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Chest mobility, cough strength, muscle strength, physical activity, and quality of life in parkinson's patients who had COVID-19

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Abstract

Background Some symptoms of COVID-19 may persist for a long time in individuals who had COVID-19. Since effects of COVID-19 on chest mobility, cough strength, grip strength, physical activity, and quality of life in Parkinson's patients are still unclear, current study aimed to investigate this issue.

Methods Parkinson's patients with and without a history of COVID-19 ($n = 17$, 66.65 ± 12.01 years versus $n = 21$, 68.71 ± 10.35 years) were included in this study. Cognitive functions (Mini-Mental State Examination), severity and disability status of Parkinson's disease (Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Modified Hoehn and Yahr Scale (MHYS)), chest mobility (chest circumference measurement with a tape measure), cough strength (a PEFmeter), hand grip strength (a hand-dynamometer), physical activity level (a pedometer) and quality of life (Parkinson's Disease Questionnaire-39 (PDQ-39)) were evaluated in all individuals.

Results Parkinson's patients with COVID-19 history had lower subcostal chest circumference measurement difference, grip strength and step count measured on 1st day, and higher MDS-UPDRS part I and PDQ-39 scores than patients without COVID-19 history ($p < 0.05$). Cognitive functions, MHYS, other parts of MDS-UPDRS, axillar and epigastric chest circumference measurement differences, cough strength and average step counts values were similar between groups ($p > 0.05$).

Conclusions Disease severity due to non-motor symptoms, abdominal respiration, peripheral muscle strength, daily step count and quality of life worsened in Parkinson's patients with COVID-19 history compared to those without COVID-19 history and these parameters should be therefore monitored regularly. Chest respiration and cough strength were preserved in these individuals.

Keywords Cough, COVID-19, Muscle strength, Parkinsonism, Physical activity, Quality of life

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Introduction

Parkinson's disease is a disease of the central nervous system and among neurodegenerative disorders. In Parkinson's disease, motor problems occur due to the unknown death of dopamine-producing cells in the substantia nigra which is located in the middle part of the brain. As this disease progresses, movement-related motor findings such as tremors, rigidity, slowness of movements, posture disorder, and difficulty in walking and gait become evident [1]. Moreover, pulmonary system abnormalities and respiratory dysfunction such as chest wall rigidity, unstable breathing pattern, abnormal pulmonary function test results, dyspnea and hypoxia can be seen in advanced stages of Parkinson's disease. Respiratory system dysfunction is an important factor that increases morbidity and mortality rates, especially in elderly Parkinson's patients [2–4]. As the disease severity of Parkinson's disease increases, the patients experience difficulties in hand functions and walking. This situation may even cause Parkinson's patients to fall and limitations in daily living activities [1, 4].

On the other hand, the SARS-CoV-2 (COVID-19) pandemic has afflicted the health of societies all over the world, but it especially negatively affected individuals with chronic neurological diseases [5, 6]. Parkinson's patients have noticed many difficulties in their health during the COVID-19 pandemic and social restriction days. Mood disorders like more stress, anxiety and depression, increased motor and non-motor symptoms, tendency to a sedentary lifestyle and physical inactivity were observed in these patients during pandemic period compared to before pandemic [5, 7–13]. Moreover, worsening of these signs and symptoms was more pronounced in Parkinson's patients who neglected their daily exercises [8]. Increased Parkinson's symptoms including pain, tremor and rigidity, mood disturbances and physical inactivity and deterioration in quality of life (QOL) have been reported by many patients, especially during times of quarantine [14]. It is known that the COVID-19 virus can cause endothelial damage, myofibrillar destruction and muscle degradation, and thus a decrease in peripheral and respiratory muscle strength in individuals who had COVID-19 [15]. Fatigue and dyspnea may persist for a long time after exposure to COVID-19, and these symptoms are among the symptoms referred to as long-COVID [16]. Insomnia, physical inactivity, decreased exercise capacity, muscle weakness, and deterioration in QOL can be seen in individuals who had COVID-19, as well [16–18].

The literature presents limited studies showing the extent to which Parkinson's patients who had COVID-19 are affected physically, psychologically, and in terms of symptoms, compared to Parkinson's patients without a history of COVID-19. In the light of the information available to date, it is known that disease severity and symptoms increase while the QOL deteriorates more in Parkinson's patients who had COVID-19 [9, 11]. However, no study has been found in literature that comparatively examines the physical activity level, cough and handgrip strength, thoracic cage mobility and QOL between Parkinson's patients based on the presence of a confirmed history of COVID-19. Therefore, to reveal the effects of having a history of COVID-19 on these aforementioned parameters in Parkinson's patients in this study.

Materials and methods

Study design

Izmir Democracy University Non-Invasive Clinical Research Ethics Committee approved this study on 29.03.2023 with decision number 2023/04 – 01. After all approvals had been received for this study, which was planned as a cross-sectional observational analytical study, our study was executed favorably with the principles stated in the Declaration of Helsinki between May 2023 and May 2024 at the Department of Physiotherapy and Rehabilitation of the Faculty of Health Sciences of Izmir Democracy University and the Department of Neurology of the Faculty of Medicine of Bandırma Onyedi Eylül University. All Parkinson's patients were informed in detail about the purpose and method of the study, and then the patients signed consent forms. Then, the following evaluations were applied to each patient in a face-to-face interview lasting no more than one hour. Clinical trials registration number is NCT06008444.

Study population

The study population consisted of Parkinson's patients who received outpatient treatment at the Department of Neurology of the Faculty of Medicine of Bandırma Onyedi Eylül University. The study sample consisted of Parkinson's patients from this population who agreed to participate in our study voluntarily. This study included two groups: Parkinson's patients with and without a confirmed history of COVID-19. Among Parkinson's patients, 17 patients who had COVID-19 and 21 patients who had never had COVID-19 before were included in this study. The inclusion criteria for Parkinson's patients who have had COVID-19 were as follows: (i) having been diagnosed with COVID-19 at least 12 weeks ago (confirmed by a positive Polymerase Chain Reaction test result or, in cases of a negative Polymerase Chain Reaction testor chest tomography) and having recovered, (ii) volunteering to participate in the study, (iii) age ≥ 18 years, (iv) having been diagnosed with Parkinson's disease, (v) having sufficient cognitive ability to comprehend assessments (Standardized Mini-Mental Test score ≥ 24), (vi) if comorbid conditions such as hypertension or diabetes were present, these conditions had to be well-controlled, (vii) being independently ambulant and able to walk, and (viii) being classified between stages 1 and 4 according to the Modified Hoehn and Yahr Scale (MHYS). The inclusion criteria for another group differed from the inclusion criteria for the patients who have had COVID-19 in only option (i): never having been diagnosed with COVID-19 before or not having any suspicion of having COVID-19.

The exclusion criteria for individuals in both study groups were as follows: (i) sudden change in medication or dosage during the study period, (ii) being in stage 5 according to the MHYS, (iii) having a history of another neurological disease such as stroke, nerve diseases, brain tumors, head trauma, etc. other than Parkinson's disease, (iv) having had a myocardial infarction or pulmonary embolism in the last 30 days (v) having a history of any pulmonary, orthopedic, psychiatric, cardiovascular, or neuromuscular disease that could interfere with the assessments, (vi) having blood pressure values above 140/90 mmHg or below 90/50 mmHg in pre-study measurements, (vii) having severe vision loss or vestibular dysfunction, (viii) presence of arrhythmia on electrocardiography or (ix) having a history of dyspnea and/or palpitations.

Measurements

Demographic and descriptive characteristics, cognitive functions, disease severity and disability status, thoracic cage mobility, physical activity level, peak cough expiratory flow value, hand grip strength, and QOL in all patients were evaluated at one time by the physiotherapist and doctor. The QOL score was the primary outcome measure of current study, other parameters were secondary outcome measures.

Evaluation of QOL

Parkinson's Disease QOL Questionnaire (PDQ-39), which is valid and reliable questionnaire, used to assess the QOL of Parkinson's patients [19, 20]. The PDQ-39 consists of 38 items. Individuals verbally rate each item of the PDQ-39 between 0 (never), 1 (rarely), 2 (sometimes), 3 (mostly), and 4 (always). The PDQ-39 assesses how often individuals with Parkinson's disease experience difficulties in 8 domains of their daily lives. These domains include bodily discomfort, communication, cognition, social support, stigmatization, emotional well-being, daily living activities and mobility. The total score for each dimension ranges from 0 (representing never having difficulty) to 100 (always having difficulty). Higher scores for each domains indicate worse QOL. The total score was obtained from 38-item. The total score obtained from PDQ-39 is obtained by summing the scores from the sub-domains and then dividing by 8 [20].

Evaluation of cognitive functions

The Turkish version of Standardized Mini Mental Status Examination administered to Parkinson's patients is a valid and reliable test [21, 22]. The test evaluates individuals' cognitive functions under five basic headings: orientation, recording memory, attention and calculation, recall and language [22]. The maximum score that can be obtained from the test is 30. A total score between 24 and 30 indicates that the individual does not have cognitive impairment [21].

Evaluation of severity and disability status

The Hoehn and Yahr Staging Scale was developed to examine disease severity and motor symptoms in Parkinson's patients. The scale was revised by the Movement Disorder Society in 2004, and its new version was called the MHYS. This scale evaluates the course of the disease in seven stages. As the stage progresses, the disease symptoms worsen [23].

To assess progression of disease, Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) was used in current study, which is a reliable scale in Turkish population [24]. MDS-UPDRS consists of 4 parts that evaluate the severity of both symptoms and complications resulting from these symptoms. Part I, II, III and IV evaluate non-motor problems, motor problems, motor examination and motor complications, respectively. Each question item of this scale is scored between 0 and 4, and there are also yes/no question items. A higher total score obtained from this scale indicates that Parkinson's disease is more severe, meaning a worse health status. The first part includes the severity of nonmotor aspects of daily living; the second part includes the severity of motor aspects of daily living activities; the third part includes the assessment of motor manifestations of the disease by examination; and the fourth part includes the assessment of motor complications that usually arise from symptoms and anti-Parkinsonian medications. The fourth part can be evaluated when motor complications occur in the later stages of this disease [25].

Evaluation of chest mobility

Chest circumference measurement, which is a reliable and reproducible measurement, was used to evaluate chest mobility in patients [26]. Chest circumference measurements were made with a tape measure from three thoracic levels including axillary, epigastric and subcostal at rest, maximum inspiration and maximum expiration. The axillary level reference points for upper chest circumference measurement are the 3rd intercostal space (or 4th rib), the epigastric level reference point for lower chest circumference measurement is the xiphoid process level and the reference point for subcostal chest

Fig. 1 Evaluation of Cough Strength in Individuals with Parkinson's Disease

Fig. 2 Evaluation of Hand Grip Strength in Individuals with Parkinson's Disease

circumference measurement is the 10th thoracic vertebra level. The difference between maximum inspiration and expiration measurements taken at each level was recorded in centimeters. According to the difference values in each level, the depth of respiration was classified as superficial if it was less than 2 cm, normal if it was between 2 and 5 cm, and deep if it was > 5 cm [26, 27].

Evaluation of cough strength

Peak cough expiratory flow (PCEF) value of Parkinson's patients was evaluated using a peak cough flow meter called PEFmeter (ExpiRite Peak Flow Meter, China) in an upright sitting position (Fig. 1). After taking a deep breath, the individual was made to cough as forcefully as possible into the PEFmeter. The best of at least three repetitions was recorded [28]. Expected cough force values were calculated from the regression equations of Nunn and Gregg [29]. A PCEF value below 80% of the predicted value was classified as weak cough strength. A PCEF value of ≤ 153 L/min has been reported as a cut-off value for determining aspiration risk in Parkinson's patients [30].

Evaluation of hand grip strength

Maximum isometric strength of the hand and forearm muscles were measured using a standard, adjustable and portable hand dynamometer (Baseline® Standard Hydraulic Hand Dynamometer 12–0240) (Fig. 2). Grip strength measurement is valid and reliable [31]. All measurements were performed in the sitting position with the shoulder in adduction, elbow in 90° flexion, forearm in neutral, and wrist in 0–30° extension and 0–15° ulnar deviation. The measurement was repeated three times for each side. The individual was asked to rest for 15 s before each measurement, and the highest values measured for the right and left in kilogram-force (kgF) were recorded. The reference equation for adults was used to calculate the expected grip strength value. The grip strength of those whose percentage values calculated according to the reference equation values were below 80% and were considered weak [32]. Low grip strength of less than 28 kg for men and less than 18 kg for women is also defined as sarcopenia [33].

Evaluation of physical activity level

The daily physical activity level of Parkinson's patients was evaluated using a pedometer (Omron® HJ-321, Kyoto, Japan). In flat walking, the Omron HJ-321 provides accurate results with less than 1% step count error and is a reliable pedometer for step count tracking at straight walking speed [34]. Pedometers were adjusted individually according to individuals' step length, body weight and height, and individuals were informed about how to use the pedometer before the study. Although valid physical activity tracking days are considered to have at least 10 h of valid usage time [35], individuals were asked to report their three-day step count to the researcher. The number of steps was recorded in the daily step count chart of the patients. For Parkinson's patients, walking 4200 steps per day is equivalent to the physical activity guidelines' recommendations for being active [35].

Statistical analyses

Sample size analysis determined that by including minimum 21 patients exposed to COVID-19 and minimum 11 patients not exposed to COVID-19 in the groups, the median difference in the total QOL score (23.04) between the two groups could be detected with an α value of 0.05, an effect size of 1.1, and a power of 80% in this study [7, 36]. The SPSS program version of 15.0 was used to make statistical analyses. The conformity of all numerical variables recorded within the scope of the study to normal distribution was investigated through visual and analytical methods. Descriptive analyses were presented for categorical (frequency (n), percentage (%)), non-normally distributed (median, interquartile range (IQR), U values) and normally distributed (mean (×), standard deviation (sd), mean difference and 95% confidence interval (95%CI)) variables. The Independent Samples t-test, Mann-Whitney U test and Chi-square test were used to compare normally distributed, non-normally distributed, and categorical variables, respectively. The probability of errors in statistical analysis was set as $p < 0.05$.

Results

Thirty-eight out of 116 Parkinson's patients who came to the neurology outpatient clinic were included in current study. The study was completed with 17 Parkinson's patients who had COVID-19 and 21 Parkinson's patients who had not had COVID-19 (Fig. 3). Baseline descriptive and demographic features of the patients were found to be similar except for the MDS-UPDRS part I score, regular exercise status and exercise duration (Table 1, $p > 0.05$). All individuals with Parkinson's disease (100%) were right-hand dominant. Patients with a history of COVID-19 received COVID-19 treatment at home, which shows that patients had mild severity of COVID-19. The distribution of medications used specifically for Parkinson's disease was statistically similar between the groups ($p = 0.470$).

As presented in Table 2, difference value from subcostal level in chest circumference measurement, left hand grip strength and first day step counts were lower in the patients who had COVID-19 compared to others. While the daily living activities, emotional well-being, cognition, physical discomfort domains scores and total score of the PDQ-39 were statistically significantly higher in the patients who had COVID-19 compared to the patients without a history of COVID-19 ($p < 0.05$). The difference values from the axillary and epigastric levels in chest circumference measurement, PCEF, right hand grip strength, 2nd day, 3rd day, average and total step counts and the mobility, stigma, social support and communication domains scores of the PDQ-39 were similar between the groups (Table 2, $p > 0.05$).

The depth of respiration, PCEF percentage of expected value below 80%, grip strength percentage of expected value below 80%, and being physically active status were similar between the groups (Table 3, $p > 0.05$). In terms of sarcopenia, 2 (11.8%) of individuals who have had COVID-19 and 4 (19%) of those who have not had COVID-19 had low grip strength on the right side; 4 (23.5%) of individuals who have had COVID-19 and 5 (23.8%) of those who have not had COVID-19 had low grip strength on the left side ($p > 0.05$). In addition, no risk factor for aspiration was detected in individuals in both groups.

Discussion

Our study, whose primary research aim was to investigate impacts of a confirmed history of COVID-19 on muscle strength, chest mobility, physical activity, cough force, and QOL in Parkinson's patients, yielded important results. Among Parkinson population of our study, individuals with a confirmed history of COVID-19 had higher scores in the MDS-UPDRS part I and PDQ-39 (daily living activities, emotional well-being, cognition, physical discomfort domains and total score) compared to individuals without a history of COVID-19. Conversely, individuals with a history of COVID-19 had lower the difference in chest circumference measurements at the subcostal level, left-hand grip strength, and the number of steps recorded on the first day.

During the COVID-19 pandemic, worsening of stress, depression, anxiety, physical activity level, and QOL was observed in Parkinson's patients [7, 14]. Many patients have also specified deteriorations in Parkinson's motor and nonmotor symptoms such as pain, rigidity and tremor during quarantine periods. The QOL scores were worse in community-based Parkinson's patients than in hospital-based Parkinson's patients [14]. In our study, QOL and exercise duration were found to be worse in

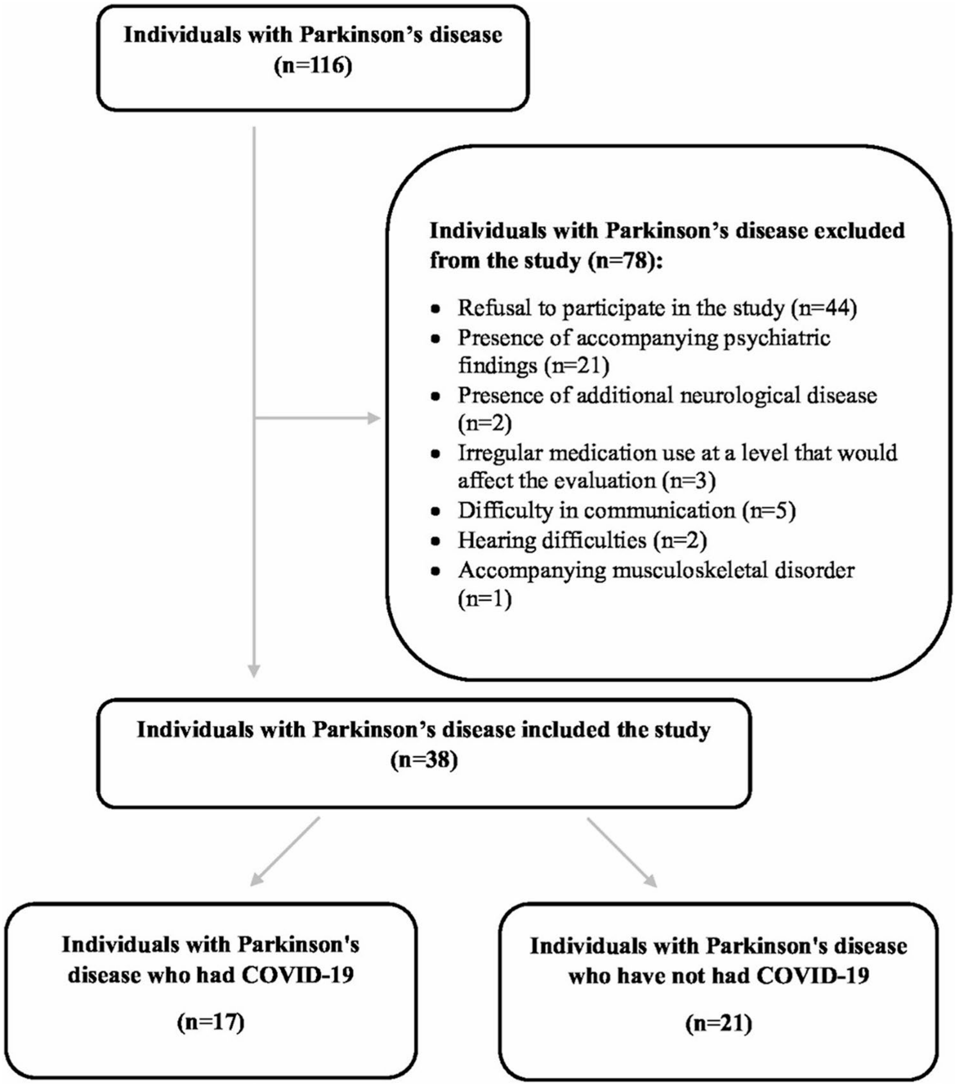

Fig. 3 CONSORT Flowchart for Individuals with Parkinson's Disease

individuals with Parkinson's disease who had COVID-19 compared to others. Similar to this result of our study, it was found that Parkinson's patients had worse QOL after quarantine, and those who had COVID-19 had higher PDQ-39 scores than Parkinson's patients who had never had COVID-19 [11]. The poorer QOL observed in Parkinson's patients with a history of COVID-19 may be attributed to the negative impact of the COVID-19 pandemic on exercise and subjective symptoms of individuals with Parkinson's disease. In these individuals, reduced exercise was associated with a subjective increase in both motor and nonmotor symptoms of Parkinson's disease. Therefore, maintenance of exercise in individuals with Parkinson's disease should be emphasized even in situations such as the COVID-19 pandemic [8]. The fact that it was obtained by comparing with controls who had no COVID-19 contact is the superior aspect of our study compared to the studies in literature. Another contribution to the literature is that the effects of the pandemic have decreased, and the late-term effects of the patients have been evaluated after a long time has passed since the disease contact. It can therefore guide the approach to Parkinson's patients with a COVID-19 history.

The first part of the MDS-UPDRS is concerned with non-motor problems experienced by individuals with Parkinson's disease in their daily lives, such as memory and cognitive functions, feelings of depression and anxiety, sleep disturbances, pain and other sensory problems, and difficulties with urinary and bowel functions [23]. Based on the results of our study, individuals with Parkinson's disease who had COVID-19 had worse MDS-UPDRS part I scores than others; that is, these individuals had a higher disease severity and poorer health status associated with non-motor symptoms [23]. A study reported that the MDS-UPDRS motor scores of

Table 1 Comparison of demographic and descriptive characteristics of groups

		Individuals who have had COVID-19 (*n* = 17)		**Individuals who have not had COVID-19 (*n* = 21)**		***p* value**
		x̄±sd Median (IQR)		**x̄±sd Median (IQR)**		
Age (year)		66.65 ± 12.01		68.71 ± 10.35		0.572
Height (m)		1.64 ± 0.06		1.67 ± 0.05		0.135
Weight (kg)		71.24 ± 12.48		70.38 ± 7.49		0.795
Body Mass Index (kg/m^2)		26.31 ± 3.92		25.14 ± 2.14		0.247
Disease Onset Age (year)		64.24 ± 11.98		64.10 ± 12.37		0.972
Time Between Evaluation Date and Parkinson's Diagnosis Date (month)		26.96 ± 17.49 23.98 (28.37)		54.82 ± 60.84 31.84 (41.92)		0.116
Exercise Duration of Individuals Who Exercise (min)		3.53 ± 8.43		19.29 ± 19.45		0.002 *
Time Between Evaluation Date and COVID-19 Diagnosis Date (month)		25.07 ± 6.64		-		-
Movement Disorders Society Unified Parkinson's Disease Rating Scale	Part I	8.71 ± 4.63 7 (8)		5.33 ± 4.36 5 (6)		0.022 ¥
	Part II	10.47 ± 7.40 8 (13)		6.48 ± 4.90 7 (8)		0.129
	Part III	25.47 ± 9.86 25 (15)		27.76 ± 9.67 26 (15.5)		0.476
	Total score	44.65 ± 18.50 40 (31.5)		39.57 ± 16.17 38 (20)		0.597
Standardized Mini Mental Status Examination	Orientation	9.65 ± 0.49		9.62 ± 0.50		0.863
	Recording memory	3 ± 0		3 ± 0		-
	Attention and calculation	2.94 ± 1.60		3.29 ± 1.74		0.533
	Recall	2.12 ± 0.60		2.05 ± 0.81		0.768
	Language	8.47 ± 1.07		8.48 ± 0.68		0.984
	Total score (0–30)	26.12 ± 2.12		26.67 ± 2.31		0.455
Gender		*n*	%	*n*	%	*p* value
	Female	10	58.8	6	28.6	0.060
	Male	7	41.2	15	71.4	
Disease Onset Side	Right	6	35.3	13	61.9	0.231
	Left	7	41.2	6	28.6	
	Bilateral	4	23.5	2	9.5	
Modified Hoehn and Yahr Scale	Stage 1	1	5.9	1	4.8	0.410
	Stage 1.5	0	0	0	0	
	Stage 2	15	88.2	18	85.7	
	Stage 2.5	0	0	0	0	
	Stage 3	0	0	2	9.5	
	Stage 4	1	5.9	0	0	
	Stage 5	0	0	0	0	
Smokers		3	17.6	2	9.5	0.640
Alcohol Users		3	17.6	1	4.8	0.307
People Who Exercise Regularly		3	17.6	13	61.9	0.009 #
Users of Assistive Devices (Cane)		4	23.5	4	19	1.000
People with Systemic Diseases		12	70.6	13	61.9	0.575

x̄ mean, *sd* standard deviation, *IQR* interquartile range, *n* frequency, % percentage, *Mean Difference* mean difference, *CI* confidence interval

Independent Samples t-test $^{*}p < 0.05$, Mann-Whitney U test $^{¥}p < 0.05$, Chi-square test $^{\#}p < 0.05$

Parkinson's patients increased in the post-COVID period compared to the pre-COVID period [11]. In addition, parallel to the results of our study, the increase in the MHYS score, post-COVID period MDS-UPDRS motor scores, and the total score of the PDQ-39 in Parkinson's patients who had COVID-19 compared to those who had not had COVID-19 was also found to be significant [11]. Individuals with Parkinson's disease who had COVID-19 reported greater worsening of motor symptoms (63% vs. 43%) and non-motor symptoms (75% vs. 52%) than others [9]. It has been reported by another study that motor and non-motor clinical symptoms of Parkinson's

Table 2 Comparison of chest circumference measurement, PCEF, hand grip strength, step count and quality of life values between groups

	Individuals who have had COVID-19 (*n* = 17)	**Individuals who have not had COVID-19 (*n* = 21)**		
	x±sd Median (IQR)	x±sd Median (IQR)	U value/ Mean difference [95%CI]	p value
Δ Axillary (cm)	5.35 ± 1.27 5 (2)	5.71 ± 1.19 6 (2)	147	0.341
Δ Epigastric (cm)	4.77 ± 1.15 5 (1)	5.43 ± 1.43 6 (3)	126	0.115
Δ Subcostal (cm)	3.65 ± 2.12 3 (2)	5.14 ± 1.62 5 (2.5)	101.5	0.020 #
PCEF (L/dk)	330.58 ± 68.99 325 (105)	368.10 ± 77.37 370 (90)	119	0.080
PCEF (%)	85.82 ± 16.25 91 (19)	87.33 ± 13.28 87 (18)	−1.51 [(−11.22)-(8.20)]	0.754
Right hand grip strength (kgF)	25.08 ± 5.58 24.95 (9.07)	28.73 ± 7.08 29.48 (10.21)	−3.65 [(−7.92)-(0.63)]	0.092
Right hand grip strength (%)	73.60 ± 16.67 72.95 (16.82)	74.76 ± 14.56 78.40 (25.86)	−1.16 [(−11.44)-(9.12)]	0.820
Left hand grip strength (kgF)	24.15 ± 4.94 24.95 (9.07)	28.62 ± 6.31 29.48 (10.21)	−4.47 [(−8.27)-(−0.67)]	0.022 *
Left hand grip strength (%)	71.41 ± 17.65 70.35 (26.01)	74.80 ± 14.45 71.19 (23.31)	−3.39 [(−13.95)-(7.16)]	0.518
Step count on day 1	5588.12 ± 1472.98 5435 (1794.5)	6955.19 ± 1872.67 7002 (3136)	−1367.07 [(−2496.31)-(−237.84)]	0.019 *
Step count on day 2	6434.35 ± 1762.71 6433 (2529)	6320.29 ± 2002.30 6129 (3230.5)	168	0.758
Step count on day 3	5784.47 ± 2032.09 5160 (2008.5)	6293.48 ± 1626.27 6283 (1818.5)	142	0.284
Average step count	5935.65 ± 1495.22 6012.33 (1445.83)	6522.98 ± 1564.40 6238 (2444.5)	136	0.212
Total step count	17806.94 ± 4485.67 18,037 (4337.5)	19568.95 ± 4693.20 18,714 (7333.5)	136	0.212
PDQ-39 Mobility (0-100%)	25.15 ± 18.88 25 (33.75)	16.55 ± 10.62 17.5 (17.5)	135.5	0.204
PDQ-39 Daily living activities (0-100%)	31.13 ± 20.42 33.33 (25)	15.68 ± 15.81 12.5 (16.67)	88.5	0.008 #
PDQ-39 Emotional well-being (0-100%)	46.08 ± 22.07 50 (35.42)	28.37 ± 17.71 25 (35.42)	99.5	0.020 #
PDQ-39 Stigmatization (0-100%)	6.25 ± 7.97 6.25 (9.38)	3.57 ± 6.12 0 (9.38)	139.5	0.193
PDQ-39 Social support (0-100%)	9.80 ± 14.50 0 (20.83)	2.78 ± 6.63 0 (0)	133	0.095
PDQ-39 Cognition (0-100%)	20.09 ± 10.23 16.67 (16.67)	12.30 ± 11.67 8.33 (25)	112	0.046 #
PDQ-39 Communication (0-100%)	19.12 ± 20.15 16.67 (25)	12.69 ± 12.53 16.67 (20.83)	153.5	0.447
PDQ-39 Bodily discomfort (0-100%)	51.96 ± 16.54 50 (20.83)	32.14 ± 19.24 33.33 (33.33)	79	0.003 #
PDQ-39 Total score (0-100%)	26.19 ± 8.14 25.10 (14.61)	15.51 ± 7.07 14.79 (12.01)	59.5	< 0.001 #

Δ difference between deep inspiration and deep expiration, *cm* centimeter, *PCEF* peak cough expiratory flow value, *kgF* kilogram force, % percent, *PDQ-39* Parkinson's Disease Quality of Life Questionnaire-39, *x* mean, sd: standard deviation, *IQR* interquartile range, *CI* confidence interval, Independent Samples t test $^{*}p < 0.05$, Mann-Whitney U test $^{\#}p < 0.05$

Table 3 Comparison of the depth of respiration, expected percentage values of PCEF and hand grip strength and being physically active status between the groups

		Individuals who have had COVID-19 (*n* = 17)		Individuals who have not had COVID-19 (*n* = 21)		p value
		n	%	n	%	
Depth of respiration	Superficial	0	0	0	0	0.224
	Normal	9	52.9	7	33.3	
	Deep	8	47.1	14	66.7	
PCEF value	Those <%80	5	29.4	5	23.8	0.727
	Those ≥%80	12	70.6	16	76.2	
Hand grip strength	Those <%80	12	70.6	15	71.4	1.000
	Those ≥%80	5	29.4	6	28.6	
Physical activity	Inactive	1	5.9	1	4.8	1.000
	Active	16	94.1	20	95.2	

n frequency, % percentage, Chi-square test $^{\#}p < 0.05$

patients worsened, the amount, duration and frequency of exercise decreased and the number of individuals who did not exercise increased during the pandemic period [8]. When individuals who performed continuous and reduced exercise were compared, although there was no significant difference between the MDS-UPDRS part 3 scores, patients in the reduced exercise group reported greater motor and non-motor deterioration than the others [8]. Although the individuals in our study were evaluated after a long time had passed since the pandemic, in parallel with result of this study [8], approximately 62% of Parkinson's patients without a history of COVID-19 had higher exercise times (about 20 min per a day) than others, while the deterioration in non-motor symptoms of those was lower. The lower incidence of non-motor symptoms in individuals with Parkinson's disease who exercise regularly may be attributed to the positive effects of physical activity on neuroplasticity, dopamine regulation, and general brain health. These factors contribute to improved motor function, cognitive abilities, and emotional health, potentially reducing the development and severity of non-motor symptoms such as depression, anxiety, and sleep disorders [37].

Pulmonary system problems that are frequently seen in Parkinson's patients include chest wall rigidity/abnormalities, posture disorders, respiratory muscle weakness, central respiratory dysfunction, impaired respiratory sensation, and dyspnea as a side effect of medications such as levodopa [2]. These impairments lead to reduced chest wall mobility, decreased lung volumes and capacities, and increased difficulty in performing breathing activities [2]. In our study, although the respiratory depth was found to be similar in the groups, the difference value of the chest circumference measurement from the subcostal level in individuals with Parkinson's disease who had COVID-19 was found to be lower than the others. When the literature was examined, no study investigating the thoracic cage mobility in individuals with Parkinson's disease who had COVID-19 during the pandemic period has yet been found. The result of an online study, which is that motor symptoms are more pronounced in Parkinson's patients with COVID-19 [9], is consistent with the result of our study of a significant decrease in subcostal breathing in Parkinson's patients with COVID-19. It was also observed that Parkinson's patients who had COVID-19 were more likely to smoke (5.9% vs. 1.6%) and to have the histories of heart (20% vs. 8.2%) and lung (14% vs. 8.1%) diseases in the study of Fox Insight [9]. In contrast to these results, in our study, smoking and alcohol use and chronic disease history were similar in groups. Symptoms may worsen in individuals with Parkinson's disease exposed to infections such as COVID-19 [38]. The decline in respiratory function observed in individuals with Parkinson's disease who have any infectious disease may be attributed to systemic inflammation, altered dopaminergic signaling, impaired drug absorption, or changes in drug pharmacokinetics [39]. A study proved that breathing exercises applied regularly to Parkinson's patients increase chest mobility by increasing the difference between deep inspiration and deep expiration in chest circumference measurements taken from the axillary, epigastric and subcostal regions, as well [40]. For this reason, rehabilitation programs including breathing exercises and trunk mobility for Parkinson's patients can be adapted to the specific needs of each patient through online services in cases of high risk of infection such as COVID-19 [10, 40].

The PCEF measurement can predict the risk of aspiration or impairments in respiratory muscles (trunk muscles etc.) and reflects disease severity in individuals with Parkinson's disease [41]. It was found that young individuals who had been infected with COVID-19 in the last 6 months had weakness in the respiratory and upper extremity peripheral muscles and similar values in pulmonary function test compared to controls who had not had COVID-19 [16, 42, 43]. Similar to the results of these studies, in our study, it was observed that the PCEF value did not differ between the groups. As in other studies, the individuals with Parkinson's disease who had

COVID-19 in our study were individuals who had been diagnosed with COVID-19 at least 12 weeks ago and had recovered. However, although the individuals in our study were older and had a neurological disease, unlike the population in these studies [16, 42, 43], the preservation of the PCEF value in individuals with Parkinson's disease can be attributed to the fact that approximately 25 months have passed since COVID-19 contact and that they had mild COVID-19. Likewise, the results of a study that included a larger sample, a wider age range, and more severe COVID-19 cases (those that developed acute respiratory distress syndrome (ARDS) are striking [6]. Individuals with ARDS who developed pneumonia had lower oxygen saturation and total lung capacity, and higher dyspnea rates [6]. The change in pulmonary functions following contact to COVID-19 appears to be more pronounced in patients who develop ARDS and require invasive mechanical ventilation [6]. Pulmonary function deterioration is greater in individuals with Parkinson's disease compared to healthy individuals, and this deterioration increases as the severity of Parkinson's disease increases [4]. Considering that both the diagnosis of COVID-19 has negative effects on the respiratory system and respiratory system problems such as cough strength insufficiency are important disorders seen in patients with Parkinson's disease, we recommend regular monitoring of lung functions and chest mobility in these patients. As known, regular exercise can improve ventilatory parameters in Parkinson's disease patients [44]. Therefore, individual exercise planning may be recommended to improve the decreased ventilation in the lung bases, especially in Parkinson's disease patients who had COVID-19.

In people exposed to COVID-19 infection, the SARS-CoV-2 virus leads to a decrease in peripheral and respiratory muscle strength by causing an increase in caspase 3, which is suggestive of muscle apoptosis [15]. It is also known that there is a linear relationship between increased endothelin-1 synthesis and sarcopenia [45]. Our results show that most individuals with Parkinson's disease (disease duration of approximately 2–3 years) have muscle weakness regardless of COVID-19 history, but those who had COVID-19 have a greater decrease in upper extremity muscle strength, even though approximately 1 year has passed since the infection. In line with the results of our study, a study showed that 39.6% of adult patients who had COVID-19 had weakness in hand grip muscles and 35.4% had weakness in quadriceps femoris muscle [18]. Additionally, peripheral muscle weakness was found to be more evident in individuals with moderate COVID-19 compared to those with mild COVID-19 [18]. In young adults who had at least 6 months of post-COVID-19, respiratory and shoulder abduction muscle strength were found to be lower compared to controls who had not been exposed to COVID-19 [16]. The fact that muscle weakness continues to be seen days to months after COVID-19 may be attributed to the systemic effect of the viral infection, muscle weakness and deconditioning due to long-term underlying chronic disease, and other combined effects of COVID-19, including decreased physical activity during the recovery process. The basis of these destructive effects of COVID-19 is myofibrillar destruction, muscle degradation and muscle apoptosis [15]. Therefore, it is recommended that individuals with Parkinson's disease be evaluated regularly and in detail, considering their advanced age, COVID-19 history, and related disorders, and that they be directed to rehabilitation programs in line with their identified needs.

It is a striking finding in our study that left-hand grip strength was found to be significantly lower in individuals with Parkinson's disease who had a history of COVID-19, without any difference in the right-hand grip strength, compared to individuals without a history of COVID-19. This asymmetric finding may be partly explained by hand dominance, as all Parkinson's patients included in our study were right-hand dominant, and typically the right-dominant limb is stronger and has higher functional reserve [46]. Furthermore, Parkinson's disease itself is a disease characterized by asymmetrical motor symptom onset and progression, often starting and remaining more severe on one side of the body [47]. However, since no significant difference was found between our groups regarding the side of disease onset, this may not have contributed to the observed asymmetry in grip strength. Variability in fatigue perception across repeated measurements may be another possible contributing factor, particularly in patients with neurological motor disorders such as Parkinson's disease. Patients with Parkinson's disease may experience fatigue due to low dopamine, as well. Therefore, familiarization, depending on how it is performed, may result in greater fatigue before the tests are performed [48]. It is also plausible that COVID-19-related muscle deconditioning or inflammatory effects may have had an uneven impact depending on pre-existing lateralized weakness or disuse. Future studies that include detailed data on hand dominance, symptom laterality, and side-specific muscle strength in individuals with Parkinson's disease who had COVID-19 may help clarify the mechanisms underlying this asymmetry.

Parkinson's patients were vulnerable to physical inactivity and inactivity-related adverse health outcomes due to social distancing recommendations during the COVID-19 pandemic [5]. During the first wave of the pandemic, Leavy et al. found that individuals with Parkinson's disease took an average of approximately 5900 steps per day, and 40% of these individuals took less than

5000 steps per day [5]. In line with the results of this study, the average daily step count of the individuals in our study was approximately 6000 steps, and individuals in both groups were physically active. Although individuals with Parkinson's disease in our study were assessed several years after the first wave of the pandemic, the fact that the average daily step count of the individuals included in our study was over 4200 steps, regardless of their COVID-19 history, also coincides with the recommendations of physical activity guidelines to be active [33]. On the other hand, studies conducted on Parkinson's patients during the pandemic period have stated that the majority of these individuals reduced their physical activity compared to before the pandemic and these individuals were less active [10, 12, 13]. During the COVID-19 pandemic, a decrease in physical activity was observed in Parkinson's patients due to lack of motivation and social restrictions. We recommend regular physical activity monitoring in these patients, not only during the pandemic period, to prevent a sedentary lifestyle that may worsen motor and mood symptoms.

This study has several limitations that should be acknowledged. First, due to its cross-sectional design, causal inferences between a history of COVID-19 and the observed impairments in non-motor symptoms, abdominal breathing, peripheral muscle strength, daily step count, and QOL in individuals with Parkinson's disease cannot be made. Although a significant amount of time has passed since the COVID-19 infection, the temporal sequence between COVID-19 contact and outcomes remains unclear. It is also possible that unmeasured confounding factors such as differences in disease severity, comorbidities, or access to rehabilitation services may have influenced the results. Therefore, these findings should be interpreted with caution, and prospective longitudinal studies are needed to further investigate potential causal relationships. Another limitation may be that all participants were recruited from a single outpatient neurology clinic. This may limit the generalizability of our findings to other populations, such as patients in different geographic regions or healthcare systems. Finally, another limitation is the inability to reach the targeted number of individuals with Parkinson's disease who have had COVID-19. However, since the literature suggests the probability of COVID-19 in individuals with Parkinson's disease is approximately 1% [9] and patients were recruited from a single center, this number may not have been reached. Further multicenter studies are needed to confirm the findings in more diverse cohorts.

Conclusion

In our study, it was found that Parkinson's patients with a COVID-19 history had increased severity of non-motor symptoms, decreased abdominal breathing, weaker peripheral muscle strength, a tendency to decrease in daily step count and poorer QOL compared to controls without any COVID-19 history, despite a long time having passed since COVID-19 contact. The superior aspect of our study compared to the studies in literature is that these results were obtained by comparing them with controls who had not had COVID-19. However, due to the cross-sectional design of this study, causal relationships between prior COVID-19 and the observed outcomes cannot be established. On the other hand, it was also determined that COVID-19 history did not affect upper and lower chest breathing and cough strength in individuals with Parkinson's disease. Therefore, it is important to carefully assess both motor and non-motor symptoms of Parkinson's patients, especially those with a history of COVID-19 and to encourage them to exercise. Rehabilitation practices including deep breathing exercises, progressive resistance exercises, and physical activity counseling may be considered for Parkinson's patients with a history of COVID-19.

Abbreviations

COVID-19	SARS-CoV-2
QOL	Quality of life
MHYS	Modified hoehn and yahr scale
MDS-UPDRS	Movement disorders society unified parkinson's disease rating scale
PCEF	Peak cough expiratory flow
kgF	Kilogram-force
PDQ-39	Parkinson's disease quality of life questionnaire
n	Frequency
%	Percentage
IQR	Interquartile range
×	Mean
sd	Standard deviation
95%CI	95% Confidence interval
ARDS	Acute respiratory distress syndrome

Supplementary Information

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Supplementary material 1.

Supplementary material 2.

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Authors' contributions

MŞ and GB designed the study; MŞ, GB, YÜ and ÖÇÖ conducted the study, MŞ and YÜ collected the data; MŞ and GB analyzed the data; MŞ, GB, YÜ and ÖÇÖ contributed to the writing; GB, YÜ and ÖÇÖ reviewed critically. All authors read and approved the final manuscript.

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Data availability
The data that supports the findings of this study are available from the corresponding author upon reasonable request. The data is not publicly available due to privacy or ethical restrictions.

Declarations

Ethics approval and consent to participate
Izmir Democracy University Non-Invasive Clinical Research Ethics Committee approved this study on 29.03.2023 with decision number 2023/04 – 01. Informed consent forms were obtained from all participants.

Consent for publication
Our participants gave written informed consent for the publication of their personal or clinical information and descriptive images with eyes closed in this study.

Competing interests
The authors declare no competing interests.

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