







## Effects of Inspiratory Muscle Training in Patients with post-COVID-19

## COVID-19 Geçirmiş Hastalarda Solunum Kas Eğitiminin Etkileri

Fulden SARI<sup>1</sup> , Selin BAYRAM<sup>2</sup> , Gamze Gülsün PALA<sup>2</sup> , Fatma COMCE<sup>3</sup>   
Hamit KUCUK<sup>4</sup> , Deran OSKAY<sup>2</sup> 

<sup>1</sup>Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Bingöl University, Bingöl, TÜRKİYE

<sup>2</sup>Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Gazi University, Ankara, TÜRKİYE

<sup>3</sup>Department of Pulmonary Medicine, Özel Versa Hospital Nevşehir, TÜRKİYE

<sup>4</sup>Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Gazi University, Ankara, TÜRKİYE

## Abstract

**Background:** The aim of this study is to investigate the effectiveness of inspiratory muscle training on exercise capacity, lower muscle strength, dyspnea, anxiety-depression, quality of life, physical activity and fatigue in coronavirus disease 2019 (COVID-19) patients with respiratory involvement

**Materials and Methods:** Twenty-four patients were included in the study. The patients were randomly separated into two groups as treatment group (13 patients) and control group (11 patients). Breathing exercise, resistance training and inspiratory muscle training were performed for 6 weeks in the treatment exercise group. Breathing exercise and resistance training consisted of control exercise group for 6 weeks. For the patients to follow the exercises, a video explaining the individual exercises was sent to each group and video interviews were faceted regularly every week. All patients were evaluated at baseline and at the end of sixth week in terms of exercise capacity, lower muscle strength, dyspnea, quality of life, fatigue, physical activity and anxiety-depression.

**Results:** Demographic and clinical features of the patient groups were similar ( $p>0.05$ ). An increase in the functional capacity, lower muscle strength and decrease in anxiety-depression level ( $p<0.05$ ) were observed in both groups. In fact; the improvements in the treatment group were statistically more significant than the control group in functional capacity, lower muscle strength and anxiety-depression level ( $p<0.05$ ). Hand grip strength (with the exception of control group), physical activity and quality of life levels were increased while dyspnea and fatigue were decreased in both groups ( $p<0.05$ ). However, there was no statistical difference between the groups for these parameters ( $p>0.05$ ).

**Conclusions:** Inspiratory muscle training improves exercise capacity and lower muscle strength and decreases anxiety-depression in the COVID-19 patients with respiratory involvement.

**Key Words:** Dyspnea, Exercise, Fatigue, Functional capacity, Muscle strength, Rehabilitation

## Öz

**Amaç:** Bu çalışmanın amacı pulmoner etkilenimi olan COVID-19 geçirmiş hastalarda inspiratuar kas eğitiminin egzersiz kapasitesi, alt ekstremitte kas kuvveti, nefes darlığı, yaşam kalitesi, yorgunluk, fiziksel aktivite ve anksiyete-depresyonu üzerindeki etkinliğini araştırmaktır.

**Materyal ve Metod:** Yirmi dört hasta çalışmaya dahil edildi. Hastalar randomize edilerek tedavi (13 hasta) ve kontrol (11 hasta) grubu olmak üzere iki gruba ayrıldı. Tedavi grubuna 6 hafta boyunca solunum egzersizleri, kuvvetlendirme ve inspiratuar kas eğitimi egzersizlerinden oluşan egzersiz programı uygulandı. Kontrol grubuna ise solunum ve kuvvetlendirme egzersizlerinden oluşan 6 haftalık egzersiz programı verildi. Hastaların egzersizleri takip edebilmeleri için her gruba bireysel egzersizleri açıklayan youtube videosu link olarak gönderildi ve her hafta düzenli olarak görüntülü görüşmeler yapıldı. Hastalar tedavi öncesi ve 6 hafta sonra egzersiz kapasitesi, alt ekstremitte kas kuvveti, nefes darlığı, yaşam kalitesi, yorgunluk, fiziksel aktivite ve anksiyete-depresyon açısından iki kez değerlendirildi.

**Bulgular:** Hasta gruplarının demografik ve klinik özellikleri benzerdi ( $p>0.05$ ). Her iki grupta da fonksiyonel kapasitede, alt ekstremitte kas kuvvetinde artış ve anksiyete-depresyon düzeyinde düşüş gözlemlendi ( $p<0.05$ ). Hatta; fonksiyonel kapasitede, alt ekstremitte kas kuvvetinde ve anksiyete-depresyon düzeyindeki değişiklikler kontrol grubuna göre daha üstün bulundu ( $p<0.05$ ). Her iki grupta da el kavrama kuvveti (kontrol grubu hariç), fiziksel aktivite ve yaşam kalitesi düzeyi artarken, nefes darlığı ve yorgunluk düzeyi azaldı ( $p<0.05$ ). Ancak bu parametreler açısından gruplar arasında istatistiksel fark yoktu ( $p>0.05$ ).

**Sonuç:** Inspiratuar kas eğitimi, pulmoner etkilenimi olan COVID-19 geçirmiş hastalarda egzersiz kapasitesi ve alt ekstremitte kas kuvvetini artırırken anksiyete-depresyon düzeyini azaltır.

**Anahtar Kelimeler:** Nefes darlığı, Egzersiz, Fonksiyonel kapasite, Kas kuvveti, Rehabilitasyon

## Corresponding Author/ Sorumlu Yazar

Dr. Fulden SARI

Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Bingöl University, Bingöl, TÜRKİYE

E-mail: fuldensari@hotmail.com

Received / Geliş tarihi: 28.06.2022

Accepted / Kabul tarihi: 10.10.2022

DOI: 10.35440/hutfd.1136549

## Introduction

The coronavirus disease 2019 (COVID-19) that first appeared in Wuhan has outbroken contagious pulmonary disease (1, 2). According to Worldometer data (26 April 2022), there were 510.323.728 confirmed infected cases worldwide, of which 6.247.006 deaths were reported and 463.638.758 recovered individuals (3). While symptoms such as fever, fatigue, dry cough and dyspnea are common in COVID-19 patients, uncommon symptoms such as headache, sore throat, chills, myalgia, arthralgia, nausea, vomiting, nasal congestion, diarrhea, hemoptysis and conjunctival obstruction have also been reported (4, 5).

According to the world health organization's (WHO)s report, COVID-19 can be asymptomatic and cause severe viral pneumonia or death (4). Patients with viral pneumonia due to COVID-19 are at risk for lung damage, other organ injuries, psychological and physical complications. Patients may experience severe muscle weakness, fatigue, dysphagia, decreased mobility, severely worsened quality of life and fall as a result of prolonged hospitalization or long-term social isolation (6, 7). Furthermore, severe respiratory symptoms such as cough (57.6%) and dyspnea (45.6%) have been seen in COVID-19 patients (8). For all of these reasons, some patients require pulmonary rehabilitation as a result of COVID-19. In the literature, the effectiveness of pulmonary rehabilitation in patients with COVID-19 has been investigated in a few studies (9, 10).

In the study of Shukla et al.; they followed-up patients with COVID-19 by giving breathing exercises (diaphragmatic breathing, pursed-lip breathing, etc.) at home (9). In a randomized controlled study conducted by Gonzalez-Gerez et al., it was found that patients' forced expiratory volume in first second, peak expiratory flow, 6-minute walk test (6-MWT) and 30-second sit and stand test (30 STS) were increased significantly and dyspnea complaints was decreased according to the results of the pulmonary telerehabilitation program in home-based COVID-19 patients (11).

In several studies, inspiratory muscle training, which is one of the components of pulmonary rehabilitation, has been known to improve a variety of clinical symptoms, including respiratory muscle strength, tiredness, and dyspnea (12-14). However a few researches have investigated the effects of inspiratory muscle training (IMT), inspiratory muscle weakness and its clinical symptoms in patients with COVID-19 (11, 15). The aim of this study is to investigate the effectiveness of the pulmonary exercise program to be applied with the inspiratory muscle training exercise program on the exercise capacity, peripheral muscle strength, dyspnea, quality of life, fatigue, physical activity and anxiety-depression in individuals with post-COVID-19.

## Materials and Methods

### Patient Selection and Method

This study is a prospective, double-blind, randomized controlled clinical study. Literate patients aged 18-65 years,

who had post-COVID-19 pulmonary involvement, were included.

Patients who could not cooperate with the evaluation, and had a previous diagnosis of respiratory disease and orthopedic and/or neurological complaints that would affect the assessment of exercise capacity were excluded.

Patients were randomized using the numbering system of the Research Randomiser web program. It was randomized as treatment group (TG) or control group (CG), by an investigator blinded to patient identity and not knowing which study group patients were in. The investigator who was responsible for the randomization was not in data collection or data analysis. Different researchers, blinded to assignment, did all the measurements and intervention in this study.

### Data collection tools

Demographic information (gender, age, body mass index), subtype of disease (cough, dyspnea, sputum), intensive care unit, hospital, O<sub>2</sub> uptake and smoking history of all the patients were recorded. Primary and secondary assessments were evaluated on the same day. The primary outcomes were exercise capacity and 30 second sit to stand test. Secondary outcomes were dyspnea, hand grip muscle strength, anxiety-depression, quality of life, physical activity and fatigue level. Measurements were assessed in the first and sixth weeks of the interventions.

*Functional Exercise Capacity:* It was assessed with the 6-MWT. Oxygen saturation, heart rate, respiratory frequency, dyspnea and fatigue were assessed. The norm values calculated by Enright et al. were taken as reference (16).

*30 second sit to stand test:* It is a test that evaluates the 30 STS and lower extremity strength of the participant. Total score gives the score of the test (17).

*Dyspnea:* Modified Medical Research Council (MMRC) dyspnea scale comprises 5 items about dyspnea, scored between 0-4 (18).

*Hand grip muscle strength:* According to the criteria determined by the American Association of Hand Therapists; hand grip muscle strength was assessed from non-dominant side using digital hand dynamometer (J-Tech™ Midvale, USA). While the non-dominant limb was in 90° flexion, maximum contraction was requested during maintaining a time of 5 seconds. Three repeated measurements were repeated and the highest value reached was taken (19).

*Anxiety-Depression:* A valid and reliable Turkish Hospital Anxiety and Depression Scale (HADS) was used to determine the anxiety-depression level of the participants. Anxiety (HADS-A) and depression (HADS-D) have two subgroups. The higher the score, the worse the anxiety and depression (20).

*Quality of life:* The Nottingham Health Profile (NHP) comprises of 38 items. The higher the score means, the worse the quality of life (21).

*Physical activity level:* Physical activity level was evaluated

with International Physical Activity (IPAQ) questionnaire. It comprises 7 questions and gives in total score of metabolic equivalent (MET)-minutes. It is separated as 'inactive', 'minimally active' and 'very active' (22).

**Fatigue:** Fatigue Severity Scale (FSS) comprises 9 items. The higher the total score, the worse the fatigue perception (23).

**Intervention:** Post-COVID-19 patients with pulmonary involvement were divided into two groups as TG and CG.

Breathing exercises were diaphragmatic breathing, thoracic expansion, and exercises to increase chest compliance with respiratory control with exercise band. Respiratory control and "pursed-lip" breathing were shown to patients. Diaphragmatic breathing and thoracic expansion were explained together with pursed-lip breathing. Patients were told to hold at maximum inspiration at the end of inspiration exercise for 3 seconds. Breathing exercises were practiced for 5-10 repetitions, 1 set and approximately 5-10 minutes. It was performed for 10 repetitions, 3 sets/day.

Resistance training included exercises for the quadriceps muscle strengthening exercises which were squat and clinical pilates-based bridge exercise. Resistance exercises were performed 6 weeks, every day, 10 repetitions, 3 sets/day and approximately 10 minutes.

Inspiratory muscle training (T-IMT) (Threshold IMT, Philips-Respironics, Pittsburgh, PA, USA) is used for strength and endurance of the respiratory muscles. In the TG, the T-IMT resistance was determined as 3-4 according to the Modified Borg Scale for every patient. The patients were interviewed via Zoom Meeting or WhatsApp Messenger (according to the patient's preference) every week. They worked regularly 30 minutes, 3 times, 7 days for 6 weeks. Patients were taught to continue deeply diaphragmatic breathing for 8-10 breaths. The loading resistance was increased every week.

In the CG; breathing and quadriceps muscle strengthening exercises were given.

For the patients to follow the exercises, a youtube video explaining the individual exercises was sent to each group and video interviews were faceted regularly every week.

### Ethics

Our study was approved by the local Ethics Committee of the Gazi University (31.05.2021/535) and applied according to standards of the Declaration of Helsinki. All participants signed informed consent about the study which conforms to the Helsinki Declaration to participate in the study. Our study was also registered to ClinicalTrials.gov (ID: NCT04972864).

### Statistical analysis

A priori sample size was calculated using G-Power (Version 3.1.9.2, University of Dusseldorf, Dusseldorf, Germany) software. A type I error level of 5% was accepted as statistically significant. To obtain a power of 85% with a probability of a 2-tailed type I error of 0.05, the sample of patients to be included was calculated as 11 patients in the TG and 11 pa-

tients in the CG, a total of 22 participants. All data were analyzed using SPSS 15.0 (SPSS, Chicago, Illinois). Data normality was assessed using the Shapiro-Wilk/ Kolmogorov-Smirnov test. Non-normally distributed variables were expressed as median (25-75. interquartile range [IQR]) were used and compared with the Mann-Whitney U test. Wilcoxon Signed Rank test was used for within-group comparisons. Statistical significance has been determined as  $p < 0.05$ .

### Results

Between March and June 2021, twenty-six post-COVID-19 patients with pulmonary involvement were randomly assigned to two groups (Figure 1). 24 of 26 patients with post-COVID-19 pulmonary involvement completed the study. The study was completed with 13 recipients in the TG (10 males and 3 females) and 11 recipients in the CG (6 males and 5 females). The medical conditions of the patients were assessed using the Charlson comorbidity scale (treatment group= 4 diabetes mellitus patients, control group= 1 diabetes mellitus and 1 rheumatoid arthritis patient). The chronic disease evaluations of the groups were statistically similar ( $p > 0.05$ ). None of the patients in both groups had exercise habits. Patients' conditions were low and similar at the beginning treatment ( $p > 0.05$ ). There were similarities in demographic and clinical characteristics between the groups and none of the recipients needed O<sub>2</sub> uptake at the time of assessment (Tables 1,  $p > 0.05$ ).

**Table 1.** Demographic and baseline post-COVID-19 patients' characteristics

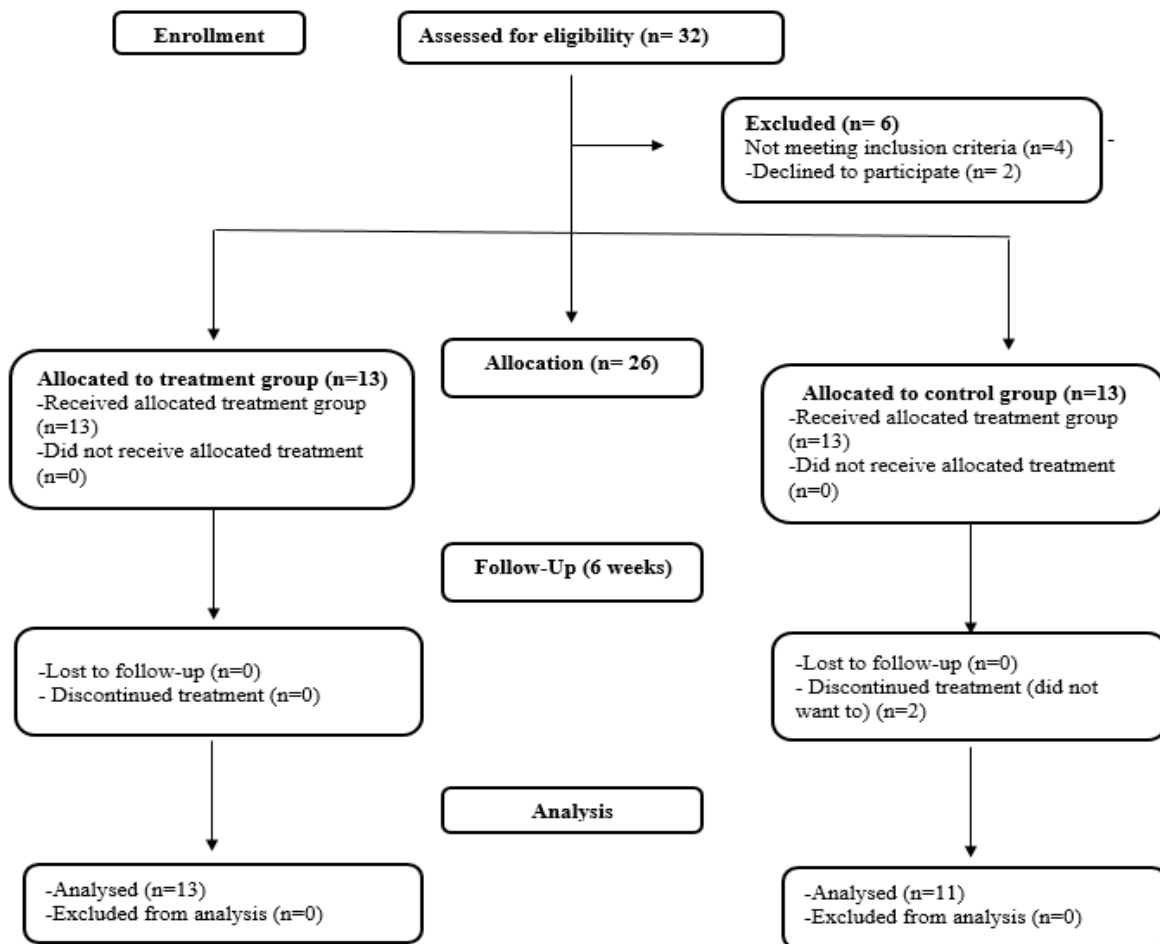
	Treatment Group (n=13)	Control group (n=11)	P*
Age (year)	54 (46-60.5)	58 (55-64)	0.25
Height (cm)	172 (161-178)	173 (160-175)	0.62
Weight (kg)	87 (71-100)	82 (75-88)	0.50
BMI (kg/m <sup>2</sup> )	29.2 (27.03-32)	29.4 (27.7-31.7)	0.75
Duration (months)	1.5 (1-2)	1.5 (1-2)	0.91
CCI	0 (0-1)	0 (0-0)	0.59
	Treatment Group (n=13) n (%)	Control group (n=11) n (%)	p <sup>§</sup>
ICU (yes-no)	2 (15.38)- 11 (84.62)	2 (18.18)- 9 (81.82)	0.85
Hospital (yes-no)	11 (84.62)- 2 (15.38)	9 (81.82)- 2 (18.18)	0.85
O <sub>2</sub> uptake (yes-no)	10 (76.92)- 3 (23.08)	6 (54.54)- 5 (45.46)	0.38
Smoking (ex-smoker-non)	6 (46.15)- 7 (53.85)	4 (30.76)- 7 (69.24)	0.62
Cough (yes-no)	3 (23.07)- 10 (76.93)	5 (45.45)- 6 (54.55)	0.24
Dyspnea (yes-no)	10 (76.93)- 3 (23.07)	7 (63.63)- 4 (36.37)	0.47
Sputum (yes-no)	3 (23.07)- 10 (76.93)	2 (18.18)- 9 (81.82)	0.76

\*Mann-Whitney U Test. cm: centimeter. kg: kilogram. m: meter. BMI: Body-mass index. IQR 25-75: interquartile range 25-75.

CCI: Charlson comorbidity index. <sup>§</sup>Chi-Square Test. ICU: intensive care unit. O<sub>2</sub>: oxygen.  $p < 0.05$

6-MWT distance significantly increased within TG ( $p<0.001$ ) and CG ( $p<0.05$ ) after treatment. The walking distance increased  $90.99 \pm 56.94$  m (from 531.57 m to 622.56 m) in the TG whereas the increase of  $38.74 \pm 58.52$  m (from 482.72 m to 521.47 m) in the CG. When the effect of the treatment between groups was analyzed, it significantly improved in the TG compared to the CG ( $p<0.05$ ). Within TG ( $p<0.001$ ) and CG ( $p<0.05$ ) significant improvements were observed in 30 second sit to stand test. In addition, here was a significant

increase in the TG compared to the CG among the groups ( $p<0.001$ ). No significant changes were shown in MMRC dyspnea scale between TG and CG ( $p=0.87$ ), however MMRC dyspnea scale significantly decreased within the TG after treatment ( $p<0.05$ ). According to the modified borg scale, 10 (76.93%) patients in the TG had dyspnea before treatment, while 7 (63.63%) patients in the CG had dyspnea. The two groups were statistically similar before treatment ( $p>0.05$ , Table 1).



**Figure 1.** Flow diagram of the patients

However; after treatment, 2 (15.38%) patients in the TG had dyspnea, while 6 (54.54%) patients in the CG had dyspnea. The difference between the two groups was significant after treatment ( $p<0.05$ ). Hand grip muscle strength significantly increased within TG ( $p<0.05$ ), whereas, a statistical difference was not shown in hand grip muscle strength between TG and CG after treatment ( $p>0.05$ , Table 2). HADS-A, HADS-D and HADS-T scores decreased significantly in the TG and CG ( $p<0.05$ , Table 2). Significant difference was not shown in NHP questionnaire between the TG and the CG after treatment ( $p>0.05$ ). However, NHP questionnaire significantly decreased within the TG and CG after treatment ( $p<0.05$ , Table 2). Statistical difference was not shown in IPAQ scores between the two groups ( $p>0.05$ ), however IPAQ score increased significantly within TG and CG ( $p<0.05$ ,

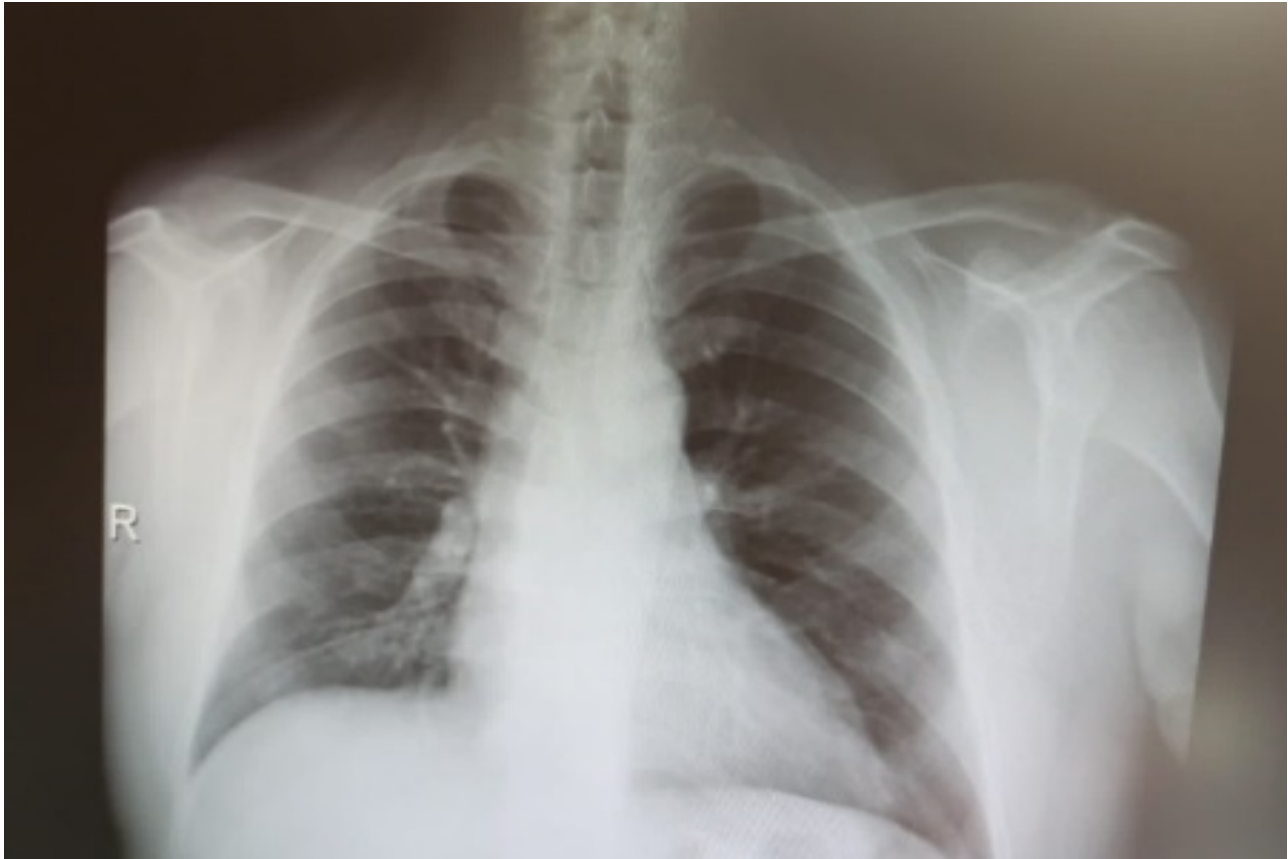
Table 2) after treatment. Before the treatment, 10 patients (76.92%) in the TG and 9 patients (81.81%) in the CG were inactive. After the treatment 6 patients (46.15%) in the TG and 5 patients (45.45%) in the CG were inactive for IPAQ category. FSS scores decreased significantly within the two groups ( $p<0.05$ ). However significant difference was not found between the two groups ( $p>0.05$ , Table 2). Eleven patients (84.61%) in the TG and nine patients (81.81%) in the CG reached minimal clinically important difference for FSS. One patient in the TG had bilateral sequelae fibrotic changes in the posteroanterior (PA) chest view in the first month after post-COVID-19 (Figure 2a), while the same patient' PA chest view was normal in the 1st month after the TG (Figure 2b).

**Table 2.** Before and after treatment changes within and between groups

	Treatment Group (n=13)			Control group (n=11)			Treatment Group	Control group	Treatment Effect ( $\Delta$ )
	Before	After	Group Difference	Before	After	Group Difference	Change ( $\Delta$ )	Change ( $\Delta$ )	
	Median (IQR 25-75)	Median (IQR 25-75)	$p^{\delta}$	Median (IQR 25-75)	Median (IQR 25-75)	$p^{\delta}$	Median (IQR 25-75)	Median (IQR 25-75)	
6MWT	554.4 (482.4-607.85)	623.4 (604.8-658.2)	<b>0.001</b>	540 (330-551.4)	540.6 (480-599.4)	<b>&lt;0.05</b>	70.2 (50.4-119.4)	30 (26-75.6)	<b>&lt;0.05</b>
30STS	12 (10.5-14.5)	17 (16-19.5)	<b>0.001</b>	13 (11-14)	15 (13-19)	<b>&lt;0.05</b>	5 (4-7)	2 (1-4)	<b>0.001</b>
mMRC	1 (1-2)	1 (0-1)	<b>&lt;0.05</b>	2 (0-2)	1 (0-1)	<b>&lt;0.05</b>	-1 (-1-0)	-1 (-2-0)	0.87
Hand grip strength (non-dominant)	35.2 (21.7-42.6)	40.1 (26.3-45.7)	<b>&lt;0.05</b>	32.1 (20.6-37.8)	28.3 (21.1-40)	0.26	3.5 (1.1-5.1)	0.9 (-1.7-4.6)	0.16
HADS-D	13 (5-16.5)	1 (0-2)	<b>0.001</b>	5 (3-9)	3 (1-8)	<b>&lt;0.05</b>	-9 (-15- -4.5)	-1 (-4- -1)	<b>&lt;0.05</b>
HADS-A	8 (4.5-18.5)	2 (0-4)	<b>0.001</b>	5 (4-8)	4 (2-7)	<b>&lt;0.05</b>	-7 (-15.5- -3)	-3 (-4- -1)	<b>&lt;0.05</b>
HADS-T score	23 (9.5-32.5)	3 (0-6)	<b>0.001</b>	11 (7-17)	7 (4-15)	<b>&lt;0.05</b>	-20 (-31.5- -8)	-4 (-9- -2)	<b>&lt;0.05</b>
NHP	106.99 (55.38-170.54)	21.67 (5.24-69.85)	<b>&lt;0.05</b>	91.28 (36.48-215.44)	39.36 (0-184.33)	<b>&lt;0.05</b>	-70.3 (-100.2- -24.1)	-19.8 (-83.1-3.4)	0.30
IPAQ score	89.5 (10-544.5)	594 (272.25-1188)	<b>&lt;0.05</b>	132 (0-594)	693 (247.5-2653.2)	<b>&lt;0.05</b>	372 (99-907.5)	693 (0-2244)	0.61
FSS	35 (19.5-39)	18 (13.5-30)	<b>&lt;0.05</b>	39 (23-51)	19 (5-33)	<b>&lt;0.05</b>	-14 (-19.5- -4.5)	-9 (-23- -4)	0.95

\*Mann-Whitney U Test.  $^{\delta}$ Wilcoxon Signed Rank. IQR 25-75: interquartile range 25-75.  $\Delta$ : Delta. 6MWT: 6-minute walking test. 30STS: 30 second sit to stand test. mMRC: the Modified Medical Research Council dyspnea scale. HADS-D: Hospital Anxiety and Depression Inventory- Depression. HADS-A: Hospital Anxiety and Depression Inventory- Anxiety. HADS-T: Hospital Anxiety and Depression. NHP: Nottingham Health Profile. IPAQ: International Physical Activity questionnaire. FSS: Fatigue Severity Scale.  $p < 0.05$

**Figure 2a.** PA chest view of a patient after post COVID-19



**Figure 2b.** PA chest view of the patient after the IMT treatment group

## Discussion

The aim of this study was to investigate the effects of respiratory muscle training exercise program on exercise capacity, lower extremity muscle strength, shortness of breath, anxiety-depression, fatigue, quality of life and physical activity in post COVID-19 patients with pulmonary involvement. The current study shows that 6-week IMT increases functional exercise capacity and lower extremity muscle strength whereas decreases anxiety, depression and dyspnea perception (the modified borg scale) in post-COVID-19 patients with pulmonary involvement. The 6-week IMT did not have an effect on quality of life, physical activity and fatigue.

There may be seen decreased lung function, increased degree of fibrosis on chest computed tomography, worsening symptoms and quality of life in patients post COVID-19 pulmonary involvement (24). Consequently; It is important to strengthen the respiratory muscles of COVID-19 pulmonary involvement patients.

IMT increases strength and endurance of respiratory muscles, decreases dyspnea perception and increases functional exercise capacity. Therefore; Significant advances in exercise capacity following IMT have been indicated in patients with chronic obstructive pulmonary disease (COPD), asthma, sarcoidosis, and bronchiectasis (12, 13, 25, 26). Our study demonstrated that a significant improvement in 6MWT walking distance was in the TG. The walking distance was increased by  $90.99 \pm 56.94$  m (from 531.57 m to 622.56

m) in the TG whereas the increase of  $38.74 \pm 58.52$  m (from 482.72 m to 521.47 m) in the CG. Similarly; Abodonya et al. (15) who conducted a study evaluating the effect of IMT for recovered COVID19 patients after weaning from mechanical ventilation, found that 2 weeks of IMT training increased the 6-MWT distance significantly in these patients compared to the CG.

The 30 STS is a valid and reliable method for assessing and measuring lower muscle strength (27). The increase in the post-TG was clinically significantly more than in the CG. Similarly, in a randomized controlled study in hemodialysis patients, 30 STS was found to be higher after IMT training compared to the CG (28). In addition, contrary to other studies (29, 30), hand grip muscle strength increased both statistically and clinically in the group with respiratory muscle training after treatment. However, the groups were statistically similar after treatment.

MMRC and modified Borg scale are effective, valid and reliable questionnaires that can be used to reduce the dyspnea perception after IMT training. In current studies, it was found that the perception of dyspnea after IMT training decreased compared to the result of the evaluation with the modified borg scale (26, 31, 32). Similarly, in our study, dyspnea perception was significantly reduced in the TG according to CG when evaluated by the modified borg scale, whereas MMRC score was significantly reduced in both group after treatment.



A review demonstrated that depression-anxiety was related to quality of life, dyspnea perception, and exercise capacity (33). It was reported that respiratory muscle training reduced anxiety-depression levels in patients due to reducing dyspnea and increasing exercise capacity (34). In our study, HADS scores were also significantly decreased in the TG according to CG after treatment.

Previous researches have shown that IMT improves quality of life, physical activity level, and fatigue in patients (35-37). However; there was no significant difference between the groups. Nevertheless, there was a significant decrease in the number of patients with inactive physical activity level after treatment in both groups. On the other hand, it demonstrated an improvement in fatigue perception and an increase to minimal clinical significance for FSS in both groups. As a result; no changes were observed significant clinical differences between groups in NHP, IPAQ and FSS scores. The effects of IMT on quality of life, physical activity, and fatigue should be explored in a larger post-COVID-19 population with a longer treatment program.

There were some limitations in our study. Firstly; respiratory muscle strength/endurance and pulmonary function tests were not evaluated. Unfortunately, we were not able to evaluate the differences in these assessments between the groups after treatment. Effects evaluation on respiratory muscle strength/endurance and pulmonary function tests of IMT training may be researched in further studies. Secondly; The inspiratory muscle strength program was supervised for only 6 weeks which was a short period for treatment effects. A longer randomized controlled exercise program could have proved the long-term IMT program effects for post COVID-19 patients. Thirdly; for ethical reasons, we did not have a third control group that did not apply any rehabilitation-type intervention. Finally, cardiopulmonary exercise tests were not applied in our study.

## Conclusions

IMT as a useful, practical and safe exercise method increased exercise capacity and lower muscle strength whereas decreased dyspnea perception, anxiety and depression in patients post-COVID-19 at 6-weeks. However, IMT does not indicate to have an effect on quality of life, physical activity and fatigue in our study. Consequently, we hope that; it will be useful for further studies that will investigate the benefits of long-term inspiratory muscle training in COVID-19 patients with pulmonary involvement.

## Acknowledgements

Thank you to all our patients who completed the study.

**Ethical Approval:** Our study was approved by the local Ethics Committee of the Gazi University (31.05.2021/535).

### Author Contributions:

Concept: F.S.

Literature Review: F.S.

Design : F.S., D.O.

Data acquisition: S.B., G.G.P., F.Ç., H.K.

Analysis and interpretation: F.S.

Writing manuscript: F.S.

Critical revision of manuscript: D.O.

**Conflict of Interest:** The authors declare that they have not conflict of interest.

**Financial Disclosure:** Authors declared no financial support.

## References

1. Cruz MP, Santos E, Cervantes MV, Juárez ML. COVID-19, a worldwide public health emergency. *Rev Clin Esp.* 2021; 221:55-61.
2. Assessment ER. Outbreak of Acute Respiratory Syndrome Associated with a Novel Coronavirus, China: First Local Transmission In The EU/EEA—Third Update. 2020.
3. Update C. 2,503,392 cases and 171,796 deaths from COVID-19 virus pandemic-Worldometer [Internet]. Worldometers info. 2020. Available from: <https://www.worldometers.info/coronavirus/>.
4. Organization WH, Organization WH. Report of the WHO-China joint mission on coronavirus disease 2019 (COVID-19). Geneva. 2020.
5. Zhang J-j, Dong X, Cao Y-y, Yuan Y-d, Yang Y-b, Yan Y-q, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy.* 2020; 75(7):1730-41.
6. Stam HJ, Stucki G, Bickenbach J. Covid-19 and post intensive care syndrome: a call for action. *J Rehabil Med.* 2020; 52:1-4.
7. Medica EM. First impact on services and their preparation. "Instant paper from the field" on rehabilitation answers to the Covid-19 emergency. *Eur J Phys Rehabil Med.* 2020.
8. Yan CH, Faraji F, Prajapati DP, Boone CE, DeConde AS. Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms. *Int Forum Allergy Rhinol.* 2020; 806-13.
9. Shukla M, Chauhan D, Raj R. Breathing exercises and pranayamas to decrease perceived exertion during breath-holding while locked-down due to COVID-19 online randomized study. *Complement Ther Clin Pract.* 2020; 41:101248.
10. Gonzalez-Gerez JJ, Bernal-Utrera C, Anarte-Lazo E, Garcia-Vidal JA, Botella-Rico JM, Rodriguez-Blanco C. Therapeutic pulmonary telerehabilitation protocol for patients affected by COVID-19, confined to their homes: study protocol for a randomized controlled trial. *Trials.* 2020; 21:1-9.
11. Liu K, Zhang W, Yang Y, Zhang J, Li Y, Chen Y. Respiratory rehabilitation in elderly patients with COVID-19: A randomized controlled study. *Complement Ther Clin Pract.* 2020; 39:101166.
12. Liaw MY, Wang YH, Tsai YC, Huang KT, Chang PW, Chen YC, et al. Inspiratory muscle training in bronchiectasis patients: a prospective randomized controlled study. *Clin Rehabil.* 2011; 25:524-36.
13. Karadallı MN, Boşnak-Güçlü M, Camcıoğlu B, Kokturk N, Türkteş H. Effects of inspiratory muscle training in subjects with sarcoidosis: a randomized controlled clinical trial. *Respir Care.* 2016; 61:483-94.
14. Keles MN, Elbasan B, Apaydin U, Aribas Z, Bakirtas A, Kokturk N. Effects of inspiratory muscle training in children with cerebral palsy: a randomized controlled trial. *Braz J Phys Ther.* 2018; 22:493-501.
15. Abodonya AM, Abdelbasset WK, Awad EA, Elalfy IE, Salem HA, Elsayed SH. Inspiratory muscle training for recovered

- COVID-19 patients after weaning from mechanical ventilation: A pilot control clinical study. *Medicine*. 2021; 100(13).
16. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med*. 1998; 158:1384-87.
  17. Zanini A, Aiello M, Cherubino F, Zampogna E, Azzola A, Chetta A, et al. The one repetition maximum test and the sit-to-stand test in the assessment of a specific pulmonary rehabilitation program on peripheral muscle strength in COPD patients. *Int J Chron Obstruct Pulmon Dis*. 2015; 10:2423.
  18. Stenton C. The MRC breathlessness scale. *Occupational Medicine* 2008; 58:226-7.
  19. Fess E. Grip strength Second ed. Chicago: American Society of Hand Therapists, 1992:6-25.
  20. Aydemir Ö, Guvenir T, Kuey L, Kultur S. Validity and reliability of Turkish version of hospital anxiety and depression scale. *Turk Psikiyatri Derg*. 1997; 8:280-7.
  21. Küçükdeveci A, McKenna S, Kutlay S, Gürsel Y, Whalley D, Arasil T. The development and psychometric assessment of the Turkish version of the Nottingham Health Profile. *Int J Rehabil Res*. 2000; 23:31-8.
  22. Sağlam M, Arikan H, Savci S, Inal-Ince D, Bosnak-Guclu M, Karabulut E, et al. International physical activity questionnaire: reliability and validity of the Turkish version. *Percept Mot Skills*. 2010; 111:278-84.
  23. Armutlu K, Korkmaz NC, Keser I, Sumbuloglu V, Akbiyik DI, Guney Z, et al. The validity and reliability of the Fatigue Severity Scale in Turkish multiple sclerosis patients. *Int J Rehabil Res*. 2007; 30:81-5.
  24. Spagnolo P, Balestro E, Aliberti S, Cocconcelli E, Biondini D, Della Casa G, et al. Pulmonary fibrosis secondary to COVID-19: a call to arms? *The Lancet Respiratory Medicine*. 2020; 8:750-2.
  25. Gosselink R, De Vos J, Van Den Heuvel S, Segers J, Decramer M, Kwakkel G. Impact of inspiratory muscle training in patients with COPD: what is the evidence? *Eur Respir J*. 2011; 37:416-25.
  26. Duruturk N, Acar M, Doğrul MI. Effect of inspiratory muscle training in the management of patients with asthma. *J Cardiopulm Rehabil Prev*. 2018; 38:198-203.
  27. Csuka M, McCarty DJ. Simple method for measurement of lower extremity muscle strength. *Am J Med*. 1985; 78:77-81.
  28. Figueiredo PHS, Lima MMO, Costa HS, Martins JB, Flecha OD, Gonçalves PF, et al. Effects of the inspiratory muscle training and aerobic training on respiratory and functional parameters, inflammatory biomarkers, redox status and quality of life in hemodialysis patients: A randomized clinical trial. *PLoS One*. 2018; 13: e0200727.
  29. Marco E, Ramírez-Sarmiento AL, Coloma A, Sartor M, Comin-Colet J, Vila J, et al. High-intensity vs. sham inspiratory muscle training in patients with chronic heart failure: a prospective randomized trial. *Eur J Heart Fail*. 2013; 15:892-901.
  30. Turquetto ALR, Dos Santos MR, Agostinho DR, Sayegh ALC, de Souza FR, Amato LP, et al. Aerobic exercise and inspiratory muscle training increase functional capacity in patients with univentricular physiology after Fontan operation: A randomized controlled trial. *Int J Cardiol*. 2021; 330:50-8.
  31. Soumyashree S, Kaur J. Effect of inspiratory muscle training (IMT) on aerobic capacity, respiratory muscle strength and rate of perceived exertion in paraplegics. *J Spinal Cord Med*. 2020; 43:53-9.
  32. Langer D, Ciavaglia C, Faisal A, Webb KA, Neder JA, Gosselink R, et al. Inspiratory muscle training reduces diaphragm activation and dyspnea during exercise in COPD. *J Appl Physiol*. 2018; 125:381-92.
  33. Panagiotti M, Scott C, Blakemore A, Coventry PA. Overview of the prevalence, impact, and management of depression and anxiety in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2014; 9:1289.
  34. Saka S, Gurses HN, Bayram M. Effect of inspiratory muscle training on dyspnea-related kinesiphobia in chronic obstructive pulmonary disease: A randomized controlled trial. *Complementary Ther Clin Pract*. 2021; 44:101418.
  35. Pellizzaro CO, Thomé FS, Veronese FV. Effect of peripheral and respiratory muscle training on the functional capacity of hemodialysis patients. *Ren Fail*. 2013; 35:189-97.
  36. Aslan GK, Akinci B, Yeldan I, Okumus G. A randomized controlled trial on inspiratory muscle training in pulmonary hypertension: Effects on respiratory functions, functional exercise capacity, physical activity, and quality of life. *Heart Lung*. 2020; 49:381-7.
  37. Hossein Pour AH, Gholami M, Saki M, Birjandi M. The effect of inspiratory muscle training on fatigue and dyspnea in patients with heart failure: A randomized, controlled trial. *Jpn J Nurs Sci*. 2020; 17:e12290.