

Original Article

Post-COVID Pulmonary Function Test Evaluation

Emine Afsin¹, Muhammed Emin Demirkol²

¹Department of Chest Diseases, Abant İzzet Baysal University Hospital, Bolu, Turkey ²Department of Internal Medicine, Abant İzzet Baysal University Hospital, Bolu, Turkey

Cite this article as: Afsin E, Demirkol ME. Post-COVID pulmonary function test evaluation. Turk Thorac J. 2022;23(6):387-394.

Abstract **OBJECTIVE:** Since the lung is the most affected organ by COVID-19 disease, we aimed to evaluate the pulmonary function test, presence of hypoxemia, and Post-COVID-19 Functional Status Scale in 3- to 6-month post-COVID period.

MATERIAL AND METHODS: Post-COVID-19 Functional Status Scale, pulse oxygen saturation, and pulmonary function test were evaluated in 67 outpatients/inpatients after 3-6 months following COVID-19 (positive reverse transcription-polymerase chain reaction on nasopharyngeal swab) disease. Pre-COVID pulmonary function test parameters were available in 33 patients, and these were compared with post-COVID pulmonary function test parameters.

RESULTS: We found 20.9% (14 patients) restrictive and 11.9% (8 patients) obstructive patterns in pulmonary function test. Of those with forced vital capacity < 80%, 53.3% were patients without known lung diseases. When pulmonary function test values before and after COVID-19 were compared, only a loss of 130 mL in forced expiratory volume in 1 second was determined (P = .005). About 65.4% of the patients with dyspnea were in the group without a lung disease (P = .002) and 66.7% of patients with forced expiratory volume in 1 second and forced vital capacity of <80% had dyspnea complaint (P = 0.048, P = 0.012). Oxygen saturation was lower in patients with lung disease (P = .012) and was significantly lower in patients with forced vital capacity < 80% (P = .023). No correlation was found between Post-COVID-19 Functional Status Scale and pulmonary function test parameters (P > .05). Smoking, hospitalization, oxygen support, and the severity of computed tomography involvement did not impact pulmonary function test.

CONCLUSION: In post-COVID patients, the major disorder in the respiratory function test was determined as a restriction. However, advanced tests such as lung volumes and carbon monoxide diffusing capacity (DLCO) measurement and high-resolution lung tomography are needed to differentiate in terms of physical functional limitation or parenchymal fibrosis.

 KEYWORDS: COVID-19, pulmonary function test, Post-COVID-19 Functional Status Scale

 Received: October 7, 2021
 Accepted: July 23, 2022
 Publication Date: September 12, 2022

INTRODUCTION

Since the World Health Organization declared coronavirus disease 2019 (COVID-19) a pandemic on March 11, 2020, approximately 20% of infected patients required hospitalization and 6% need to be monitored in intensive care and invasive respiratory support.¹ Epidemiological reports have shown that 8.2% of total cases are admitted with rapid and progressive respiratory failure, similar to acute respiratory distress syndrome (ARDS).² Lungs are the organs most affected by COVID-19, with different pathophysiological events including extensive alveolar epithelial destruction, hyaline membrane formation, capillary damage and bleeding, alveolar septal fibrous proliferation, and pulmonary consolidation.³ COVID-19 may cause lung fibrosis and/or pulmonary hypertension.^{4,5} These results suggest that lung injury should be evaluated even in discharged patients.

Pulmonary function tests (PFT), such as spirometry, diffusion test, and lung volumes, are most commonly used to evaluate lung functions.⁶ Recent clinical guidelines recommend that patients with severe pneumonia should be followed up with PFT 12 weeks after discharge.⁷ Restrictive disorder and minor airway dysfunction, which may be permanent and not related to disease severity, were found in PFT.⁸ Mo et al³ reported restrictive respiratory disorder and decreased diffusion capacity, associated with the severity of the disease in patients during discharge. As with previous coronavirus infections such as severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome , it is thought that patients may experience permanent deterioration in respiratory functions for months or even years after discharge.^{9,10}

In previous coronavirus infections, muscle weakness, lethargy, pain, depressive mode, anxiety, and various degrees of deterioration in the quality of life were also observed after discharge.¹¹⁻¹³ A new "Post COVID-19 Functional Status Scale (PCFS)" is recommended in the COVID-19 pandemic and suggested that it could be used to evaluate the functional sequelae of COVID-19.

Our study aimed to retrospectively investigate the development of restrictive or obstructive patterns in patients after polymerase chain reaction (PCR)-positive COVID-19 infection and to evaluate the functional status of patients.

Corresponding author: Emine Afsin, e-mail: emineafsin@yahoo.com



MATERIAL AND METHODS

In Pulmonary Diseases clinic between January 2021 and March 2021, among the outpatients or inpatients who were treated and who had passed 3-6 months after their COVID-19 disease (positive reverse transcription-PCR on nasopharyngeal swab), 67 patients for whom anamnesis, PCFS, PFT (results for the pre-COVID-19 period were also obtained in 33 patients), and computed tomography (CT) data were available in the files were included in the study. Demographic, radiological data, PFT parameters, PCFS grade, comorbidities, and oxygen therapy needs of the patients were recorded. Post-COVID-19 Functional Status Scale was graded from 0 to 4.14 Spirometry tests were performed following the guidelines of the American Thoracic Society/European Respiratory Society. Disposable bacteria and virus filters were used for each patient during PFT. Using Global Lung Function Initiative 2012 reference values, forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) were found to be 80%, FEV1/FVC was 70%, and maximal mid-expiratory flow (MMEF) was 65%. Approval was sought from Abant İzzet Baysal University Ethics Committee (date: July 27, 2021, no: 2021/203), and written informed consent was obtained from all participants enrolled in the study.

Statistical Method

The analysis of the data obtained as a result of the research was performed using the Statistical Package for Social Sciences version 20.0 software (IBM Corp.; Armonk, NY, USA). Descriptive statistical methods (frequency, arithmetic mean, standard deviation, median, minimum, maximum, and crosstabs) were used, and the compliance to normal distribution was evaluated using Kolmogorov-Smirnov test. Independent sample t-test was used for 2 independent groups by comparing the arithmetic means of the normally distributed groups. A comparison of 2 dependent groups was evaluated using paired sample *t*-test. The Mann–Whitney U test compared 2 independent groups by the median values of the groups that did not show normal distribution. A comparison of 2 dependent groups was performed using Wilcoxon test. The chi-square test examined the relationship between categorical variables. Statistical significance level was accepted as a *P*-value of <.05.

The relationship between post-COVID pulmonary function test parameters and independent variables was examined by linear regression analysis (enter method). In order to detect the multiple correlations problem, the limits of variance inflation factor < 10, tolerance < 2, and Durbin–Watson < 2.5

MAIN POINTS

- Major pulmonary function test disorder was found to be a restriction in those who had dyspnea in the 3- to 6-month post-COVID period.
- However, since this restriction may be associated with physical functional limitation, tests such as lung volume measurement, DLCO, and high-resolution computed tomography are needed for parenchymal diseases.
- Post-COVID-19 Functional Status Scale was not found to be effective in predicting respiratory dysfunction.

were checked, and the conformity of the residuals to the normal distribution was examined based on the skewness-kurtosis ± 1 range.

RESULTS

In total, 55.2% of the patients were male, and in men, the mean age was higher, the need for hospitalization and oxygen support was higher, and the oxygen saturation in the control visit was lower (Table 1). Dyspnea (38.8%), weakness–fatigue (13.4%), myalgia (4.5%), cough (3%), and taste–smell disorder (1.5%) were the most common symptoms. The complaints of fatigue were significantly higher in women than in men (Table 1).

When the patients were examined in terms of underlying lung disease (asthma, chronic obstructive pulmonary disease, interstitial lung disease), those with lung disease were found to be older, and their SpO₂ was lower (P = .012) (Table 2). SpO₂ was significantly lower in patients with FVC < 80% (P = .023, Table 3).

PCFS was categorized as 0 in 43.3%, 1 in 47.8%, and 2 in 9% of patients. There was no significant difference between male and female patients (Table 1).

Of the patients with dyspnea, 65.4% were in the group without lung disease, and this difference was statistically significant (P = .002). Although all patients with fatigue had no previous lung disease, the difference was not statistically significant (P = .336). Of those with FVC < 80%, 53.3% were patients without lung disease. Of those with FEV1 < 80%, 58.3% were those with lung disease, but the difference was not statistically significant as the results did not meet the chi-square assumption. Thirty-three of the patients had PFT records from the pre-COVID period in the hospital data system. When the pre-and post-COVID PFT values of 33 patients were compared using the Wilcoxon test, a statistically significant decrease of 130 mL was determined in FEV (P = .005) (Table 4).

When the factors affecting PFT parameters were examined, FEV1, FVC, and MMEF were significantly lower in the elderly. Forced expiratory volume in 1 second was lower in patients with lung disease, and MMEF was lower in patients without lung disease, but the difference did not meet the test's assumptions. Forced vital capacity was lower in the group without lung disease (P = .001). Forced expiratory volume in 1 second and FVC values were found below normal in patients with dyspnea (Table 3).

In the post-COVID 3- to 6-month period, the FEV1% variable was significant for the age and lung disease regression model and was lower in those with advanced age and lung disease (Table 5), as demonstrated by scatter plots (Figure 1). For the FVC% variable, the variables included in the model were not found to be significant. Forced expiratory volume in 1 second/FVC% was significant for the age regression model, but this value was lower in older age groups (Table 5), as indicated with scatter plots (Figure 2). The MMEF% variable was significant only for the lung disease regression model and was lower in those with lung diseases (Table 5).

	Female (n = 30)	Male (n = 37)	Total (n = 67)	Р
Age	45.47 ± 10.7	53.59 ± 15.81	49.95 ± 14.26	.042
Smoking status				
Non-smoker	24 (80%)	15 (40.5%)	39 (58.2%)	<.00
Ex-smoker	1 (3.3%)	17 (45.9%)	18 (26.9%)	
Smoker	5 (16.7%)	5 (13.6%)	10 (14.9%)	
Pulmonary disease				
Yes	5 (16.7%)	6 (16.2%)	11 (16.4%)	.608
No	25 (83.3%)	31 (83.8%)	56 (83.6%)	
CT involvement				
CT not performed	19 (63.3%)	15 (40.6%)	34 (50.7%)	.174
<50% involvement	4 (13.3%)	9 (24.3%)	13 (19.4%)	
>50% involvement	7 (23.3%)	13 (35.1%)	20 (29.9%)	
Symptoms				
Dyspnea	10 (33.3%)	16 (43.2%)	26 (38.8%)	.283
atigue	7 (23.3%)	2 (5.4%)	9 (13.4)	.037
Faste-smell disorder	1 (3.3%)	0 (0%)	1 (1.5%)	.448
Myalgia	2 (6.7%)	1 (2.7%)	3 (4.5%)	.421
Cough	1 (3.3%)	1 (2.7%)	2 (3%)	.699
Need hospitalization	9 (30%)	21 (56.8%)	30 (44.8%)	.029
No	21 (70%)	37 (43.2%)	37 (55.2%)	
Need for O ₂ support	9 (30%)	21 (56.8%)	30 (44.8%)	.029
No	21 (70%)	16 (43.2%)	37 (55.2%)	
EV1 < 80%	5 (16.7%)	7 (18.9%)	12 (17.9%)	.811
$EV1 \ge 80\%$	25 (83.3%)	30 (81.1%)	55 (82.1%)	
EVC < 80%	6 (20%)	9 (24.3%)	15 (22.4)	.673
$VC \ge 80\%$	24 (80%)	28 (75.7%)	52 (77.6%)	
FEV1/FVC < 70%	6 (20%)	2 (24.3%)	8 (11.9%)	.073
FEV1/FVC \geq 70%	24 (80%)	35 (75.7%)	59 (88.1%)	
MMEF < 65%	12 (40%)	8 (21.6%)	20 (29.8%)	.102
$MMEF \ge 65\%$	18(60%)	29(78.4%)	47(70.1%)	
PCFS				
)	11 (36.7%)	18 (48.6%)	29 (43.3%)	.616
1	16 (53.3%)	16 (43.2%)	32 (47.8%)	
2	3 (10%)	3 (8.1%)	6 (9%)	
SpO ₂	97 (95-99)	97 (76-99)	97 (76-99)	.037

Table 1. Demographic, Clinical, and PFT Evaluation of Patients According to Gende

CT, computed tomography; SpO₂ oxygen saturation measured by pulse oximetry; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; MMEF, maximal mid-expiratory flow; PCFS, Post-COVID-19 Functional Status Scale; PFT, pulmonary function test. Bold values indicate $P \le .05$.

There were 14 patients with FEV1/FVC above 70% and FVC and FEV1 below 80%, and the restrictive pattern rate was 20.9%, while FEV1/FVC was <70% in 8 patients, and the obstructive pattern rate was 11.9%.

DISCUSSION

Different degrees of destruction in the alveolar structure and pulmonary interstitial fibrosis were observed in the autopsy series of COVID-19 patients.¹⁵ Data published so far have

investigated the pulmonary function of patients recovering from COVID-19 at discharge,³ a few weeks after discharge,⁵ and after 6 weeks of pulmonary rehabilitation,¹⁶ and between 60 and 100 days after symptom onset.¹⁷ No data on longterm follow-up are yet available, except for 1 study¹⁸ comparing post-COVID tenth-week and sixth-month. The British Thoracic Society guide recommends PFT at the third month after discharge, especially for those with suspected interstitial disease.⁷ Our study is critical in terms of evaluating the post-COVID third- to sixth-month period.

	With Previous Pulmonary Disease (n = 11)	With No Previous Pulmonary Disease (n = 56)	Total Patients $(n = 67)$	Р
Age	58 (24-87)	47 (20-89)	48 (20-89)	.025
CT involvement				
CT not performed	4 (11.8%)	30 (88.2%)	34 (50.7%)	.057
<50% involvement	5 (38.5%)	8 (61.5%)	13 (19.4%)	
>50% involvement	2 (10%)	18 (90%)	20 (29.9%)	
Hospitalization need				
Yes	6 (20%)	24 (80%)	30 (44.8%)	.523
No	5 (13.5%)	32 (86.5%)	37 (55.2%)	
Need for O_2 support				
Yes	6 (20%)	24 (80%)	30 (44.8%)	.523
No	5 (13.5%)	32 (86.5%)	37 (55.2%)	
Dyspnea				
Yes	9 (34.6%)	17 (65.4%)	26 (38.8%)	.002
No	2 (4.9%)	39 (95.1%)	41 (61.2%)	
Fatigue				
Yes	0 (0%)	9 (100%)	9 (13.4%)	.336
No	11 (19%)	47 (81%)	58 (86.6%)	
FEV1 < 80%	7 (58.3%)	5 (41.7%)	12 (17.9%)	<.001
$EV1 \ge 80\%$	4 (7.3%)	51 (92.7%)	55 (82.1%)	
EVC < 80%	7 (46.7%)	8 (53.3%)	15 (22.4%)	.001
$VC \ge 80\%$	4 (7.7%)	48 (92.3%)	52 (77.6%)	
FEV1/FVC < 70%	3 (37.5%)	5 (62.5%)	8 (11.9%)	.117
FEV1/FVC \geq 70%	8 (13.6%)	51 (86.4%)	59 (88.1%)	
MMEF < 65%	8 (40%)	12 (60%)	20 (29.9%)	.002
MMEF $\geq 65\%$	3 (6.4%)	44 (93.6%)	47 (70.1%)	
PCFS				
)	1 (3.4%)	28 (96.6%)	29 (43.3%)	.034
1	9 (28.1%)	23 (71.9%)	32 (47.8%)	
2	1 (16.7%)	5 (83.3%)	6 (9%)	
SpO ₂	96 (76-98)	97 (92-99)	97 (76-99)	.012

*Does not meet the chi-square test assumptions.

CT, computed tomography; SpO2, oxygen saturation measured by pulse oximetry; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; MMEF, maximal mid-expiratory flow; PCFS, Post-COVID-19 Functional Status Scale; PFT, pulmonary function test. Bold values indicate $P \leq .05$.

Bold values indicate $P \le .05$.

In severe acute respiratory syndrome, persistent anomalies in respiratory functions have been reported in 25%-40% of patients 1 year after discharge.^{10,19} In a meta-analysis, 15% restrictive and 7% obstructive patterns were reported in COVID-19.²⁰ Our study determined the restrictive pattern to be 20.9% and the obstructive pattern to be 11.9% in 3- to 6-month post-COVID period. Chronic obstructive pulmonary disease was the underlying lung disease in 2 of 8 patients for whom an obstructive pattern was found. Some of the patients (33 patients) had PFT from the pre-COVID period, and when PFT parameters were compared, 130 mL loss was found only in FEV1 (P = .005), while no significant difference was found in FVC and FEV1/FVC (P = .454, P = .066). In severe COVID-19, oxygen toxicity and ventilator-induced lung injury lead to fibrosis. Patients who develop post-COVID fibrosis have extensive radiological lung involvement and therefore require high concentrations of oxygen for a long time, often during the acute phase of their illness. Prolonged exposure to high concentrations of oxygen increases the production of oxygen-derived free radicals that can damage the pulmonary epithelium.²¹ In the study by Masson et al⁵ involving 45 post-COVID patients, they found a higher rate of PFT abnormality in patients with severe disease. However, in SARS, no significant difference was observed in FVC and DLCO when inpatients and non-inpatients were compared.²² In our study, the severity of CT involvement, the need for oxygen support, and the history of hospitalization were not associated with PFT abnormalities.

	FEV1 < 80%, n = 12	FEV1 ≥ 80%, n = 55	FVC < 80%, n = 15	FVC ≥ 80%, n = 52	FEV1/FVC < 70%, n = 8	FEV1/FVC ≥ 70%, n = 59	MMEF < 65%, n = 20	MEEF ≥ 65%, n = 47	
Age (n = 67)	61 (42-87)	47 (20-89)	59 (32-87)	46.5(20-89)	49 (36-60)	48 (20-89)	53 (36-87)	47(20-89)	
	<i>P</i> = .001		P = .008		<i>P</i> = .961		<i>P</i> =	P = .025	
Smoking status									
Non-smoker	5 (41.7%)	34 (61.8%)	7 (46.7%)	32 (61.5%)	4 (50%)	35 (59.3%)	9 (45%)	30 (63.8%)	
Ex-smoker	5 (41.7%)	13 (23.6%)	6 (40%)	12 (23.1%)	2 (25%)	16 (27.1%)	7 (35)	11 (23.4%)	
Smoker	2 (16.7%)	8 (14.5%)	2 (13.3)	8 (15.4)	2 (25%)	8 (13.6%)	4 (20%)	6 (12.8%)	
	P =	.385	<i>P</i> = .424		<i>P</i> = .693		<i>P</i> = .359		
Had pulmonary disease	7 (58.3%)	4 (7.3%)	7 (46.7%)	4 (7.7%)	3 (37.5%)	8 (13.6%)	8 (40%)	3 (6.4%)	
No	5 (41.7%)	51 (92.7%)	8 (53.3%)	48 (92.3%)	5 (62.5%)	51 (86.4%)	12 (60%)	44 (83.6%)	
	<i>P</i> <	.001*	<i>P</i> =	.001	P =	.117	<i>P</i> =	.002*	
Hospitalization nee	ed								
Yes	8 (66.7%)	22 (40%)	9 (60%)	21 (40.4%)	1 (12.5%)	29 (49.2%)	8 (40%)	22 (73.3%)	
No	4 (33.3%)	33 (60%)	6 (40%)	31 (59.6%)	7 (87.5%)	30 (50.8%)	12 (60%)	25 (53.2)	
	P =	.092	<i>P</i> = .178		<i>P</i> = .066		<i>P</i> = .608		
CT involvement									
CT not performed	4 (33.3%)	30 (54.5%)	5 (33.3%)	29 (55.8%)	6 (75%)	28 (47.5%)	11 (55%)	23 (48.9)	
<50% involvement	3 (25%)	10 (18.2%)	4 (26.7%	9 (17.3%)	1 (12.5%)	12 (20.3%)	3 (15%)	10 (21.3%)	
>50% involvement	5 (41.7%)	15 (27.3%)	6 (40%)	14 (26.9%)	1 (12.5%)	19 (32.2%)	6 (30%)	14 (29.8%)	
	P =	.408	<i>P</i> =	.309	P =	.334	P =	.824	
The need for O_2 su	pport								
	8 (66.7)	22 (40%)	9 (60%)	21 (40.4%)	1 (12.5%)	29 (49.2%)	8 (40%)	22 (46.8%)	
No	4 (33.3%)	33 (60%)	6 (40%)	31 (59.6%)	7 (87.5%)	30 (50.8%)	12 (60%)	25 (53.2%)	
	P =	.092	<i>P</i> = .178		<i>P</i> = .066		<i>P</i> = .608		
Dyspnea									
Yes	8 (66.7%)	18 (32.7%)	10 (66.7%)	16 (30.8%)	4 (50%)	22 (37.3%)	10 (50%)	16 (34%)	
No	4 (33.3%)	37 (67.3%)	5 (33.3%)	36 (69.2%)	4 (50%)	37 (62.7%)	10 (50%)	31 (66%)	
	P =	.048	<i>P</i> = .012		<i>P</i> = .489		<i>P</i> = .220		
PCFS									
0	3 (25%)	26 (47.3%)	4 (26.7%)	25 (48.1%)	2 (25%)	27 (45.8%)	5 (25%)	24 (51.1%)	
1	8 (66.7%)	24 (43.6%)	8 (53.3%)	24 (46.2%)	6 (75%)	26 (44.1%)	14 (70%)	18 (38.3%)	
2	1 (8.3%)	5 (9.1%)		3 (5.8%)		6 (10.2%)	1 (5%)	5 (10.6%)	
	<i>P</i> =	.328	<i>P</i> = .136		<i>P</i> = .231		<i>P</i> = .059		
SpO ₂	96 (76-99)	97 (92-99)		97 (92-99)		97 (76-99)		97 (90-99)	
. 2		.154		.023		.013	P =		

Table 3. Factors Affecting Post-COVID Pulmonary Function Test Parameter

CT, computed tomography; SpO2, oxygen saturation measured by pulse oximetry; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; MMEF, maximal mid-expiratory flow; PCFS, Post-COVID-19 Functional Status Scale; PFT, pulmonary function test. Bold values indicate $P \le .05$.

Fatigue was reported in at least one-third of patients in 2 studies with a follow-up period of 18 months²³ and 40 months²⁴ in previous coronavirus pandemics. Fatigue and dyspnea have been reported in 30%-60% of individuals in the post-COVID period.^{17,25} In our study, dyspnea (38.8%) and weakness– fatigue (13.4%) were the most common complaints in the post-COVID 3- to 6-month follow-up. 65.4% of the patients with dyspnea were in the group without a lung disease, and this difference was statistically significant (P = .002). Although all patients with fatigue were without lung disease, it was not statistically significant. Of those with FVC < 80%, 53.3% were patients without lung disease (P = .001).

Table 4. The Comparison of the Pre- and Post-COVID-19 PFT Parameters of 33 Patients with PFT Available in the Pre-COVID-19 Period

	FEV1*	FVC**	FEV1/FVC*
Pre-COVID	2.83 (1.04-4.83)	3.62 ± 0.95	84.6 (62.7-106.0)
Post-COVID	2.73 (1.00-5.00)	3.57 ± 1.01	82.0 (63.0-97.0)
Р	.005	.454	.066

*Wilcoxon test: **Paired sample t-test.

FVC, forced vital capacity; FEV1, forced expiratory volume in

Bold values indicate $P \leq .05$.

In patients who recovered from ARDS and described dyspnea, long-term physical function limitation was observed disproportionate to the degree of pulmonary dysfunction.²⁶ The results we obtained suggest non-pulmonary factors such as post-COVID fibrosis or critical illness neuromyopathy. Quarantine conditions and isolated hospitalization may also cause muscle weakness. Findings of dyspnea disproportionate to respiratory dysfunction have been reported in many COVID-19 survivors, even those with milder disease. It is unknown whether post-COVID-19 symptoms are more closely related to physical dysfunction than permanent lung function decrease.²⁷

Skeletal muscle damage was observed during acute disease in 19% of patients with COVID-19.²⁸ Pulmonary function test

Table 5. Elifeat Regression Analysis for Fost-COVID IT Francheters								
	FEV1 %		FVC %		FEV1/FVC %		MMEF %	
	B**	Sig	B**	Sig	B**	Sig	B *	Sig
Constant	115.335	0.183	4.752	0.961	178.186	<0.001*	220.530	0.215
Age	-0.468	0.032*	-0.410	0.097	-0.265	0.020*	-0.650	0.143
Smoking	2.573	0.388	3.490	0.306	-1.328	0.394	6.127	0.319
Pulmonary disease	-18.940	0.004*	-10.419	0.151	-5.697	0.087	-37.919	0.005*
СТ	3.962	0.580	1.325	0.871	3.918	0.296	22.458	0.130
O2 support	2.847	0.229	-0.049	0.985	1.417	0.251	6.314	0.196
Dyspnea	-3.912	0.501	-3.284	0.620	-3.287	0.280	-8.412	0.482
PCFS	1.759	0.683	1.522	0.757	-0.163	0.942	-2.011	0.820
SpO ₂	0.010	0.990	1.131	0.243	-0.856	0.055	-1.126	0.517
Р	.00	2*	.01	9*	.03	0*	.00	6*
Model R ²	0.3	37	0.2	59	0.2	43	0.2	95
Durbin-Watson	2.0	58	1.8	55	1.8	83	1.9	63
Residuals	±	1	±	1	±	1	±	1

*Statistically significant; **Unstandardized coefficients.

CT, computed tomography; SpO2, oxygen saturation measured by pulse oximetry; PCFS, Post-COVID-19 Functional Status Scale; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; MMEF, maximal mid-expiratory flow. Bold values indicate $P \le .05$.

 $\mathbf{r}_{\mathbf{r}} = \mathbf{r}_{\mathbf{r}} +$

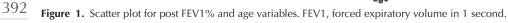


 Table 5. Linear Regression Analysis for Post-COVID PFT Parameters

¹ second; PFT, pulmonary function test.

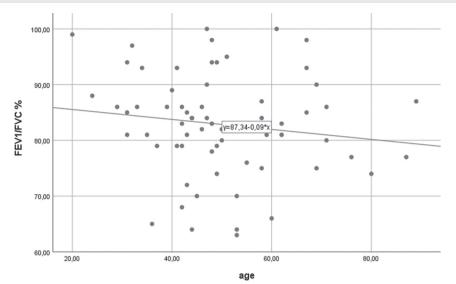


Figure 2. Scatter plot for FEV1/FVC % and age variables. FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second.

6-8 weeks after hospital discharge following SARS revealed a mild or moderate restrictive pattern consistent with muscle weakness in 6%-20% of patients.²⁹ In our study, FEV1 and FVC values were found to be below 80% in patients with dyspnea complaints. However, since this restriction was determined more frequently in the group without lung disease who also had symptoms of weakness–fatigue, it raises the question, "Is the restriction due to loss of physical function?" Although Hall et al³⁰ physicians did not identify any radiological or physiological abnormalities in 60% of 200 patients, they reported persistent subjective symptoms, and this situation is called "post-COVID-19 syndrome."

In our study, SpO₂ was significantly lower in patients with FVC < 80% and those with lung diseases (P = .023 and P =.012, respectively). When the literature is reviewed, we could not find any study on post-COVID hypoxemia. Hypoxemia may occur in both fibrotic disorders, obstructive pulmonary diseases, and neuromuscular disorders.³¹

The validity of PCFS has been tested, and it was reported that it could be used to refer patients to specialist clinics or rehabilitation programs.³² Post-COVID-19 Functional Status Scale can be used after discharge from the hospital, 4-8 weeks after discharge, and in the 6th month.¹⁴ In 444 patients who recovered from COVID-19, PCFS was reported as grade 0 in 20% of cases, grade 1 in 63.1%, grade 2 in 14.4%, grade 3 in 2%, and grade 4 in 0.5%.33 In our study, PCFS was categorized as grade 0 in 43.3%, grade 1 in 47.8%, grade 2 in 9% of patients, and no patients were grade 3 or 4. There was no significant difference between male and female patients (Table 1). It was reported that PCFS is affected by age, gender, periodic influenza vaccination, smoking status, time from the onset of symptoms, presence of comorbidities, oxygen therapy, and need for intensive care unit.33 However, we could not find any literature on its relationship with PFT. In our study, no significant relationship was found between PCFS and PFT parameters.

Post-COVID fibrosis is associated with advanced age, severe illness, long-term intensive care/hospital stay, mechanical

ventilation, smoking history, and chronic alcoholism.^{34,35} In our study, smoking and hospitalization history were not correlated with changes in PFT values (P < .05).

The limitations of our study are the absence of PFTs belonging to the pre-COVID period of all patients and that it is a single-center, retrospective study. It should be considered that previous respiratory diseases, obesity and smoking, and environmental pollution will also cause an impairment in lung functions. The restriction should also be investigated by lung volumes, DLCO measurements, and radiologically.

CONCLUSION

Major PFT disorder was found to be a restriction in those who had dyspnea in 3- to 6-month post-COVID period. However, since this restriction may be associated with physical functional limitation, tests such as lung volume measurement, DLCO, and HRCT are needed for parenchymal diseases. Post-COVID-19 Functional Status Scale was not found to be effective in predicting respiratory dysfunction.

Ethics Committee Approval: This study was approved by Ethics committee of Abant İzzet Baysal University: (Date: July 27, 2021, No: 2021/203).

Informed Consent: Verbal and written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – E.A.; Design – E.A.; Supervision – E.A.; Funding – E.A., M.E.D.; Materials – E.A., M.E.D.; Data Collection and/or Processing – E.A., M.E.D.; Analysis and/or Interpretation – E.A., M.E.D.; Literature Review – E.A., M.E.D.; Writing – E.A.; Critical Review – E.A.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

REFERENCES

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China.*Lancet.* 2020;395(10223):497-506. [CrossRef]
- Namendys-Silva SA. ECMO for ARDS due to COVID-19. Heart Lung. 2020;49(4):348-349. [CrossRef]
- Mo X, Jian W, Su Z, et al. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J*. 2020;55(6):Article 2001217. [CrossRef]
- Venkataraman T, Frieman MB. The role of epidermal growth factor receptor (EGFR) signaling in SARS coronavirus-induced pulmonary fibrosis. *Antiviral Res.* 2017;143:142-150. [CrossRef]
- Frija-Masson J, Debray MP, Gilbert M, et al. Functional characteristics of patients with SARS-CoV-2 pneumonia at 30 days post infection. *Eur Respir J.* 2020;56(2):2001754. [CrossRef]
- Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. *Eur Respir J.* 2005;26(5):948-968.
 [CrossRef]
- British Thoracic Society. British Thoracic Society guidance on respiratory follow up of patients with a clinico-radiological diagnosis of COVID-19 pneumonia [internet]; 2020. Available at: https://www.brit-thoracic.org.uk/document-library/quali ty-improvement/covid-19/resp-follow-up-guidance-post-co vid-pneumonia/
- Hui DS, Joynt GM, Wong KT, et al. Impact of severe acute respiratory syndrome (SARS) on pulmonary function, functional capacity and quality of life in a cohort of survivors. *Thorax*. 2005;60(5):401-409. [CrossRef]
- Ong KC, Ng AWK, Lee LSU, et al. 1-year pulmonary function and health status in survivors of severe acute respiratory syndrome. *Chest.* 2005;128(3):1393-1400. [CrossRef]
- Tansey CM, Louie M, Loeb M, et al. One-year outcomes and health care utilization in survivors of severe acute respiratory syndrome. *Arch Intern Med.* 2007;167(12):1312-1320.
 [CrossRef]
- Ngai JC, Ko FW, Ng SS, To KW, Tong M, Hui DS. The longterm impact of severe acute respiratory syndrome on pulmonary function, exercise capacity and health status. *Respirology*. 2010;15(3):543-550. [CrossRef]
- Neufeld KJ, Leoutsakos J-MS, Yan H, et al. Fatigue symptoms during the first year following ARDS. *Chest.* 2020;158(3):999-1007. [CrossRef]
- Klok FA, Boon GJAM, Barco S, et al. The post-COVID-19 Functional Status scale: a tool to measure functional status over time after COVID-19. *Eur Respir J.* 2020;56(1):2001494. [CrossRef]
- Yao XH, Li TY, He ZC, et al. A pathological report of three COVID-19 cases by minimally invasive autopsies. *Zhonghua Bing Li Xue Za Zhi = Chin J Pathol.* 2020;49:E009.
- Liu K, Zhang W, Yang Y, Zhang J, Li Y, Chen Y. Respiratory rehabilitation in elderly patients with COVID-19: a randomized controlled study. *Complement Ther Clin Pract.* 2020;39:101166. [CrossRef]
- 17. Sonnweber T, Sahanic S, Pizzini A, et al. Cardiopulmonary recovery after COVID-19 an observational prospective multicenter trial. *Eur Respir J.* 2020;57. Available at: http://erj.ersj ournals.com/lookup/doi/10.1183/13993003.03481-2020.

- Stylemans D, Smet J, Hanon S, et al. Evolution of lung function and chest CT 6 months after COVID-19 pneumonia: real-life data from a Belgian University Hospital. *Respir Med.* 2021;182:106421. [CrossRef]
- Hui DS, Wong KT, Ko FW, et al. The 1-year impact of severe acute respiratory syndrome on pulmonary function, exercise capacity, and quality of life in a cohort of survivors. *Chest.* 2005;128(4):2247-2261. [CrossRef]
- 20. Castro RT, Castillo LV, Restoy XA, et al. Respiratory function in patients post-infection by COVID-19: a systematic review and meta-analysis. *Pulmonology*. 2020. [CrossRef]
- 21. Mach WJ, Thimmesch AR, Pierce JT, Pierce JD. Consequences of hyperoxia and the toxicity of oxygen in the lung. *Nurs Res Pract.* 2011;2011:260482. [CrossRef]
- Ong K-CC, Ng AW, Lee LS-USU, et al. Pulmonary function and exercise capacity in survivors of severe acute respiratory syndrome. *Eur Respir J.* 2004;24(3):436-442. [CrossRef]
- Lee SH, Shin HS, Park HY, et al. Depression as a mediator of chronic fatigue and post-traumatic stress symptoms in middle east respiratory syndrome survivors. *Psychiatry Investig.* 2019;16(1):59-64. [CrossRef]
- Lam MH, Wing YK, Yu MW, et al. Mental morbidities and chronic fatigue in severe acute respiratory syndrome survivors: long-term follow-up. *Arch Intern Med.* 2009;169(22):2142-2147. [CrossRef]
- 25. Borst BV, Peters J, Brink M, et al. Comprehensive health assessment three months after recovery from acute COVID-19. *Ann Med.* 2020;0:1-14. [CrossRef]
- Orme J, Romney JS, Hopkins RO, et al. Pulmonary function and health-related quality of life in survivors of acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 2003;167(5):690-694). [CrossRef]
- 27. Lutchmansingh DD, Knauert MP, Antin-Ozerkis DE, et al. A clinic blueprint for post-COVID-19 RECOVERY: learning from the past, looking to the future. *Chest.* 2021;159(3):949-958.
- Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 2020;77(6):683-690. [CrossRef]
- Chan KS, Zheng JP, Mok YW, et al. Sars: prognosis, outcome and sequelae. *Respirology*. 2003;8(suppl):S36-S40. [CrossRef]
- Hall J, Myall K, Lam JL, et al. Identifying patients at risk of post-discharge complications related to COVID-19 infection. *Thorax*. 2021;76(4):408-411. [CrossRef]
- 31. Hancı P, Öcal S, Mekanik Ventilasyon NHN. 9102017153 726-020-Makale.pdf. Available at: solunum.org.tr.
- Machado FVC, Meys R, Delbressine JM, et al. Construct validity of the post-COVID-19 Functional Status Scale in adult subjects with COVID-19. *Health Qual Life Outcomes*. 2021;19(1):40. [CrossRef]
- Aliae AR, Hussein M, Galal I, et al. Functional Status: Relation to Age, Smoking, Hospitalization and Previous Comorbidities. [CrossRef]
- Yu M, Liu Y, Xu D, Zhang R, Lan L, Xu H. Prediction of the development of pulmonary fibrosis using serial thin-section CT and clinical features in patients discharged after treatment for COVID-19 pneumonia. *Korean J Radiol.* 2020;21(6):746-755. [CrossRef]
- Ojo AS, Balogun SA, Williams OT, Ojo OS. Pulmonary fibrosis in COVID-19 survivors: predictive factors and risk reduction strategies. *Pulm Med.* 2020;2020:6175964. [CrossRef]