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EXERCISE CAPACITY, MUSCLE FUNCTION, FUNCTIONAL BALANCE, AND COGNITIVE STATUS IN PATIENTS WITH POST COVID-19 SYNDROME COMPARED TO HEALTHY CONTROLS

POST COVID-19 SENDROMU OLAN HASTALARIN SAĞLIKLI KONTROLLERE GÖRE EGZERSİZ KAPASİTESİ, KAS FONKSİYONU, FONKSİYONEL DENGE VE BİLİŞSEL DURUMU

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ABSTRACT

Objective: There is limited data on the effect of post-COVID-19 syndrome on functional outcomes compared with healthy uninfected individuals. This study aimed to compare the muscle function, exercise capacity, and quality of life of patients with post-COVID-19 syndrome with that of healthy controls.

Method: Twenty patients with post-COVID-19 syndrome and twenty healthy controls participated in the study. The Incremental Shuttle Walk Test (ISWT) was used to measure exercise capacity, and the Timed Up and Go Test (TUG) was used to assess functional balance. Quadriceps muscle strength (QMS) and handgrip strength (HGS) were measured. Assessment tools included the McGill Pain Questionnaire (SF-MPQ) for pain, the Tampa Scale for Kinesiophobia (TSK) for movement fear, the Modified Medical Research Council Dyspnea Scale (mMRC) for dyspnea, the Fatigue Severity Scale (FSS) for fatigue perception, and the Cognitive Failures Questionnaire (CFQ) for cognitive status.

Results: The mMRC dyspnea, TSK, FSS, SF-MPQ total scores, and pain severity of patients with post-COVID-19 syndrome were higher than those of healthy controls ($p<.05$). Compared to the healthy group, the ISWT and %ISWT distances were significantly lower in the post-COVID-19 group ($p<.05$).

Conclusion: Exercise capacity is negatively affected; anxiety, pain, fatigue severity, dyspnea, and kinesiophobia levels are increased in patients with post-COVID-19 syndrome compared with healthy groups. However, muscle strength, balance, and cognitive function are preserved in individuals with mild-to-moderate COVID-19 infection. Pulmonary rehabilitation programs should be designed on the basis of these multiple influences with a multidisciplinary approach in the long-term rehabilitation of individuals with COVID-19 infection.

Key Words: COVID-19, Functional status, Pandemics, Exercise test, Post-COVID-19

ÖZ

Amaç: Sağlıklı, enfekte olmamış bireylerle karşılaştırıldığında, COVID-19 sonrası sendromun fonksiyonel sonuçlar üzerindeki etkisine ilişkin sınırlı veri bulunmaktadır. Bu çalışma, post COVID-19 sendromu olan hastaların kas fonksiyonunu, egzersiz kapasitesini ve yaşam kalitesini sağlıklı kontrollerle karşılaştırmayı amaçladı.

Yöntem: Çalışmaya post COVID-19 sendromu olan 20 hasta ve 20 sağlıklı kontrol katıldı. Egzersiz kapasitesini ölçmek için Artan Hızda Mekik Yürüme Testi (ISWT), fonksiyonel dengeyi değerlendirmek için Zamanlı Kalk ve Yürü Testi (TUG) kullanıldı. Quadriseps kas kuvveti (QMS) ve el kavrama kuvveti (HGS) ölçüldü. Değerlendirme araçları arasında; ağrı için McGill Ağrı Anketi (SF-MPQ), hareket korkusu için Tampa Kinezyofobi Ölçeği (TSK), nefes darlığı için Modifiye Medical Research Council dispne skalası (mMRC), yorgunluk algısı için Yorgunluk Şiddet Ölçeği (FSS) ve bilişsel durum için Bilişsel Durum Ölçeği (CFQ) yer aldı.

Bulgular: Post-COVID-19 sendromlu hastaların mMRC nefes darlığı, TSK, FSS, SF-MPQ toplam skorları ve ağrı şiddeti sağlıklı kontrollere göre daha yüksekti ($p<.05$). Sağlıklı grupla karşılaştırıldığında ISWT ve %ISWT mesafeleri, post COVID-19 grubunda anlamlı derecede düşüktü ($p<.05$).

Sonuç: Sağlıklı gruplarla karşılaştırıldığında, post COVID-19 sendromlu hastalarda egzersiz kapasitesi olumsuz etkilenmekte; anksiyete, ağrı, yorgunluk şiddeti, nefes darlığı ve kinezyofobi düzeyleri artmaktadır. Ancak hafif-orta şiddette COVID-19 enfeksiyonu olan bireylerde kas gücü, denge ve bilişsel işlevler korunmaktadır. COVID-19 enfeksiyonu olan bireylerin uzun süreli rehabilitasyonunda pulmoner rehabilitasyon programları bu çoklu etkiler dikkate alınarak multidisipliner bir yaklaşımla tasarlanmalıdır.

Anahtar Kelimeler: COVID-19, Fonksiyonel statü, Pandemi, Egzersiz testi, Post-COVID-19

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INTRODUCTION

The multisystemic condition known as "long COVID or post-COVID-19 syndrome" is characterized by severe symptoms that last longer than three months after the first symptom onset [1]. Most cases occur in nonhospitalized individuals with mild acute illness. Common symptoms include dyspnea, chronic smell and taste problems, fatigue, pain, and neuropsychological symptoms like headache, memory loss, poor thinking, anxiety, and depression [1,2]. In a study of 1,077 hospitalized COVID-19 survivors, five months after discharge, 48% reported ongoing fatigue, 41% experienced dyspnea, and 21-28% sustained palpitations and chest pain [3].

Three months after discharge, COVID-19 survivors' exercise capacity remained unaffected by disease severity, despite preserved ventilatory efficiency. Exercise capacity is mildly reduced across severity groups [4]. A study in patients with severe COVID-19 six months after ICU discharge revealed significantly lower respiratory function, exercise capacity, and quality of life than healthy controls. These patients also experienced higher fatigue levels, and their balance and mobility were negatively impacted [5]. For up to two years following infection, physical function and activity may worsen in patients withpost-COVID-19 syndrome, as well as lower fitness levels [2]. Instead of vertigo, balance problems associated to dizziness affect about 20% of patients with post-COVID-19 syndrome. Even though their somatosensory and vestibular scores are comparable to those of controls, patients with long-COVID had poorer overall visual scores [6].

Current data show that even in mild/moderate COVID-19 cases and young survivors, muscle function, physical activity, physical performance, exercise capacity, balance, sleep quality, and psychosocial status are adversely affected [4,5,7]. Evidence on long-term functional consequences remains limited. While some studies have compared survivors' extrapulmonary functions based on severity [7] and healthy controls [5], more research is required to completely comprehend the long-term impacts of COVID-19. Thus, this study aimed to compare exercise capacity, muscle function, balance, pain, kinesiophobia levels, quality of life, and cognitive status of long-term COVID-19 survivors with those of healthy controls who had never been infected. The strength of this study was that extrapulmonary effects of patients with post-COVID-19 syndrome were compared to healthy controls who had never-infected with COVID-19 infection at the beginning of pandemic period.

METHOD

Study Design and Participants

Between February 2021 and February 2022, this study was conducted in collaboration with the Hacettepe University Faculty of Physical Therapy and Rehabilitation, Department of Cardiorespiratory Physiotherapy and Rehabilitation, and the Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of General Internal Medicine. Twenty cooperative patients between the ages of 18 and 65 years who had been diagnosed with COVID-19 infection at least 12 weeks earlier, showed persistent symptoms, were in clinical stability, and had well-managed concurrent conditions were recruited. These were non-ICU hospitalized COVID-19 patients. Exclusions comprised those with recent positive COVID-19 Polymerase chain reaction (PCR) tests, myocardial infarction, pulmonary embolism in the last 30 days, orthopedic/neurological disorders hindering walking, or neurological/psychiatric disorders impacting cooperation. The healthy group comprised 20 volunteers matched in age and gender, free from chronic diseases, orthopedic, or other walking impairments, and without COVID-19 infection at the study time and before the study.

Firstly, the participants' age, gender, body weight, height, body mass index (BMI), comorbid diseases, smoking exposure, medical history, family history, occupation, accompanying illnesses, and working status were recorded. Secondly, clinical tests and questionnaires were administered to participants.

The sample size of our study was determined with the G*Power analysis system (G*Power Software version 3.1.9.3, Heinriche Heine University, Düsseldorf Germany) based on findings of physical functions assessed by 1-minute sit-to-stand test in COVID-19 survivors by Belli et al [8]. Accordingly, it was determined that the sample size of our study should have been at least 12 participants for each group in order to reach 90% power at the medium effect level (d=0.50).

Outcome Measures

Body Composition: Body composition was evaluated using an OMRON BF-511 Body Composition Monitor (Omron Corporation, Japan). Body weight and visceral fat level (VFL), fat-free mass (FFM), and body fat (FM) were recorded [9].

Comorbidity and Dyspnea Level: The Modified Charlson Comorbidity Index (CCI) score was calculated and recorded [10]. The modified Medical Research Council (mMRC) scale score was recorded [11].

Exercise Capacity: The incremental shuttle walk test (ISWT) was used to evaluate exercise capacity. The distance was expressed in meters and as a percentage of the expected distances, and the number of shuttles was noted [12].

Muscle Strength: For peripheral muscle function, the hand grip strength (HGS) and quadriceps muscle strength (QMS) were tested. HGS was performed using a Jamar hand dynamometer (Jamar®, California, USA), and the result was expressed in kgF. The QMS was measured and recorded in kilos using the Lafayette Manual Muscle Test System (Model-01165, Lafayette Instrument Company, USA). The dominant side underwent three sets of measurements, with the best results for peripheral muscle strength being noted [13,14].

Functional Status: The Turkish valid and reliable version of the Post-COVID-19 Functional Status Scale (PCFS) was used to evaluate the functional status and activity limitations of COVID-19 survivors [15].

Balance: The timed-up and go test (TUG) evaluated functional mobility and balance. Using a stopwatch, the total TUG time was measured in seconds. On the same day, the TUG test was administered twice, with the best test duration being recorded as the final score [16].

Pain: Participants' pain characteristics and severity were evaluated using the Short Form of the McGill Pain Questionnaire (SF-MPQ), translated into Turkish. The sum of the sensory, emotional, and overall pain descriptors yielded the final score. The overall SF-MPQ score ranges from 0 to 45 and higher scores denote worse pain. Lastly, the Visual Analog Scale (VAS) was used to assess the patient's pain threshold [17].

Fatigue Perception and Fear of Movement: The Turkish version of the Fatigue Severity Scale (FSS) assessed participants' fatigue levels. A total FSS score≥4 indicates severe fatigue [18]. The subjects' fear of movement was measured using the Turkish translation of the Tampa Scale for Kinesiophobia (TSK). Overall, the TSK score on the rating system ranges from 17 to 68. A TSK score of less than 37 indicates kinesiophobia [19].

Cognitive Function: The 25 items of the Cognitive Failures Questionnaire (CFQ) are used to self-report perception, memory, and motor function problems in order to assess cognitive state. Scores vary from 0 to 100, with higher numbers denoting more cognitive dysfunction [20].

Psychosocial Status: Using the Turkish translation of the Hospital Anxiety and Depression Scale (HADS), the participants' anxiety and depressive symptoms were evaluated. Between 0 and 7, the HADS score is considered normal; 8–10 is borderline; and ≥11 indicates significant anxiety or depression [21].

Quality of Life: Quality of life was assessed among participants using the Short Form-36 (SF-36) questionnaire. Higher ratings indicate a higher quality of life; values range from 0 to 100 [22].

Work Productivity: According to VAS, based on pre-pandemic and post-pandemic periods, the work productivity of COVID-19 survivors and healthy individuals was evaluated with the following questions: (i)"I can easily focus on my tasks at work," (ii)"I feel productive at work," and (iii)"I can quickly adjust to changes in the work I do."

Ethical Approval

The Hacettepe University Non-Interventional Clinical Research Ethics Committee approved the study on 02.02.2021, with the decision number 2021/03-03. All participants were informed about the study protocol and signed the informed consent. The authors declare that the procedures were followed according to the regulations established by the Ethics Committee and to the Helsinki Declaration of the World Medical Association. This study was registered in ClinicalTrials.gov: NCT04836767.

Statistical Analysis

The statistical analyses were performed using the Windows-based statistical package program Statistical Package for the Social Sciences (SPSS) 23.0 (IBM, Ver.23.0, Newyork, USA). When comparing quantitative data between groups, regularly distributed data was compared using the Student's t-test; non-normally distributed data was compared using the Mann-Whitney U test. The chi-square test was utilized to analyze qualitative data. A $p<0.05$ criterion for significance was set. A post hoc power analysis was performed using the ISWT distance data from the COVID-19 and healthy groups. The power [1-β] of the study was 99%.

RESULTS

A flowchart of the study is presented in Figure 1.

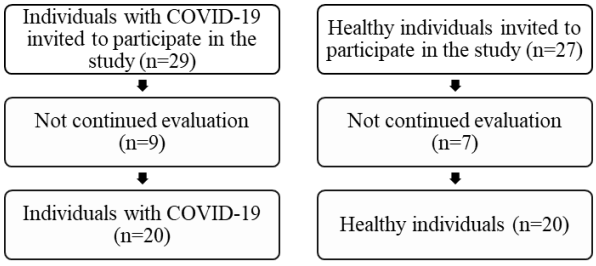

Figure 1. Flow chart of the study

Twenty COVID-19 survivors and 20 healthy, never-infected controls were included in the study. The severity of COVID-19 infection was mild/moderate in all survivors. The groups' mean age, height, body weight, BMI, smoking exposure, FFM, and FM values and modified CCI scores were similar ($p>.05$, Table 1).

Twenty percent of patients with post-COVID-19 syndrome had chronic rhinosinusitis, 5% had visual and hearing problems, 5% had gastrointestinal disorders, and 5% had DM. In both groups, 85% of the participants were females and 15% were males. The VFL of the healthy group was significantly lower than that of the COVID-19 group ($p<.05$, Table 1).

According to the PCFS score, 65% of patients with post-COVID-19 syndrome had negligible, 10% had mild, 10% had moderate, and 5% had severe functional limitations (Table 1).

There was no significant difference in QMS and HGS between groups ($p>.05$, Table 2). The TUG time was similar between groups ($p>.05$, Table 2). The ISWT distance and %ISWT distance were significantly lower in the COVID-19 group than in the healthy group ($p<.05$, Table 2). Although the changes in dyspnea, leg fatigue, and general fatigue perceptions were similar between groups ($p>.05$, Table 2), the increase in HR was lower, and the decrease in oxygen saturation (SpO_2) levels was greater in COVID-19 survivors ($p<.05$, Table 2).

Table 1. Physical characteristics, comorbidity and functional status in patients with post COVID-19 syndrome and healthy controls

Parameters	**Post COVID-19 Syndrome (n=20)**	**Healthy (n=20)**	**t/z**	**p**
	Mean±SD	**Mean±SD**		
Age (years)	28.80±8.26	26.90±4.10	-.920[&]	.363
Height (cm)	165.53±8.35	166.50±7.29	.391[&]	.698
Body weight (kg)	68.45±10.52	64.55±10.52	1.188[&]	.242
BMI (kg/m^2)	24.91±3.28	23.20±2.79	1.828[&]	.076
FM (%)	28.10±6.41	25.42±6.63	-1.296[&]	.203
FFM (%)	29.94±5.37	30.83±1.18	-.636[a]	.525
VFL	5.45±2.01	4.05±1.46	-2.513[&]	**.016***
Smoking history (Packs-year)	0.50±2.23	0.50±2.23	.000[a]	1.000
Parameters	**Median (Min-Max)**	**Median (Min-Max)**	**t/z**	**p**
Modified CCI score	0 (0-3)	0 (0-0)	-1.777[a]	.076
PCFS score	**n (%)**			
0	2 (10)			
1	13 (65)			
2	2 (10)			
3	2 (10)			
4	1 (5)			

**p<0.05, [&]t: Student-t test, [a]z:Mann-Whitney U test, BMI:Body Mass Index, CCI:Charlson Comorbidity Index, FM:Fat mass, FFM:Fat-free mass, VF:Visceral fat level, PCFS:Post-COVID-19 Functional Status (PCFS) Scale*

The mMRC, TSK, FSS, SF-MPQ, total scores, and VAS pain severity scores were significantly higher in the post-COVID-19 syndrome group than in the healthy group ($p<.05$, Table 3). The distribution of pain is presented in Figure 2. Although kinesiophobia was observed in 60% of the patients with post-COVID-19 syndrome, 75% of them had severe fatigue. Patients with post-COVID-19 syndrome had significantly lower SF-36 total and subdimension scores than healthy controls ($p<.05$, Table 3). Otherwise, the HADS anxiety and depression scores and CFQ scores were comparable between groups ($p>.05$, Table 3). According to the HADS anxiety cut-off scores, 50% of patients with post-COVID-19 syndrome had abnormal anxiety levels, whereas 10% of healthy controls had abnormal anxiety levels ($p<.05$, Table 3), there was not any significant difference based on the HADS depression cut-off scores ($p>.05$, Table 3). According to the statistical analysis of work productivity, the decrease in work productivity in patients with post-COVID-19 syndrome was significantly greater than that in healthy controls after the pandemic ($p<.05$, Table 3).

DISCUSSION

Our study highlights increased dyspnea, fear of movement, fatigue, anxiety, and pain perception in post-COVID-19 patients with mild/moderate symptoms compared with healthy controls. Despite preserved cognitive function, balance, and mobility, patients experienced reduced exercise capacity, psychosocial well-being, quality of life, and work productivity. This study examined long-term extrapulmonary effects in post-COVID-19 patients compared with never-infected healthy individuals.

Table 2. Exercise capacity, peripheral muscle function and functional balance and mobility in patients with post COVID-19 syndrome and healthy controls

Parameters	Post COVID-19 Syndrome (n=20) X̄±SS	Healthy (n=20) X̄±SS	t/z	p
Muscle function				
QMS (kg)	25.42±6.47	23.82±4.45	-1.853[a]	.064
%QMS	52.60±12.11	49.79±7.60	-.865[&]	.393
HGS (kgF)	29.30±5.81	32.80±6.65	-1.771[&]	.085
%HGS	89.07±14.52	81.88±19.73	1.312[&]	.197
Functional balance and mobility				
TUG (sec)	7.11±0.82	6.72±0.87	1.459[&]	.267
Exercise capacity				
%ISWT distance	56.80±8.30	73.32±10.23	-5.608[&]	**<.001***
ISWT distance (m)	571.00±114.74	765.95±131.07	-5.005[&]	**<.001***
ΔHR (beats/min)	68.20±27.17	84.35±20.77	-2.111	**.041***
ΔSpO_2 (%)	-2.15±1.72	0.05±1.63	-4.136	**<.001***
ΔDyspnea	3.87±1.02	4.42±1.85	-1.159[a]	.256
ΔGeneral fatigue	3.10±1.34	3.12±1.67	-.052[a]	.959
ΔLeg fatigue	3.37±1.58	2.55±1.73	1.570[a]	.125

**p<0.05, [&]t: Student-t test, [a]z:Mann-Whitney U test, ISWT:Incremental Shuttle Walk Test, HR:Heart Rate, SpO2:Oxygen Saturation, QMS:Quadriceps Muscle Strength, HGS:Hand Grip Strength, TUG:Time up and Go Test*

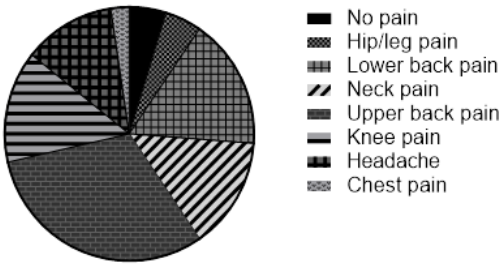

Figure 2. Distribution of pain in patients with post-COVID-19 syndrome

Watanabe et al. found that visceral fat could indicate poorer clinical outcomes in patients with COVID-19 [23]. A higher visceral fat ratio in the post-COVID-19 syndrome group confirms these findings. All participants had similar height, body weight, BMI, fat, and muscle ratio.

Anaya et al. reported that >20% of patients with post-COVID-19 syndrome experience shortness of breath [24]. Similarly, Pavli et al. determined a dyspnea incidence ranging from 10% to 40% among patients with post-COVID-19 syndrome [25].

Table 3. Dyspnea, fatigue severity, pain, kinesiophobia, quality of life, cognitive status, psychosocial status and work productivity in patients with post COVID-19 syndrome and healthy controls

Parameters	Post COVID-19 Syndrome (n=20)	Healthy (n=20)	t/z/χ^2	p
Dyspnea- Median (Min-Max)				
mMRC score (0-4)	1 (0-3)	0 (0-1)	-5.466	**<.001***
Fatigue (X̄±SS)				
FSS score (0-7)	4.78±1.63	2.61±1.33	4.608[&]	**<.001***
Pain (X̄±SS)				
SF-MPQ total score (0-45)	26.25±14.96	15.85±12.54	-2.033[a]	**.042***
VAS score (0-10)	5.30±2.49	3.00±2.15	-2.943[a]	**.003***
Kinesiophobia (X̄±SS)				
TSK (17-68)	38.05±7.61	32.25±6.80	2.539[&]	**.015***
Quality of life (SF-36) (0-100) (X̄±SS)				
Physical functioning	72.50±19.76	98.25±3.35	-4.884[a]	**<.001***
Physical role functioning	33.00±36.68	97.50±7.69	-4.850[a]	**<.001***
Bodily pain	49.75±29.17	85.75±14.57	-3.721[a]	**<.001***
General health	49.75±20.09	79.50±12.65	-5.602[&]	**<.001***
Vitality	35.50±24.16	65.50±18.41	-3.553[a]	**<.001***
Social functioning	51.87±25.41	82.50±17.86	-3.579[a]	**<.001***
Emotional role functioning	36.64±35.69	78.32±36.32	-3.230[a]	**.001***
Mental health	52.20±25.11	72.40±14.03	-3.140[&]	**.004***
Psychosocial status (X̄±SS)				
HADS-anxiety (0-21)	8.80±5.54	5.85±3.29	-1.725[a]	.084
HADS-depression (0-21)	7.70±5.10	5.25±3.9	-1.506[a]	.132
Cognitive status (X̄±SS)				
CFQ (0-100)	42.35±19.49	30.90±15.87	-1.841[a]	.066
Work productivity (X̄±SS)				
I can easily focus on my tasks at work	-3.74±2.19	-1.22±1.50	-3.478[a]	**<.001***
I feel productive at work	-4.36±2.19	-1.07±1.31	-4.368[a]	**<.001***
I can quickly adjust to changes in the work I do	-3.90±2.05	-1.06±1.35	-4.002[a]	**<.001***
Anxiety status according to HADS (X̄±SS)				
Normal	9 (%45)	14 (%70)		
Borderline	1 (%5)	4 (%20)	8.220[ɣ]	**.016***
Abnormal	10 (%50)	2 (%10)		
Depression status according to HADS (X̄±SS)				
Normal	11 (%55)	15 (%75)		
Borderline	3 (%15)	2 (%10)	1.815[ɣ]	.403
Abnormal	6 (%30)	3 (%15)		

**p<0.05, [&]t:Student-t test, [a]z:Mann-Whitney U test, [ɣ]:Chi-square test, mMRC:Modified Medical Research Council dyspnea scale, TSK:Tampa Scale for Kinesiophobia, FSS:Fatigue Severity Scale, SF-MPQ:Short Form of the McGill Pain Questionnaire, VAS:Visual Analog Scale, SF-36:Short Form-36, HADS:Hospital Anxiety and Depression Scale, CFQ:Cognitive Failures Questionnaire*

In a study evaluating patients with and without the need for ICU in the post-acute period of COVID-19, dyspnea (42%) and fatigue (55%) were the most frequently reported symptoms in a cohort of 120 patients [26]. Whereas the rate of dyspnea gradually decreases within 6 months, fatigue and neurological and mental symptoms persist for a longer period of time [27]. The dyspnea and fatigue scores, as shown by the mMRC and FSS scores, were meaningfully increased in patients with post-COVID-19 syndrome, and 75% of our patients without ICU stay had severe fatigue, as previously reported [5]. The mean-modified CCI score was 0.7±0.9 in 48 mild/moderate post-COVID-19 patients with 39.2±7.9 years [7]. The minimum and maximum modified CCI scores in the post-COVID-19 group were 0-3, respectively. Comorbid conditions, such as DM or hypertension, increase the risk of a more severe course and progression of COVID-19 disease [28]. Our participants' comparable and low comorbidity severity could be due to their relatively younger age and mild/moderate COVID-19 disease severity. Therefore, our results are consistent with findings from existing studies [7,27,28].

Sirayder et al. showed that nearly 81% of COVID-19 survivors' 6MWT distance was lower than that of controls with similar physical activity levels. The patient group had lower SpO2 values and higher dyspnea, general fatigue, and leg fatigue scores after 6MWT. Balance and functional mobility determined by TUG were also adversely affected in the COVID-19 group [5]. Raman et al. reported that a significant portion of COVID-19 patients had limited exercise capacity in their study [29]. The TUG and dual task-TUG performance were shown to be poorer in the severe and critical COVID group than in patients with chronic lung disease [30]. Beyer et al. showed that patients with post-COVID-19 syndrome and severe fatigue walked significantly lower distance in 6MWT and oxygen consumption values of patients were also lower according to reference values [31]. ISWT and %ISWT distances declined in post-COVID-19 patients with mild/moderate symptoms and severe fatigue in our study, confirming existing data on exercise capacity impairment and deconditioning [5,29,31].

39.6% of the subjects had handgrip weakness, and 35.4% had quadriceps muscle weakness in the study by Tanriverdi et al. with 48 patients after mild/moderate COVID-19 infection [7]. The patients with moderate-severity disease had significantly higher muscle weakness than the mild group 12 weeks after infection [7]. Sirayder et al. showed that 57.6% of COVID-19 survivors with ICU stay had QMS levels lower than the 95% confidence interval of the controls and handgrip weakness [5]. Blokland et al. reported that peripheral muscle strength decreased in 70% of patients in the post-COVID-19 period who were connected to mechanical ventilation [32]. Because the patients with post-COVID-19 syndrome in our study had mild-to-moderate disease severity and no history of a severe illness requiring ICU care, their peripheral muscle strength was equivalent across the two groups. Otherwise, 52.60±12.11 and 49.79±7.60 percent of predicted QMS in post-COVID-19 and healthy groups could have been related to decreased physical activity levels during the pandemic. We also explain that maintaining peripheral muscular strength, any need for ICU admission, and related immobilization processes account for the comparable functional mobility and balance of the post-COVID-19 and healthy groups.

In a systematic review, the most frequently reported symptoms were fatigue and weakness, followed by shortness of breath, disruption of normal activity, loss of taste and/or smell, depression, muscle and/or joint pain, sleep disturbance, anxiety, cough, and headache [33]. Thirty-two percent of COVID-19 patients still experienced fatigue, and 22% had cognitive impairment 12 weeks after the infection, as reported in another report [27,34]. In addition, 40% of the patients with long COVID had poor concentration, 31% had poor memory, 25% had poor attention, and 6% had confusion 24 weeks after acute infection. After 24 weeks, 67% of the patients still performed below their pre-COVID functional levels; whereas 44.9% of the patients were ambulatory, able to take care of all personal needs, but unable to perform any job-related tasks, and 38% of them were only able to perform minimal self-care, spending over 50% of their awake hours in bed or a chair [35]. In our study, any significant difference in cognitive level between the groups could be related to our patient group's relatively younger age and mild/moderate disease severity. In a study about occupation status of 214 patients with post-COVID-19 syndrome, 18% of patients were working, 40% of them were working with diffuculty and 35% had stopped working due to symptoms [36]. Despite limited evidence regarding the effect of long COVID on work productivity, there was a substantial decrease in concentration, adaptation to changes, and productivity in our patients. Increased dyspnea and fatigue perceptions, minimal cognitive impairment, decreased exercise capacity, and deconditioning could have decreased work productivity in line with findings of Green et al [36].

The most reported pain in the post-COVID-19 period was back pain, followed by neck pain, backache, knee pain, and headaches. Musculoskeletal symptoms such as headache, myalgia, and arthralgia are also common in the post-COVID-19 period [1,27]. Pain may persist for weeks or months in patients who recover from COVID-19 [27]. We also confirmed previous findings that the most reported pain regions were the upper back, lower back, and neck, respectively [1]. Higher pain intensity scores in post-COVID-19 syndrome patients could have been a result of a higher proportion of females [85%] and increased anxiety levels. There are limited data on kinesiophobia during the post-acute or acute phase in COVID-19 patients. Nearly 60% of COVID-19 survivors experienced post-COVID-19 pain associated with kinesiophobia. Furthermore, higher levels of kinesiophobia are associated with pain catastrophizing, symptoms related to sensitization, and anxiety levels [37]. Sixty percent of our patients with post-COVID-19 syndrome also presented with kinesiophobia. Increased fear of movement was an expected finding in the post-COVID-19 group, with accompanying pain and anxiety symptoms. The lack of detailed knowledge among patients about COVID-19 and the effectiveness of exercise during the post-COVID-19 period, along with an increased perception of breathlessness in daily life, may also have contributed to kinesiophobia.

Our previous data showed that the PCFS score is associated with the mMRC dyspnea score and personal care, housework, physical activity, and leisure time daily life activity scores in post-acute COVID-19 patients without ICU admissions. In total, 63.1% of patients had negligible, 14.4% had mild, 2% had moderate, and 0.5% had severe functional limitations [14]. A study with patients with post COVID-19 syndrome reported that those with PCFS 3-4 had meaningful lower functional capacity, impaired quality of life and especially negative effects on pain, and social aspects, higher need for ICU admission and prolonged hospitalization stays compared to those with PCFS 1-2 [38]. In addition, 65% of patients with mild/moderate disease severity had negligible functional limitations. This could be related to the relatively younger age and dyspnea/fatigue symptoms and any need for ICU in the post-COVID-19 group. Anxiety and depression disorders were observed in 52.2% and 47.8% of post-COVID-19 patients, respectively, according to HADS [7]. Although depression levels were similar, anxiety levels of post-COVID-19 patients were greater than those in the current data [5,7,35]. The higher proportion of female participants and dyspnea and pain intensity levels could have led to these findings [7]. The negatively affected quality of life and participation limitations in both physical and emotional roles in our patients could be a result of increased and ongoing dyspnea, fatigue, pain, anxiety symptoms, cognitive decline, and impaired exercise capacity, which confirms previous data [5,31].

Limitations

The main limitation of our study was that despite the reasonable post-power value of our study, the fact that we reached a limited number of individuals who had never had a COVID-19 infection and volunteered to participate during the study period limits the generalizability of the results. Nonetheless, it stands as the pioneering research conducted at

the pandemic's onset, evaluating exercise capacity, muscle function, balance, and cognitive status in post-COVID-19 patients with mild-to-moderate symptoms and uninfected healthy individuals during the chronic phase.

CONCLUSION

In conclusion, our study revealed diminished long-term exercise capacity and quality of life in post-COVID-19 patients compared with uninfected individuals. Anxiety, pain, fatigue, and dyspnea perception increased in post-COVID-19 cases, yet muscle strength, balance, cognitive function, and depression remained similar to those in healthy subjects. Effective rehabilitation post-COVID-19 should integrate pulmonary programs addressing pain, fatigue, dyspnea, and psychosocial factors, alongside tailored exercise regimens and multidisciplinary care reflecting individual capacities and needs.

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