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ORIGINAL ARTICLE

Predictors of reduced incremental shuttle walk test performance in patients with long post-COVID-19

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ABSTRACT

Objective: One of the common limitations after COVID-19 pneumonia is the decrease in exercise capacity. The identification of the factors affecting exercise capacity and the assessment of patients at risk are important for determining treatment strategy. This study was conducted to determine the predictors of decreased exercise capacity in long post-COVID-19 patients. **Methods:** We investigated the association of exercise capacity as measured by the incremental shuttle walk test (ISWT) with age, sex, spirometric variables, respiratory and peripheral muscle strength, quality of life, fatigue, hospital anxiety depression scale, chest X-ray involvement, and hospitalization. The patients were divided into three groups: outpatients, inpatients, and ICU patients. Regression analysis was used to determine which parameters were significant predictors of exercise capacity. **Results:** Of the 181 patients included in the study, 56 (31%) were female. The mean ISWT in percentage of predicted values (ISWT%pred) was 43.20% in the whole sample, whereas that was 52.89%, 43.71%, and 32.21% in the outpatient, inpatient, and ICU patient groups, respectively. Linear regression analysis showed that predictors of decreased ISWT%pred were sex (β = 8.089; p = 0.002), mMRC scale score (β = −7.004; p ≤ 0.001), FVC%pred (β = 0.151; p = 0.003), and handgrip strength (β = 0.261; p = 0.030). **Conclusions:** In long post-COVID-19 patients, sex, perception of dyspnea, restrictive pattern in respiratory function, and decrease in peripheral muscle strength are predictors of reduced exercise capacity that persists three months after COVID-19. In this context, we suggest that pulmonary rehabilitation might be an important therapy for patients after COVID-19.

Keywords: COVID-19; Exercise; Muscle strength; Rehabilitation; Walk test.

INTRODUCTION

Post-acute illness symptoms in patients with COVID-19 can persist for months. The term long post-COVID-19 syndrome has been proposed to describe clinical symptoms lasting more than 12 weeks after the onset of acute symptoms.[1] The underlying causes of this situation are not fully understood. The most common symptoms are fatigue and dyspnea.[2,3] Severe limitations occur in some of these patients. One of them is the decrease in exercise capacity. Although studies are still ongoing, it has been suggested that various factors such as cardiac sequelae, decrease in diffusion capacity, limited lung function, and muscle weakness may be factors that might limit exercise capacity.[4,5] In another study, decreased exercise capacity three months after severe COVID-19 infection has been associated with respiratory limitation and decreased skeletal muscle mass and function rather than cardiac causes.[6,7] Moreover, studies in non-COVID-19 patients have demonstrated that decreased exercise capacity is an independent predictor of mortality.[8,9] In patients with chronic respiratory disease, normal exercise capacity improves quality of life and participation in daily activities while decreasing respiratory symptoms, anxiety, frequency of hospital visits and of hospitalizations, and social isolation. So, the determination of the factors affecting the limitation of exercise capacity and the prediction of which patients are at risk are important for managing treatment strategy. The application of an incremental shuttle walk test (ISWT) does not require the use of any specialized equipment. However, the estimated peak oxygen consumption (Vo_{2peak}) obtained by the ISWT revealed a moderate to strong correlation with maximal exercise performance as evaluated by the cardiopulmonary exercise test (CPET). The ISWT has been found to be a reliable test of cardiopulmonary exercise capacity, especially in COPD, and to produce a physiological response similar to the CPET.[10]

The aim of our study was to examine the relationship between the decrease in exercise capacity determined by ISWT and clinical, functional, or emotional factors in a patient cohort who recovered after COVID-19. A secondary aim was to discover predictors of decreased exercise capacity in long post-COVID-19 patients. Our hypothesis was that decreased exercise capacity in long post-COVID-19 patients would be predominantly related to muscle strength loss.

METHODS

This was a cross-sectional, prospective, single-center study. Between April 15, 2022, and June 14, 2022, a

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total of 217 patients who were seen at our pulmonary rehabilitation center with complaints of dyspnea and had COVID-19 at least three months but no more than six months prior to their visit were evaluated. The patients were referred to our center by the outpatient clinics which they had visited for COVID-19 control. Of the total sample, 186 patients met the inclusion criteria and agreed to participate in the study (Supplementary Material). All patients consulted with a cardiologist and underwent echocardiograms before evaluation, and myocardial dysfunction was ruled out. Three patients refused to participate in the study, and 2 patients were not approved for pulmonary rehabilitation (PR) by the cardiologist. Therefore, the final sample comprised 181 patients.

Inclusion criteria were as follows: having a confirmed diagnosis of COVID-19 by RT-PCR between three and six months before visiting our center, being diagnosed with long post-COVID by a pulmonologist, being ≥ 18 years of age, giving written consent to participate in the study, and having dyspnea at the time of admission, determined by the modified Medical Research Council (mMRC) dyspnea scale score ≥ 1. Exclusion criteria were being younger than 18 years of age; having uncontrolled psychiatric disease, orthopedic disability, movement-limiting neurological disease, active malignancy, uncontrolled hypertension, or a disease that was thought to reduce exercise capacity other than COVID-19; being a professional athlete; being pregnant; and participating in a rehabilitation or an intensive exercise program before ISWT.

In addition to demographic data, we collected information about comorbidities, length of hospital/ICU stay in days, chest X-rays, need for long-term oxygen therapy (LTOT), perception of dyspnea, body composition measurements, amount of weight loss, Borg scale score, spirometry, and peripheral and respiratory muscle strength in order to determine the factors affecting the decrease in exercise capacity of the participants. Hospital anxiety and depression scale (HADS), fatigue severity scale (FSS) and Nottingham Extended Activities of Daily Living Scale (NEADLS) were administered. Chest X-rays were evaluated visually. The use of LTOT (patients in need were started in the center to which they were referred) was recorded. The patients were divided into three groups according to the severity of the disease (outpatient, inpatient, and ICU follow-up), and their data were analyzed. Parameters that might be associated with the decrease in the percent of predicted ISWT (ISWT%pred) were investigated in all patients. Written informed consent form was obtained from all patients. The study protocol conformed to the Declaration of Helsinki and was approved by the Research Ethics Committee of the Ankara Atatürk Sanatoryum Training and Research Hospital (Protocol KAEK-15/2492).

The chest X-rays obtained during the admission process to our center were divided into six zones and their involvement was determined (bilateral, especially in the middle and lower regions, peripherally distributed, irregularly limited density increase and consolidation). The X-rays were evaluated by two different pulmonologists, and results were decided by consensus. Dyspnea was assessed using the mMRC scale.[11] BMI was calculated using the formula body mass (in kg) divided by the square of height (in m).

Exercise capacity was evaluated using the ISWT. The test was performed according to field walking test guidelines.[12] The predicted ISWT value was calculated by a reference equation,[13] which includes age, gender, and BMI. ISWT values were obtained as a percentage of the predicted value (ISWT%pred). Also, $\dot{V}O_{2peak}$ value and in percentage of the predicted value were calculated using ISWT.[14]

Dyspnea intensity was measured throughout exercise using the modified 0-10 Borg scale. Spirometry was performed to determine FVC, FEV_1, and FEV_1/FVC ratio using a spirometer (AS-507, Minato Medical Science, Tokyo, Japan) in accordance with the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.[15] Respiratory muscle strength was evaluated by measuring MIP and MEP using a Micro-RPM respiratory pressure meter (Care Fusion, Hoechberg, Germany). MIP and MEP were measured in accordance with the recommendations of the ATS/ERS.[16] The test was repeated at least three times, and the best value was recorded. To assess peripheral muscle strength of the patients, a handgrip test was performed using a hand dynamometer (Jamar Hydraulic Hand Dynamometer, Mississauga, Canada).[17] Psychological status was assessed using the HADS,[18] whereas fatigue was assessed using the FSS, and activities of daily living were assessed using the validated Turkish version of NEADLS.[19]

Statistical analyses were performed with the IBM SPSS Statistics software package, version 26.0 (IBM Corporation, Armonk, NY, USA). Normally-distributed numeric variables were expressed as means and standard variations, while non-normally distributed variables were expressed as medians. Categorical variables were expressed as absolute and relative frequencies. To determine if the variables were normally distributed, visual (histograms and probability plots) and analytical methods (Shapiro-Wilk test, skewness coefficient, and kurtosis coefficient) were used. The statistical differences of normal and non-normal quantitative variables of demographic and baseline values across groups established according to hospitalization status were assessed using ANOVA and the Kruskal-Wallis test, respectively. Tukey's honestly significant difference test and the Games-Howell test were used for post hoc analyses. The correlation between two numeric variables with normal distribution and a linear correlation was analyzed using Pearson's correlation coefficient. The correlation between variables that did not show normal distribution was evaluated with Spearman's correlation coefficient. The predictors of ISWT%pred were analyzed by using linear regression analysis. A p-value < 0.05 was used to determine statistical significance.

RESULTS

Of the 181 patients studied, 125 (69%) and 56 (31%) were male and female, respectively. During the ISWT, 141 patients were unable to complete the test, 94 of whom developed leg fatigue, 19 of whom developed dyspnea, 17 of whom developed desaturation, and 3 of whom developed tachycardia exceeding submaximal heart rate. The Vo_{2peak} calculated from the ISWT was above 80% of the predicted value in only 5 patients. The mean ISWT%pred was 43.20% ± 16.19% in the sample as a whole, whereas that in males and females, respectively, was 41.39% ± 15.57% and 47.23% ± 16.96%, and this difference was statistically significant ($p = 0.024$). The groups formed by disease severity were evaluated with one-way ANOVA. Age, comorbidities, BMI, Borg scale, HADS, and FSS results were similar among the groups. Regarding comorbidities, hypertension (in 22 patients), diabetes mellitus (in 15), coronary artery disease (in 2), and sleep apnea (in 1) were identified in the outpatient group; whereas hypertension (in 35), diabetes mellitus (in 24), coronary disease (in 2), sleep apnea (in 2), renal failure (in 1), and familial Mediterranean fever (in 1) were present in the inpatient group; and hypertension (in 15), diabetes mellitus (in 14), sleep apnea (in 2), coronary artery disease (in 1), and renal failure (in 1) were present and in the ICU group. Tables 1 and 2 provide detailed information on demographic data and other parameters evaluated, as well as p-values calculated by ANOVA for the sample as a whole and the groups by hospitalization status. ANOVA and post hoc analyses (Games-Howell) revealed statistically significant differences in ISWT%pred among the three groups ($p < 0.001$).

In the correlation analysis, ISWT%pred correlated with hospitalization status, length of hospital/ICU stay, extent of chest X-ray involvement, LTOT use, mMRC scale, amount of weight loss, Borg scale score, spirometry, handgrip strength, and NEADLS score. No relationship was found with emotional factors. Table 3 shows the parameters that correlated with ISWT%pred values in the correlation analysis performed using the whole sample. In the correlation analysis, a multivariable linear regression model was created with the parameters that correlated with the ISWT%pred. In the multiple linear regression analysis, sex, mMRC scale, FVC%pred, and handgrip strength were found to be the predictors of ISWT%pred. In the regression analysis model of ISWT%pred, the variables gender, hospitalization status, X-ray, mMRC scale, Borg scale, FVC%pred, handgrip strength, and NEADLS explained 60% of the reduced ISWT%pred (Table 4). The relationship of ISWT%pred with hospitalization status, mMRC scale, FVC%pred, and handgrip strength is seen in Figures 1 and 2.

DISCUSSION

In our study, we aimed to identify which patients with long post-COVID were at risk of having lower exercise capacity. We discovered that male gender, dyspnea perception, impaired lung function, and impaired peripheral muscle strength were the main predictors of decreased exercise capacity. Being male decreased the ISWT%pred by about 8 units. A 1-unit increase in the mMRC scale score was correlated with a 7-unit decrease in ISWT. Also, 1-unit increases in FVC%pred and in handgrip strength improved ISWT by 0.151 and 0.261 units, respectively. Because low exercise capacity negatively impacts the quality of life of patients by preventing them from regaining their pre-COVID-19 functional status, our results are crucial for identifying patients in the risk group and enabling early preventative therapy and measures to be applied.

Exercise capacity measured with field tests is also used to assess the success of pulmonary rehabilitation in addition to various indicators such as dyspnea and quality of life. Also, ISWT and endurance shuttle walk tests are used to prescribe exercise. When the reasons for test termination are considered, they might provide information about the cardiac or pulmonary causes of exercise limitation.

Previous studies have shown that ISWT performance is associated with age, FEV_1%pred, and peripheral

Table 1. Demographic characteristics and hospitalization data.[a]

Variable	Overall sample (N = 181)	Group			p	Comparison*		
		Outpatient (n = 45; 24.9%)	Inpatient (n = 92; 50.8%)	ICU (n = 44; 24.3%)		p^{1-2}	p^{2-3}	p^{1-3}
Male sex	125 (69.1)	21 (46.7)	74 (80.4)	30 (68.2)	< 0.001	< 0.001***	0.302***	0.100***
Age, years	55.7 ± 10.5	54.7 ± 10.9	55.5 ± 10.9	57.3 ± 9.2	0.502	0.897**	0.651**	0.487**
Smoking history, pack-years	27.9 ± 21.4	32.1 ± 18.2	31.4 ± 16.2	20.0 ± 12.1	0.030	0.341**	0.029**	0.487**
Comorbidities, yes	121(66.9)	34 (75.6)	58 (64.1)	29 (65.9)	0.381	0.355**	0.966**	0.599**
Length of hospital stay, days	-	-	12.6 ± 8.4	35.1 ± 16.2	-	-	-	-
Length of ICU stay, days	-	-	-	18.4 ± 13.7	-	-	-	-
X-ray, zone involvement	2.4 ± 1.9	1.6 ± 1.9	2.4 ± 1.8	3.1 ± 1.9	0.002	0.064**	0.128**	0.001**
LTOT, yes	69 (38.12)	3 (6.7)	36 (39.1)	30 (68.2)	< 0.001	< 0.001***	0.005***	< 0.001***

LTOT: long-term oxygen therapy. [a]Values expressed as n (%) or mean ± SD. *Games-Howell test: (1 = outpatient; 2 = inpatient; and 3 = ICU). **ANOVA or Kruskal-Wallis test. ***Tukey's honestly significant difference test.

Table 2. Exercise tests and other measurements/questionnaires.[a]

Variable	Overall sample (N = 181)	Group			p	Comparison*		
		Outpatient (n = 45; 24.9%)	Inpatient (n = 92; 50.8%)	ICU (n = 44; 24.3%)		p^{1-2}	p^{2-3}	p^{1-3}
mMRC (1/2/3/4)	23/44/21/12	38/58/4/0	24/44/22/10	7/30/36/27	< 0.001	< 0.001***	0.001***	< 0.001***
BMI, kg/m²	28.9 ± 5.1	28.9 ± 4.3	28.6 ± 5.0	29.6 ± 5.9	0.531	0.939**	0.499**	0.767**
Weight loss, kg	9.3 ± 5.4	6.6 ± 2.2	8.2 ± 4.4	13.7 ± 6.8	0.003	0.379***	0.051***	0.013***
ISWT, m	345 ± 141	370 ± 91	365 ± 146	249 ± 131	< 0.001	0.282***	< 0.001***	< 0.001***
ISWT, % predicted	43.2 ± 16.2	52.9 ± 10.0	43.7 ± 15.6	32.2 ± 16.1	< 0.001	< 0.001***	< 0.001***	< 0.001***
SpO_2 before ISWT	97.2 ± 1.4	97.5 ± 0.9	97.2 ± 1.4	96.7 ± 1.8	0.140	0.657**	0.397**	0.117**
SpO_2 after ISWT	92.4 ± 4.4	94.4 ± 4.1	91.7 ± 4.3	90.9 ± 4.5	0.008	0.026**	0.753**	0.013**
HR before ISWT	88.6 ± 14.2	86.4 ± 11.2	89.7 ± 15.0	89.2 ± 16.3	0.607	0.592**	0.988**	0.771**
HR after ISWT	121 ± 14	121 ± 14	122 ± 16	119 ± 15	0.326	0.385**	0.979**	0.402**
Borg at rest	0 [0.0-0.5]	0 [0.0-0.5]	0 [0.0-0.5]	0 [0-1]	0.484	1.000***	0.529***	0.631***
Borg after ISWT	4 [3-4]	4 [2-4]	4 [3-4]	4 [3-5]	0.333	0.892***	0.223***	0.620***
Vo_{2peak}, % predicted	45.1 ± 12.5	51.6 ± 8.4	45.8 ± 12.7	36.6 ± 11.1	< 0.001	0.006***	< 0.001***	< 0.00*1**
FVC, % predicted	85.5 ± 22.4	94.4 ± 18.8	86.4 ± 22.5	72.1 ± 20.3	< 0.001	0.123*	0.004**	< 0.001**
FEV_1, % predicted	83.6 ± 21.3	88.9 ± 19.6	84.4 ± 21.2	74.9 ± 21.6	0.015	0.503*	0.073**	0.012**
FEV_1/FVC	79.8 ± 11.2	77.5 ± 9.1	79.2 ± 11.4	84.4 ± 12.2	0.022	0.725*	0.057**	0.022**
MIP, cmH_2O	95.5 ± 29.4	84.2 ± 26.5	99.1 ± 25.1	99.5 ± 36.6	0.046	0.056*	0.998**	0.089**
MEP, cmH_2O	122.5 ± 34.8	108.8 ± 29.7	129.5 ± 31.1	122.7 ± 41.8	0.026	0.019*	0.626**	0.230**
Handgrip test, kg	31.5 ± 10.2	29.7 ± 10.8	33.7 ± 9.3	28.7 ± 10.4	0.016	0.101*	0.026**	0.895**
HADS-Anxiety	7.1 ± 3.7	7.9 ± 3.9	6.6 ± 3.7	7.3 ± 3.6	0.148	0.138*	0.557**	0.739**
HADS-Depression	6.9 ± 3.4	7.0 ± 3.4	6.7 ± 3.6	7.1 ± 3.3	0.854	0.918*	0.870**	0.995**
FSS	4.5 ± 1.7	4.5 ± 1.8	4.3 ± 1.7	4.6 ± 1.7	0.590	0.797*	0.595**	0.959**
NEADLS	56.8 ± 11.5	61.3 ± 5.8	56.9 ± 10.3	52.3 ± 15.8	0.002	0.010**	0.214***	0.004***

mMRC: modified Medical Research Council scale; ISWT: incremental shuttle walk test; Vo_{2peak}: peak oxygen consumption; ,HADS: Hospital Anxiety and Depression Scale; FSS: Fatigue severity score; and NEADLS: Nottingham Extended Activities of Daily Living Scale. [a]Values expressed as %, mean ± SD, or median [IQR]. *Games-Howell test: (1 = outpatient; 2 = inpatient; and 3 = ICU). **ANOVA or Kruskal-Wallis test. ***Tukey's honestly significant difference test.

muscle strength in patients with COPD. ISWT was also associated with sniff nasal inspiratory pressure and peripheral muscle strength in lung cancer.[10,20] Age, body composition, dyspnea, respiratory function, and physical activity in daily life were found to be predictors of ISWT in bronchiectasis.[21] In our study, age and BMI were not correlated with ISWT%pred. This might be because COVID-19 patients are exposed to the disease for a shorter period of time than are those with chronic diseases. Although respiratory muscles do not correlate with ISWT, the correlation of peripheral muscle strength may be associated with disease-related immobility. Finally, the correlation of other parameters with ISWT and predictors of ISWT were similar to those in non-COVID-19 diseases. In a multicenter prospective cohort study including 1,226 hospitalized patients, post-COVID-19 dyspnea was associated with lower performance on the shuttle walk test and FVC, but not with obstructive airflow limitation.[22]

Our study showed that being male with persistent symptoms is a predictor for reduced exercise capacity. Previous studies have revealed that males are likely to have more severe disease.[23,24] In our study, the rates of hospitalization and ICU stay were higher in males. Lower ISWT%pred in men may be due to more severe disease and more hospitalizations.

According to an earlier study, patients with COVID-19 had higher MRC scale scores, and those scores rise in line with the severity of the disease.[25] However, in another study, it was found that the MRC scale score did not differ between hospitalized and non-hospitalized patients.[24] In our study, the mMRC scale score was statistically significantly different among the three severity groups. In addition, the mMRC scale score was found to be a predictor for ISWT%pred.

In our study, it was found that one of the causes contributing to the reduction in exercise capacity was the decrease in FVC%pred. Restriction on spirometry has been linked to decreased exercise capacity and increased desaturation in patients with post-COVID-19 persistent dyspnea.[26] Due to their exercise-induced desaturation, post-COVID-19 patients with normoxemia at rest also resemble those having interstitial lung disease.[27] The strength of respiratory muscles may be the cause of the FVC%pred decline. ISWT%pred and respiratory muscle strength, however, did not correlate in our study. The correlation between ISWT%pred and radiological results (p = 0.001; r = −0.276) led us to believe that parenchymal injury was the cause of the decline in FVC%pred. This restrictive pattern increases with the severity of the disease.

Investigations are currently ongoing to determine the causes of decreased exercise capacity in post-COVID-19

Table 3. Correlations of the incremental shuttle walk test in % of predicted values with selected variables.

Variable	Correlation coefficient	p
Sex	0.167*	0.025
Age, years	−0.103	0.167
Smoking history, pack-years	−0.035	0.728
Comorbidities, no/yes	−0.107	0.154
Hospitalization status	−0.449**	< 0.001
Length of hospital stay, days	−0.554**	< 0.001
Length of ICU stay, days	−0.464**	0.001
X-ray, zone involvement, n	−0.330**	< 0.001
LTOT use	−0.459**	< 0.001
mMRC scale score	−0.680**	< 0.001
BMI, kg/m^2	0.104	0.171
Weight loss, kg	−0.542**	< 0.001
Borg scale score at rest	−0.208**	0.005
Borg scale score after exercise	−0.163*	0.031
FVC, % pred	0.590**	< 0.001
FEV_1, % pred	0.554**	< 0.001
FEV_1/FVC	−0.134	0.096
MIP, cmH_2O	0.030	0.744
MEP, cmH_2O	0.118	0.190
Handgrip test	0.238**	0.002
HADS-Anxiety score	−0.017	0.823
HADS-Depression score	−0.081	0.287
FSS score	−0.029	0.719
NEADLS score	0.354**	< 0.001

LTOT: long-term oxygen therapy; % pred: % of the predicted value; mMRC: modified Medical Research Council; HADS: hospital anxiety and depression scale; FSS: fatigue severity score; and NEADLS: Nottingham Extended Activities of Daily Living Scale.

Table 4. Multivariate linear regression analyses of the incremental shuttle walk test in % of predicted values.

Variable	Unstandardized coefficient (β)	Standardized coefficient	t	p	95% CI for β	
					Lower bound	Upper bound
Sex	8.089	0.246	3.133	0.002	2.978	13.201
Hospitalization status	−2.163	−0.099	−1.429	0.156	−5.159	0.834
X-ray, zone involvement, n	−0.156	−0.020	−0.304	0.761	−1.172	0.860
mMRC scale score	−7.004	−0.428	−5.525	< 0.001	−9.514	−4.495
FVC, % pred	0.151	0.220	2.991	0.003	0.051	0.251
Borg scale score at rest	0.152	0.080	0.080	0.936	−3.620	3.925
Borg scale score after exercise	−0.005	−0.001	−0.007	0.994	−1.470	1.459
Handgrip test	0.261	0.166	2.192	0.030	0.025	0.496
NEADLS score	0.153	0.107	1.644	0.103	−0.031	0.337

mMRC: modified Medical Research Council; % pred: % of the predicted value; and NEADLS: Nottingham Extended Activities of Daily Living Scale.

patients. Existing studies indicate that sarcopenia and decreased skeletal muscle strength are important reasons for limiting exercise.[6,28,29] There may be a number of causes for the decline in muscle strength. Atrophy as a result of insufficient physical activity, critical illness polyneuropathy, and muscle or central nervous system damage caused by SARS-CoV-2 are possible causes.[30] Increased length of hospital stay, probable corticosteroid use, and weight loss as the disease progresses pose a risk for sarcopenia and muscle weakness. In our study, mean handgrip strength was found to be high in hospitalized patients, but it should be noted that the majority of these patients were male. According to our results, a decrease in peripheral muscle strength is an important predictor of prolonged reduced exercise capacity after the third month in long post-COVID-19 patients. In our study, the rate of patients who terminated the exercise due to respiratory reasons was 18.8%, while the number of patients who developed leg fatigue was more than half (51.9%). This demonstrates the importance of reduction in muscle strength in limiting exercise capacity in patients with COVID-19.

Previous studies showed that decreased lung function and impaired exercise capacity were associated with

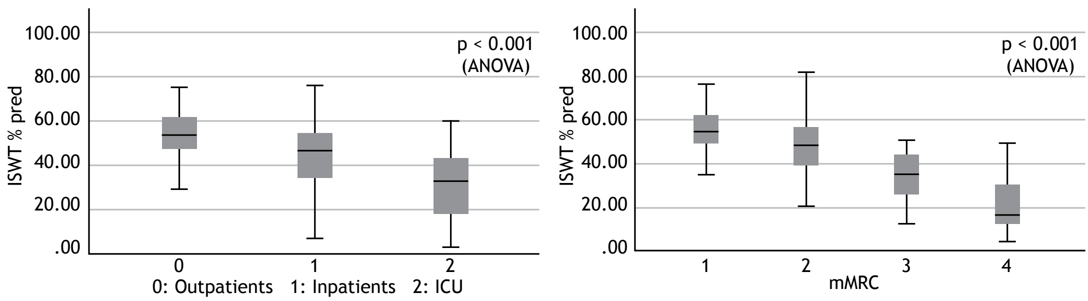

Figure 1. Incremental shuttle walk test in percentage of the predicted value (ISWT%pred) by hospitalization status and modified Medical Research Council (mMRC) scale score.

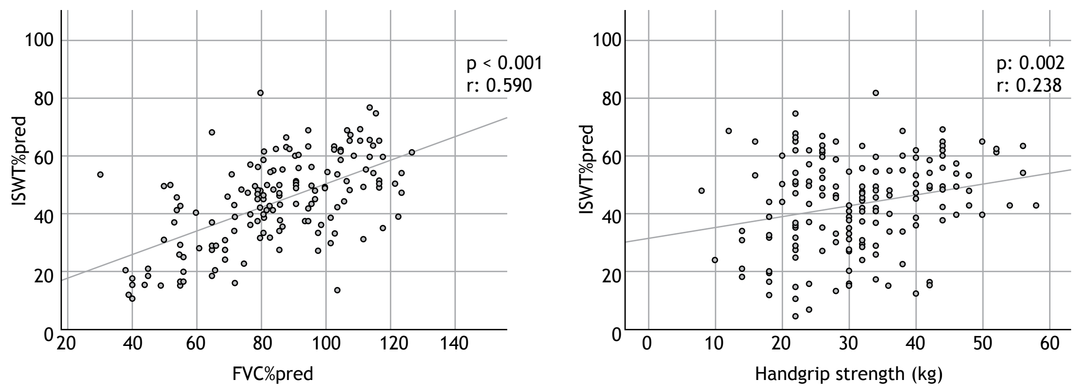

Figure 2. Incremental shuttle walk test in percentage of the predicted value (ISWT%pred) by FVC in percentage of predicted value (FVC%pred) and handgrip strength.

reduced skeletal muscle mass and function three months after COVID-19 infection. No significant deterioration in cardiac function was detected.[6] In our study, similarly to previous studies, the restrictive pattern in respiratory function and decreased skeletal muscle strength were important predictors of reduced exercise capacity. During the tests, only 3 patients developed tachycardia exceeding the submaximal heart rate.

In our study, although BMI was higher than normal in all groups, it did not differ among them. Even if the FSS score was above the normal limit in all groups, no differences were found and that was not associated with exercise capacity. According to several studies, fatigue develops at a higher rate in patients who had severe COVID-19.[31] However, there are also studies showing that persistent fatigue is independent of the severity of COVID-19 infection.[32] Previous studies presented a relationship between maximal exercise capacity and activities of daily living. Reduced exercise capacity has a negative effect on daily activities.[33] In our study, we found that exercise capacity in long post-COVID-19 patients was correlated with the NEADLS score. However, the NEADLS was not a predictor of exercise capacity.

We think that individualized pulmonary rehabilitation programs that include appropriate exercise training, as well as medical treatment, are important in the follow-up and treatment of these patients.

The most important limitation of this study is the single-center design. However, our center is a referral hospital, and patients come from all over the country. Another limitation was that our study had no control group. A cohort of non- COVID-19 patients might be beneficial for comparing baseline results. Due to the ongoing pandemic, DL_{CO} could not be performed in this study.

As a conclusion, in long post-COVID patients, male gender, perception of dyspnea, restrictive pattern in respiratory function, and decrease in peripheral muscle strength were predictors of reduced exercise capacity that persisted after three months. In addition, hospitalization was a risk factor for exercise limitation.

AUTHOR CONTRIBUTIONS

MES: literature search, data collection, study design, data analysis, manuscript preparation, and manuscript review. SS: literature search, data collection, study design, data analysis, manuscript preparation, and manuscript review. PE: literature search, study design, data analysis, manuscript preparation, and manuscript review. All authors have read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

None declared.

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