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Does the benefit from pulmonary rehabilitation differ between phenotypes in chronic obstructive pulmonary disease?

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Abstract:

INTRODUCTION: Chronic obstructive pulmonary disease (COPD) is a disease caused by airway and/or parenchymal pathology. Therefore, some patients inevitably have chronic bronchitis and some patients have emphysema. The current thinking is that exercise affects these two major phenotypes differently. In this study, we investigated the benefits of pulmonary rehabilitation (PR) in chronic bronchitis- and emphysema-predominant COPD patients.

METHODS: Retrospective data of chronic bronchitis- and emphysema-predominant COPD patients who completed an outpatient 8-week PR program between the years 2013 and 2017 in the PR unit of our hospital were examined. Demographic data (age, sex, body mass index, smoking history, long-term oxygen therapy, noninvasive ventilation, emergency admissions, and number of hospitalizations) were recorded. The patients were divided into two groups: chronic bronchitis predominant and emphysema predominant. Patients were assigned to the emphysema-predominant group based on radiology results. Patients were assigned to the chronic bronchitis-predominant group according to clinical description. The two groups were compared using the recorded data cited above.

RESULTS: Of the 146 patients, 85 (58.2%) were assigned to the emphysema-predominant group and 61 (41.8%) were assigned to the chronic bronchitis-predominant group. There was no difference between the two groups in age and gender. Pulmonary function test (PFT) parameters (forced expiratory volume in 1 s and diffusing capacity of the lungs for carbon monoxide (DLCO)), arterial blood gas values (pO_2, PCO_2, and SpO_2), 6 min of walking time, and quality of life scores were significantly improved after PR. However, there was no difference between the emphysema- and chronic bronchitis-predominant groups in terms of the improvements after PR.

CONCLUSION: In this study, it was observed that the improvement due to PR seen in COPD patients was independent of phenotype. Therefore, all COPD patients should be encouraged to participate in PR programs regardless of their phenotypes.

Keywords:

Chronic bronchitis, emphysema, pulmonary rehabilitation

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Introduction

Pulmonary rehabilitation (PR) is a comprehensive intervention based on a patient assessment performed by a qualified physician, followed by patient-tailored therapies. These therapies include, but are not limited to, exercise training, education, and behavior change. They are designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors according to the American Thoracic Society (ATS) and Europian Respiratory Society (ERS).[1]

PR has increased patient tolerance of exercise, lowered the dyspnea perception in patients, and improved the quality of life in chronic obstructive pulmonary disease (COPD) patients.[2]

COPD is preventable and treatable by preventing and/or treating the respiratory symptoms and any airflow limitation.[3] It is a leading cause of morbidity and mortality worldwide. The global incidence rate of COPD is approximately 11.7%, and it is responsible for approximately 3 million deaths annually.[4,5]

The first Spanish COPD guidelines (GesEPOC) were developed in 2012, and it was one of the very early attempts to introduce the phenotypical approach into clinical practice. A phenotypical approach to COPD is having a huge impact on everyday practice and has changed nonpharmacological and pharmacological management of COPD in the last decade.[6] The classic COPD phenotypes of chronic bronchitis and emphysema have been recognized in physician guidelines for a long time. Most patients have either chronic bronchitis or emphysema. The benefits of PR to patients diagnosed to be in these major phenotypes are also thought to be different. This study investigated the effect of PR on these two main phenotypes, which differ clinically and radiologically.

Methods

We conducted a retrospective database study of emphysema- and chronic bronchitis-predominant patients to investigate the difference in benefits from PR in those patients. These patients had completed an 8-week supervised outpatient PR program in the PR unit at Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital in İzmir, Turkey.

The study was approved by the local ethical board.

Patients included in the study completed an informed written consent form.

Patient selection

In total, 146 COPD patients were diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) definitions and guidelines. Patients who completed the PR program between the years 2013 and 2017 were chosen as participants for the study.

The inclusion criterion was a ratio of forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC) of 70% or less after bronchodilator use. The severity of COPD was determined based on the disease stages defined by the GOLD guidelines.[3]

Patients who were excluded from the study were those who were diagnosed with other pulmonary diseases (asthma, interstitial lung diseases, etc.), who chose to exit the study for some reason, or who were repeating PR.

The following patient data were recorded:

- Demographics (age, gender, and body mass index [BMI])
- Smoking history
- Long-term oxygen therapy (LTOT)
- Using noninvasive ventilation
- Emergency admissions and hospitalizations in the last year.

The definition of chronic bronchitis predominant was Chronic sputum for most days, 3 months a year, or no radiological diagnosis of emphysema for at least 2 years.

Emphysema predominant was defined as no chronic cough and sputum but having typical clinical and radiological manifestations of emphysema.[7]

The radiological definition of emphysema was made retrospectively in each patient by a physician experienced in thoracic radiology. Emphysema typing (paraseptal, centrilobular, and panlobular) and visual scoring using the Goddard classification were performed on computed tomography (CT) images that conformed to technical criteria. Patients without CT or that did not meet the technical criteria were excluded from the study.

A CT scanner with 16 sensors was used in our hospital, and the thickness of the sections ranged from 1 mm to 2 mm. For the evaluation, attention was paid to the selection of noncontrast tests, if possible, where inspiration was sufficient. Emphysema scoring was made at approximately a –700 HU window level and 1500 HU window width. For quantitative measurements, a threshold of-950 HU was accepted for emphysematous areas.

The lungs were divided into six zones. These zones were defined as:

- Upper zone – From the top of each lung to 1 cm above the arcus aorta

- Middle zone – From 1 cm above the arcus aorta to 1 cm below the carina
- Lower zone – From 1 cm below the carina to the diaphragm.

Each zone was scored separately. Scores were assigned as follows:

- Score = 0, no emphysema involvement
- Score = 1, emphysema involvement <25%
- Score = 2, emphysema involvement <50%
- Score = 3, emphysema involvement <75%
- Score = 4, emphysema involvement >75%.

When the scores of the six regions were summed, a total score from a minimum of 0 to a maximum of 24 was determined. A score of 0 or 1 was accepted as no emphysema; a score of 2 or more were evaluated as emphysema predominant.[8,9]

Respiratory function tests

The following tests were performed before PR and after PR:

- Body plethysmography (ZAN 500, Germany),
- Carbon monoxide diffusion capacity (DLCO) (ZAN 300, Germany), and
- The percentage of predicted values of FEV_1, FVC, inspiratory capacity (IC), VC, residual volume (RV), total lung capacity (TLC), DLCO, and FEV_1/FVC ratio.

Assessment of dyspnea

The Modified Medical Research Council (mMRC) dyspnea scale, which consists of five items between 0 and 4, was used to determine the severity of patient shortness of breath. The score "0" represents the least shortness of breath, and the score "4" indicates the most shortness of breath.[10] After 6 minute walk test (6MWT), the dyspnea scores were evaluated according to the Borg scale.[11]

Exercise capacity

The 6 MWT was performed according to the ATS guidelines, and the distance walked for 6 min was recorded before and after PR.[12]

Quality of life

Quality of life was assessed using two questionnaires: the St. George's Respiratory Questionnaire (SGRQ)[13] and the SF-36 Quality of Life Questionnaire.[14] The SGRQ was used to determine the disease-specific quality of life.[13] High scores represent worsening symptoms and disease. Increased SF-36 Quality of Life scores represent an improved quality of life.

Psychological symptoms

The 14-question Hospital Anxiety and Depression Scale was used to determine the psychological status of the patients. Patients were placed in the following categories:

- Normal: Anxiety and depression score 0–7
- Borderline: 8–11
- Anxiety or depression: >11.[15,16]

Interventions

All patients in the program participated in 2-h pulmonary physiotherapy and rehabilitation sessions conducted twice a week for 8 weeks. The scoring/assessment methodology for the exercise program included:

- Breathing exercises consisting of pursed-lip breathing, diaphragmatic breathing, and thoracic expansion exercises
- Relaxation and stretching exercises
- Peripheral muscle strength training
- Aerobic exercises.

In addition, patients were taught bronchial hygiene techniques and dyspnea-reducing positions. After respiratory physiotherapy education, patients performed upper and lower extremity stretching and strengthening exercises. Initially, strengthening exercises were performed using no weight. According to the Borg scale, a one half of a kilogram (0.5 kg) weight was added after every four periods of exercise. A treadmill, a stationary bicycle, and an arm ergometer were used for aerobic exercises. Patient excursion was limited to 60–90% of the maximum heart rate. In addition, the study team used Borg dyspnea scores to regulate exercise. Exercise intensity increased, and if SpO_2 fell below 90% oxygen, supplemental O_2 was provided. Aerobic exercises were performed for 30 min, consisting of 15 min on the treadmill and 15 min using the stationary bicycle. An arm ergometer was used for any patients with a joint disorder or lower extremity disability.

Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows® version 20.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were given as mean ± standard deviation or median (25^{th}–75^{th} percentiles) for continuous variables and frequency (in percent) for categorical variables. The Pearson Chi-squared test or Fisher's exact test was used to determine the association between categorical variables. When comparing continuous variables, an independent samples *t*-test and the Mann–Whitney U test were used, as applicable. The difference between the two groups for ordinal variables was assessed with McNemar–Bowker test. For variables where parametric test assumptions were provided, a repeated measures analysis of variance was used to simultaneously assess intra- and intergroup differences. A statistical significance level of $P < 0.05$ was used to determine statistical significance.

Results

Of 146 patients, 85 (58.2%) were in the emphysema-predominant group and 61 (41.8%) were in the chronic bronchitis-predominant group. There were 79 (92.9%) male and 6 (7.1%) female patients in the emphysema group and 54 (88.5%) male and 7 (11.5%) female patients in the chronic bronchitis group. The mean age of the emphysema group was 64.1 ± 7.7 years. The mean age of the chronic bronchitis group was 63.3 ± 8.8 years. There was no difference between the two groups in terms of age and gender distribution [Table 1]. BMI was significantly lower in the emphysema group [Table 1]. There were statistically significant more in GOLD group 3 and 4 patients in the emphysema group. Therefore, those patients received more LTOT treatment [Table 1]. Before PR, pulmonary function test (PFT) parameters (FEV_1, FEV_1/FVC, and DLCO) were significantly lower in the emphysema group. Arterial blood gas values were similar in both the groups [Table 2]. 6 MWTs were lower in the emphysema group before PR. In terms of quality of life assessment, SF-36 physical function scores were lower in patients with emphysema. All remaining SF-36 and SGRQ scores did not differ between the two groups. Anxiety depression scores were similar in both the groups [Table 2]. After PR, both the groups showed significant improvement in PFT parameters (FEV_1 and DLCO) and arterial blood gas values (pO_2, PCO_2, and SpO_2). There was a statistically significant increase in 6 MWT distance and dyspnea perception. Statistically significant improvement was observed in all scores of the SGRQ and the SF-36 questionnaires. Anxiety and depression scores improved significantly in both the groups [Table 2].

There was no difference within each of the emphysema and chronic bronchitis groups and also between the two groups before and after PR for mMRC (P = 0.611, P = 0.151, and P = 0.177, respectively, McNemar–Bowker test).

When the emphysema and chronic bronchitis groups were compared in terms of improvement due to PR, no difference was observed between the two groups [Table 3 and Figure 1].

Discussion

This study was performed to assess the effect of PR on COPD patients and to find which phenotype improves with PR. When the patients were compared before and after PR in both the groups, the data suggest that there were improvements in PFTs, exercise capacity, dyspnea perception, quality of life, anxiety, and depression scores. We found a statistically significant difference in improvement after PR between chronic bronchitis- and emphysema-predominant COPDs. We found that improvements were similar in patients with both phenotypes.

In this study, we found that the patients in the emphysema-predominant group were mostly in the GOLD Stage 3 or 4; they had lower pO_2 values, and more patients received LTOT treatment. We know that hypoxemia in COPD reduces a patient's quality of life and exercise tolerance, disrupts musculoskeletal functions, and increases the risk of death.[17] Diffusion capacity was also lower in the emphysema group. The decreases in diffusion capacity were associated with a decrease in pO_2 levels and a decrease in 6 MWT distances.[18] 6 MWT distances and BMIs were also lower in the emphysema group than in the chronic bronchitis group. In other words, the emphysema-predominant group had more severe disease. This suggests that their improvement from PR should be different. However, we did not find any difference between emphysema and chronic bronchitis patients.

Table 1: Comparison of demographic and clinical features between the groups

Variables	All patients (*n*=146)	Emphysema (*n*=85)	Chronic bronchitis (*n*=61)	*P*
Age (years), mean±SD	63.8±8.1	64.1±7.7	63.3±8.8	0.582*
Gender (male:female) (*n*)	133:13	79:6	54:7	0.529†
BMI (kg/m^2), mean±SD	25.1±4.1	24.5±3.9	26.5±4.0	0.001*
Smoking (pack-years), mean±SD	62.7±33.1	63.1±31.8	62.2±28.6	0.879*
O_2 inhalation, *n* (%)	22 (15.1)	18 (21.2)	4 (6.6)	0.028†
NIMV, *n* (%)	8 (5.5)	7 (8.2)	1 (1.6)	0.174†
LTOT, *n* (%)	48(32.8)	39 (45.9)	9 (14.8)	0.003†
Nebulization, *n* (%)	30 (20.5)	19 (22.4)	11 (18)	0.668†
Emergency admission (frequency/year), mean±SD	1 (0-3)	1 (0-3)	0 (0-1)	0.271**
Hospitalization (frequency/year), mean±SD	0 (0-1)	0 (0-1)	0 (0-0)	0.080**
COPD Stage 3 and 4, *n* (%)	102 (69.9)	67 (78.8)	35 (57.4)	0.021†

*Independent samples *t*-test; **Mann–Whitney U-test; †Pearson Chi-square or Fisher's exact test where applicable. BMI – Body mass ındex, NIMV – Noninvasive mechanical ventilation, LTOT – Long-term oxygen treatment, COPD – Chronic obstructive pulmonary disease, SD: Standard deviation

Table 2: Comparison of two groups before and after pulmonary rehabilitation (pulmonary function tests, blood gas analysis, exercise capacity, and quality of life)

Variables	All patients (*n*=146)	Emphysema (*n*=85)	Chronic bronchitis (*n*=61)
Pretreatment			
PFTs, mean±SD			
FEV1 (%)	41.5±17.4	38.4±17.1	45.9±17.0
FEV1/FVC (%)	56.5±12.0	53.1±10.9	61.3±11.9
TLCO (%)	34.2±17.7	29.5±16.7	40.3±17.3
ABG analysis, mean±SD			
PO_2 (mmHg)	70.2±12.7	68.3±12.6	72.9±12.6
PCO_2 (mmHg)	41.6±7.1	41.4±6.9	41.9±7.4
SpO_2 (%)	93.1±5.3	92.4±6.0	94.0±4.1
pH	7.40±0.32	7.40±0.03	7.40±0.29
6 MWT, mean±SD, distance (m)	330±117	314±120	353±109
SGRQ scores, mean±SD			
Symptoms	56.7±20.9	58.0±21.7	54.9±19.8
Activity	68.9±21.6	72.0±20.9	64.5±23.0
Impact	39.2±22.8	41.2±24.1	36.4±20.7
Total	56.7±19.9	58.8±14.4	53.9±23.0
SF-36 scores, mean±SD			
Physical function	44.5±27.7	40.1±27.1	60.9±25.5
Social function, median	62.5(37.5-87.5)	56.2 (37.5-87.5)	62.5 (50.0-87.5)
Role physical, median	0 (0-50)	0 (0-50)	25 (0-50)
Role emotion, median	33.3 (33.3-100)	66.6 (33.3-100)	33.3 (16.6-100)
General health	39.8±24.0	37.5±24.8	42.8±22.8
Mental health	62.1±22.0	64.5±21.6	58.8±22.4
Bodily pain	62 (41-90)	62 (34-90)	62 (41-84)
Vitality	49.3±25.0	50.8±24.6	47.2±25.7
HAD scores, mean±SD			
Anxiety	8.4±6.2	8.8±7.0	7.7±4.9
Depression	6.5±4.1	6.2±3.9	6.8±4.3
mMRC (*n*)			
0	8	2	6
1	28	13	15
2	42	23	19
3	37	23	14
4	31	24	7
Post-treatment			
PFTs, mean±SD			
FEV1 (%)	44.6±18.5	41.2±17.3	49.8±18.5
FEV1/FVC (%)	56.5±14.2	52.8±14.7	61.7±11.7
DLCO (%)	40.6±37.4	32.2±27.2	51.1±45.7
ABG analysis, mean±SD			
PO_2 (mmHg)	76.1±12.4	74.0±12.6	79.1±11.8
PCO_2 (mmHg)	40.0 (37.0-43.2)	40.0 (37.0-43.9)	40.0 (37.1-43.0)
SpO_2 (%)	94.0±9.2	94.1±7.3	93.8±11.5
pH	7.41 (7.39-7.43)	7.41 (7.39-7.43)	7.40 (7.38-7.42)
6 MWT, mean±SD, distance (m)	392±109	378±113	412±100
SGRQ scores, mean±SD			
Symptoms	46.1 (32.8-61.9)	49.7 (35.1-62.9)	43.4 (31.9-61.9)
Activity	60.1±23.2	62.4±22.9	57.0±23.5
Impact	39.2±22.8	41.2±24.1	36.4±20.7
Total	46.4±20.5	48.0±21.0	44.2±19.8

Contd...

Table 2: Contd...

Variables	All patients (*n*=146)	Emphysema (*n*=85)	Chronic bronchitis (*n*=61)
SF-36 scores, mean±SD			
Physical function, mean±SD	60 (35-75)	55 (30-75)	70 (45.80)
Social function, median	75 (50-100)	75 (50-100)	75 (62.5-100)
Role physical	48.9±40.6	45.9±41.2	53.0±39.8
Role emotional	51.1±38.1	51.6±37.4	50.4±39.3
General health	48.5±26.4	46.1±26.8	51.8±25.7
Mental health	69.1±21.1	70.8±21.0	66.7±21.3
Bodily pain, median	84 (54-100)	84 (46-100)	84 (62-98)
Vitality	60.9±22.0	62.2±20.9	59.1±23.4
HAD scores, mean±SD			
Anxiety	5.8±3.9	5.8±3.7	5.7±4.2
Depression, median	5 (2.5-8)	4 (2-8)	5.5 (3-8)
mMRC (*n*)			
0	6	4	2
1	27	11	16
2	39	23	16
3	45	25	20
4	29	22	7

PFT: Pulmonary function test, ABG: Arterial blood gas, 6 MWT: 6-min walk test, SGRQ: The St. George's Respiratory Questionnaire, SF-36: Short form-36, HAD: Hospital anxiety and depression, mMRC: Modified Medical Research Council, SD: Standard deviation, FEV1: Forced expiratory volume in 1 s, FVC: Forced vital capacity, DLCO: Carbon monoxide diffusion capacity

In this study, exercise capacity increased, quality of life improved, and dyspnea perception decreased in all patients who completed PR. In a study evaluating the gains from PR according to the GOLD stages, both FEV_1 and pO_2 values were significantly increased and TLC and RV values were decreased in GOLD Stage 3 and 4 patients after PR.[19] In our study, FEV_1 and pO_2 values improved after PR in all patients. Different results have been reported regarding changes in PFTs after PR. FEV_1, FVC, and FEV_1/FVC values did not change significantly in most studies.[20,21] In some other studies, FEV_1 and FVC values were observed to be more markedly improved, especially in COPD cases.[22,23] Although there were more patients in this study from GOLD Stages 3 and 4 in the emphysema-predominant group, FEV_1, FVC, FEV_1/FVC, and DLCO values were improved in both the groups.

Although there was no statistical difference between the groups, in the chronic bronchitis-predominant type, FEV_1 and DLCO improved more. This may be due to the irreversible changes that occur in emphysema. Unlike PFT parameters, improvement for 6 MWT distance after PR was found to be higher in patients with emphysema, but this increase was not statistically significant.

The majority of COPD patients have impaired quality of life, causing the restriction of daily activities and their social lives. In a study comparing the quality of life metrics for COPD phenotypes, the quality of life was found to be worse in patients with exacerbator chronic bronchitis than other clinical phenotypes.[24] In this study, the SF-36 physical function score was lower in patients with emphysema. All remaining SF-36 and SGRQ scores did not differ between the two groups. However, after PR, the quality of life scores also improved. However, there was no difference between the phenotypes. It is known that anxiety depression scores improve in patients with COPD after PR.[25] In this study, although the emphysema-predominant group had more severe disease, anxiety depression scores were significantly higher in both the groups. After PR, anxiety and depression scores improved. However, there was no difference between the groups. A study comparing improvements due to PR between the chronic bronchitis- and emphysema-predominant phenotypes was not found. In the literature, gains from PR have been evaluated mostly in the patients with emphysema. Significant improvements were observed in exercise capacity, dyspnea perception, and disease-related quality of life after PR in patients with emphysema.[26] Patients with severe emphysema before volume reduction participated in a PR program. The program was found to be effective in preparing the patient for the procedure and selecting the appropriate patient.[27]

There are studies evaluating improvements due to PR based on the severity of emphysema. It has been reported that the IC/TLC ratio is an important predictor of mortality in patients with emphysema. The risk of death increases even in those with IC/TLC ratio <0.25.[28] In a study comparing the effect of PR on IC/TLC <0.25 and above, it was observed that IC, FEV_1, quality of life, and exercise capacity were significantly improved in patients with IC/TLC <0.25. Therefore, the

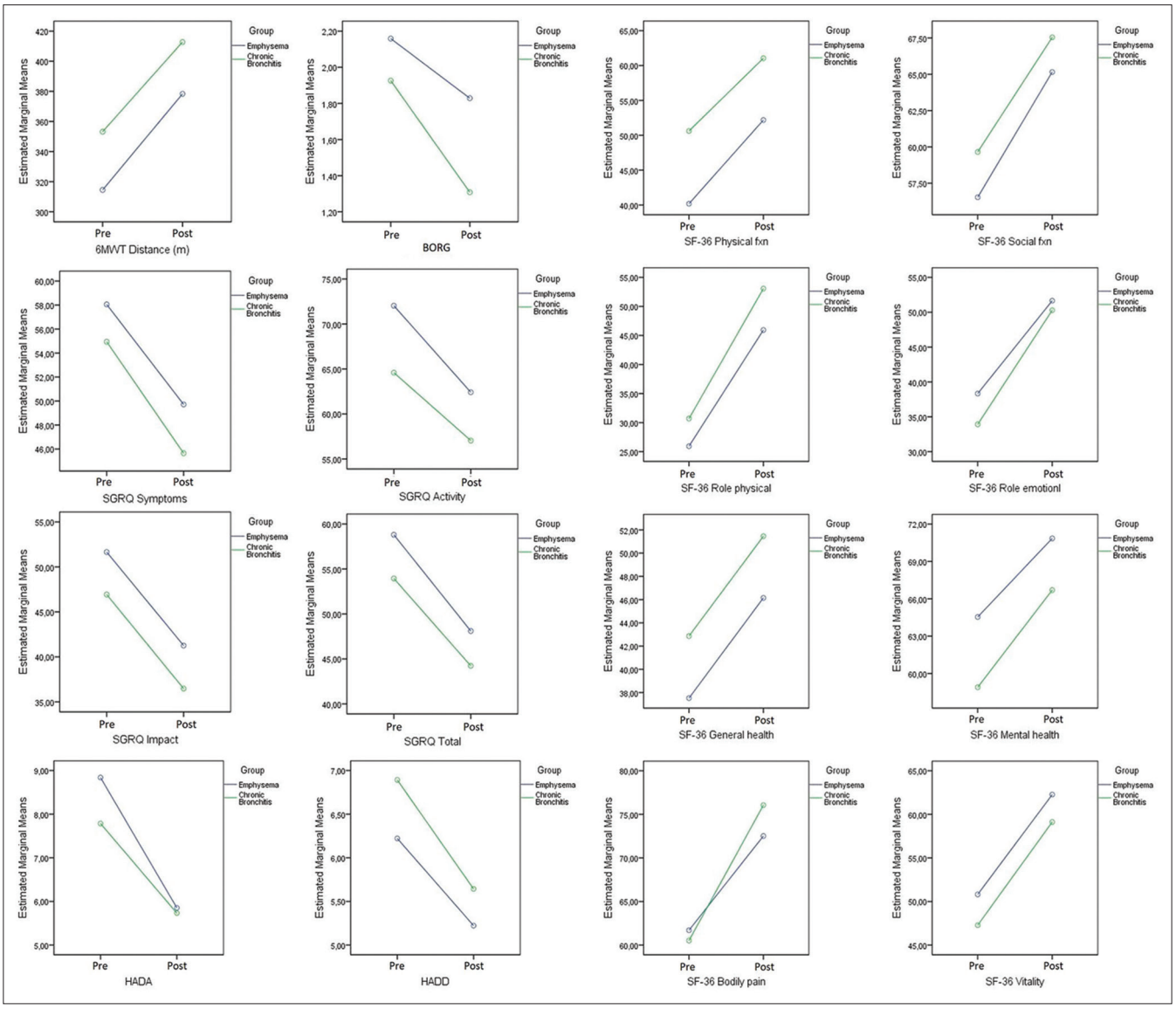

Figure 1: Emphysema and chronic bronchitis groups were compared in terms of gain from pulmonary rehabilitatıon

more severe the emphysema, the greater the gain from PR.[29] In the comparison of emphysema- and chronic bronchitis-predominant cases, there was no difference in the improvement from PR in emphysema patients versus the improvement in chronic bronchitis patients. This was thought to be due to the presence of mild, moderate, and severe emphysema patients together without stratification, as this study did not evaluate emphysema severity.

A study investigating the effect of PR on annual exacerbation rate of COPD in patients with frequent and nonfrequent exacerbators of COPD has shown that PR reduces emergency admissions and hospitalizations in patients with frequent exacerbations.[30] Although the study was not planned to compare phenotypes, they compared phenotypes with frequent and nonfrequent exacerbators, as indicated in the Spanish guidelines.[31] We compared emphysema- and chronic bronchitis-predominant phenotypes in our study.

COPD is a profoundly heterogeneous illness. Signs and symptoms are so variable that it is difficult to assign a phenotype to the severity of a patient's disease. Efforts have been made in recent years to characterize this heterogeneity. However, because COPD symptoms are so variable, many physicians have come to rely on the simplified concept of the "pink puffer" (emphysematous disease) and "blue bloater" (chronic bronchitis with or without a bronchospastic component).[32] Currently, chronic bronchitis and emphysema subtyping are still in use. In 2017, the GesEPOC described these two phenotypes as well as several other phenotypes to be used as a guide for treatment.[31] In a COPD gene study, patients were classified as airway predominant and emphysema predominant. The patients were then

Table 3: Clinical significance of pulmonary rehabilitation between emphysema and chronic bronchitis groups (repeated measures analysis of variance)

Variables	Main effect		Interaction effect	
	F	*P*	*F*	*P*
PFTs				
FEV1 (%)	22.496	<0.001	0.654	0.420
FEV1/FVC (%)	0.009	0.929	0.181	0.671
DLCO (%)	3.888	0.051	0.398	0.529
ABG analysis				
PO_2 (mmHg)	40.738	<0.001	0.069	0.794
PCO_2 (mmHg)	2.755	0.099	0.938	0.334
SpO_2 (%)	0.022	0.882	0.422	0.517
pH	0.034	0.855	1.708	0.193
6 MWT				
Distance (m)	94.464	<0.001	0.111	0.739
SGRQ scores				
Symptoms	37.887	<0.001	0.112	0.739
Activity	30.985	<0.001	0.450	0.504
Impact	59.239	<0.001	0.001	0.981
Total	64.927	<0.001	0.151	0.698
SF-36 scores				
Physical function	49.932	<0.001	0.243	0.623
Social function	22.297	<0.001	0.044	0.835
Role physical	32.090	<0.001	0.100	0.752
Role emotion	13.960	<0.001	0.147	0.702
General health	19.751	<0.001	0.000	0.994
Mental health	14.457	<0.001	0.162	0.688
Bodily pain	23.777	<0.001	0.766	0.383
Vitality	32.503	<0.001	0.009	0.925
HAD scores				
Anxiety	28.287	<0.001	0.971	0.326
Depression	11.589	<0.001	0.143	0.706

PFT: Pulmonary function test, ABG: Arterial blood gas, 6 MWT: 6-min walk test, SGRQ: The St. George's Respiratory Questionnaire, SF-36: Short form-36, HAD: Hospital anxiety and depression, mMRC: Modified Medical Research Council

subgrouped and compared for mortality risk and disease progression.

A major strength of this study is that it is the first study that evaluated the benefits of PR in patients with chronic bronchitis- and emphysema-predominant phenotypes. However, a limitation of this study is the coexistence of patients with mild, moderate, and severe emphysema patients in the emphysema-predominant group without stratification.

Conclusion

When COPD patients participate in PR programs, their dyspnea perception, exercise capacity, quality of life, and psychological status improve. There was no difference between the emphysema- and chronic bronchitis-predominant groups regarding the benefits of PR. This study showed that COPD patients benefit from PR, independent of COPD phenotype. Therefore, we believe that all patients with different phenotypes need to be encouraged to participate in PR programs.

Informed consent

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

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Conflicts of interest

There are no conflicts of interest.

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