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Can 1st and 6th month pulmonary function test follow-ups give an idea about the long-term respiratory effects of COVID-19 pneumonia?

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SUMMARY

OBJECTIVE: The aim of this study was to ascertain the long-term respiratory effects of COVID-19 pneumonia through pulmonary function tests in follow-ups at 1 and 6 months.

METHODS: Our study was conducted between August 1, 2020 and April 30, 2021. At 1 month after discharge, follow-up evaluations, PFTs, and lung imaging were performed on patients aged above 18 years who had been diagnosed with COVID-19 pneumonia. In the 6th month, the PFTs were repeated for those with pulmonary dysfunction.

RESULTS: A total of 219 patients (mean age, 49±11.9 years) were included. Pathological PFT results were noted in the 1st month for 80 patients and in the 6th month for 46 (7 had obstructive disorder, 15 had restrictive disorder, and 28 had small airway obstruction) patients. A significant difference was found between abnormal PFT results and patient-described dyspnea in the 1st month of follow-up. The 6-month PFT values (especially those for forced vital capacity) were statistically significantly lower in the patients for whom imaging did not indicate complete radiological improvement at the 1-month follow-up. No statistically significant difference was found between the severity of the first computed tomography findings or clinical condition on emergency admission and pulmonary dysfunction (Pearson's chi-square test, P=0.904; Fisher's exact test, P=0.727).

CONCLUSION: It is important that patients with COVID-19 pneumonia be followed up for at least 1 month after discharge to be monitored for potential long-term lung damage. PFTs should be administered to those in whom ongoing dyspnea, which started with COVID-19, and/or full recovery were not identified in pulmonary imaging.

KEYWORDS: Respiratory function tests. COVID-19. Lung injury. Lung diseases. Long term adverse effects.

INTRODUCTION

The long-term damage to patients with coronavirus disease 2019 (COVID-19) is slowly being revealed. It is clear that more time will be required for the completion of studies on this issue. The effects are not limited to the respiratory system. Almost all body systems are involved[1]. Individual characteristics might play a role. Many conditions, such as advanced age, diabetes, hypertension, obesity, and coronary artery disease history, are the causes of poor clinical outcomes related to respiratory tract infections during the acute period[2].

In a recent study, Anastasio et al. reported a correlation between COVID-19-related lung damage and reduced pulmonary function 4 months after acute infection[3]. The patients' recovery process should be carefully observed to prevent possible long-term problems and to establish treatment modifications. Therefore, in this study, it was aimed to investigate the usability of pulmonary function tests (PFTs) at 1- and 6-month follow-ups for early diagnosis in the development of long-term respiratory effects of COVID-19 pneumonia. The determination of the influential variables in the development of permanent lung damage was the secondary goal.

METHODS

Ethical statement

This study was approved by the local institutional review board (Approval No. B.10.1.TKH.4.34.H.GP.0.01/170). It was conducted in compliance with the World Medical Association Declaration of Helsinki. In addition, written informed consent was obtained from the participants.

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Study design and population

This single-center prospective observational study was conducted at University of Health Sciences Umraniye Training and Research Hospital between August 1, 2020 and April 30, 2021. During the first 3 months of this period, the study patients were determined, and during the succeeding 6 months, 1- and 6-month follow-up evaluations, which included PFTs, were performed. The inclusion criteria for the study were as follows: (a) application to the emergency department; (b) receipt of positive reverse transcription-polymerase chain reaction results; (c) clinico-radiological diagnosis of COVID-19 pneumonia; (d) age >18 years; (e) absence of abnormalities, such as lung disease, upper respiratory tract obstruction, neuromuscular disease, kyphoscoliosis, and ankylosing spondylitis, which could affect the PFT values; (f) absence of diseases, such as neuropsychiatric diseases, facial paralysis, mental retardation, and dementia, which could affect cooperation during PFT; and (g) presentation of the patient-signed informed consent form. Patients who did not meet these criteria and those whose records were incomplete were excluded from this study.

Patients who met the inclusion criteria were invited for a follow-up at the end of the 1st month after inpatient or outpatient COVID-19 pneumonia treatment. During the follow-ups, the status of COVID-19 pneumonia respiratory tract complaints was questioned, and the presence of ongoing symptoms was investigated. In addition, the Modified Medical Research Council (mMRC) scale, Borg rating of perceived exertion scale, control blood tests, PFTs, and pulmonary imaging (chest X-rays and/or pulmonary CT, if necessary) were administered. The evaluations of CT findings were based on the current literature[4]. We terminated the patients' follow-up whose respiratory evaluations were normal during the follow-up period and the collection of their data. Those whose respiratory evaluations indicated a lack of improvement were recalled for a 6-month follow-up, which included a PFT. Pulmonary imaging was repeated for the patients in whom radiological abnormalities were identified in the first control examination at the 6-month follow-up. Invitations to participate in follow-ups were offered face-to-face at discharge or by telephone later. In addition, the patients received a reminder telephone call during the week preceding the follow-up date. Patients who did not come to the follow-up and those who wanted to leave the study were excluded. The PFTs were performed by professionally trained respiratory technicians and interpreted by a pulmonologist with 20 years of experience. The final medical management decisions related to the post-discharge evaluations were made by the same pulmonologist.

Data collection

Data on demographics and comorbidities, clinical and vital parameters, and laboratory, radiodiagnostic, and lung function tests were obtained through real-time patient examinations and the patient records in the hospital data management system. The results of the mMRC and Borg scale, which were administered to evaluate dyspnea severity during the 1-month follow-up, were also recorded. During the telephone calls, the researchers recorded identifiable changes in the patients' health status. A Spirolab III spirometer (Medical International Research, Rome, Italy) was used for the PFTs. Several other parameters, such as FVC, forced expiratory volume in one second (FEV1), FEV1/FVC, peak expiratory flow, and forced expiratory flow (normal range 25–75%), were evaluated. Microsoft Excel® (Version 2019 for Windows, Microsoft Corp.) was used to record the patient data throughout the study period.

Statistical analysis

The statistical tests were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Conformity of the continuous data to normal distribution was determined using the Shapiro–Wilk test. The Student's *t*-test was used for intergroup comparisons of the normally distributed continuous data, and the Mann–Whitney *U*-test was used for the nonnormally distributed continuous data. The chi-square test was used for the comparisons of the categorical data. Fisher's exact test was used where necessary. The mortality-related variables were determined by logistic regression. The variables that were determined to be statistically significant by the univariate analysis and the clinically significant variables with a p-value <0.2 were included. Statistical significance was set as $P<0.05$.

RESULTS

The study included 219 patients (mean age, 49±11.9 years), 39.7% of whom were women (Table 1). It was determined that none of these patients died during the study period. PFTs were performed on all patients in the 1st month after treatment. Pathology was detected in 80 (36.5%) patients. In the 6th month, control PFTs were performed on these patients. Pulmonary dysfunction was found in 46 (21% of all patients) patients (Table 2).

At the 1-month follow-up, the patients were asked about respiratory distress. Of note, 178 patients did not experience respiratory distress. However, 41 patients did not have fully improved symptoms. They had either effort-related or noneffort-related respiratory distress. A comparison of the PFT values in the groups with and without respiratory distress indicated

Table 1. Basic characteristics of the study population.

	N (%)/Mean ±SD/Median (25–75%)
Age, years	49±11.9
Sex (female)	87 (39.7)
Background	
Diabetes mellitus	27 (12.3)
Hypertension	40 (18.3)
Chronic renal failure	5 (2.3)
Coronary artery disease	11 (5)
Congestive heart failure	3 (1.4)
Thyroid disorder	7 (3.2)
Active smoking	16 (7.3)
Pack/year ratio in smoking patients	14 (5–20)
Occupational exposure	7 (3.2)
Body mass index	
<25	49 (22.4)
25–30	95 (43.4)
>30	74 (33.8)
Complaint	
Fever	93 (42.5)
Coughing	87 (39.7)
Dyspnea	34 (15.5)
Fatigue	97 (44.3)
Hemoptysis	1 (0.5)
Other symptoms	123 (56.2)
Asymptomatic patients	8 (3.7)
Hospital admission	
Outpatient treatment	26 (11.9)
Ward admission	173 (79)
ICU admission	9 (4.1)
Hospital length of stay (days)	6 (5–10)
Total time of treatment	7.5 (5–14)
Initial computed tomography findings	
Patients underwent thoracic tomography at first admission	209 (95.4)
Presence of any pathological finding	204 (93.2)
Findings of preexisting lung disease	4 (1.8)
Typical COVID-19	180 (82.2)
Atypical COVID-19 findings	19 (8.7)

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Table 1. Continuation.

	N (%)/Mean ±SD/Median (25–75%)
Ground-glass opacification	19 (8.7)
Consolidation	113 (51.6)
Bilateral involvement	164 (74.9)
Presence of nodules	17 (7.8)
Pleural effusion	0 (0)
Thoracic lymphadenopathy	1 (0.5)
Other (calcification, cavitation, bronchiectasis, etc.)	17 (7.8)
Disease severity in terms of CT distribution	
No distribution	7 (3.2)
Mild distribution	121 (55.3)
Moderate distribution	60 (27.4)
Severe distribution	21 (9.6)
mMRC score	0 (0–0)
Borg score	0 (0–1)
Pulmonary function test results at the 1st month follow-up	
FVC, lt (for all patients)	3.28 (2.83–4.06)
FVC, % (for all patients)	88 (77.5–100)
FEV1, L (for all patients)	3.13 (2.47–3.67)
FEV1, % (for all patients)	96.7±18.1
FEV1/FVC, % (for all patients)	92.4 (87.6–96.3)
PEF, lt (for 209 patients)	6.18 (4.76–8.54)
PEF, % (for 209 patients)	81 (62–101.5)
FEF 25–75, lt (for 209 patients)	3.92 (3.4–4.9)
FEF 25–75, % (for 209 patients)	105 (87.5–125)
Obstructive pathology**	
None	39 (17.8)
Mild	6 (2.7)
Severe	1 (0.5)
Restrictive pathology**	
None	29 (13.2)
Mild	14 (6.4)
Moderate	1 (0.5)
Severe	0
Patients with small airway**	28 (12.8)
Number of patients who underwent PFT at both 1 and 6 months	80 (36.5)

Continue...

Table 1. Continuation.

	N (%)/Mean ±SD/Median (25–75%)	
Vital parameters	**Initial admission**	**Control admission**
Heart rate, beats per minute	85.5 (78–92.75)	89 (81–99.75)
Systolic blood pressure, mmHg	115 (109–120)	–
Diastolic blood pressure, mmHg	70 (67.3–80)	–
spO_2, %	96.5 (94.3–98)	98 (97–98)
Laboratory results		
Lymphocyte, $10^3/\mu L$	1.5 (1.13–2.02)	2.14 (1.82–2.61)
CRP, mg/L	1.2 (0.2–4)	0.2 (0.2–0.3)
Elevated liver enzymes	12 (5.5)	7 (3.2)
Impaired kidney function tests	4 (1.8)	4 (1.8)

*Those who had never smoked or quit for more than 1 year were considered nonsmokers. **Patients who still have pathological findings in the second pulmonary function test (PFT) results 6 months later.

statistically significantly lower PFT values in the patients who described respiratory distress (Table 2). The 6-month control PFTs revealed obstructive lung disease in 7 patients, restrictive lung disease in 15, and small-airway obstruction in 28.

The patients were clinically divided into *severe COVID-19* and *other* (mild–moderate) groups. In the 1st month, PFT abnormalities were observed in four (44.4%) of the nine patients in the severe COVID-19 group and 76 (36.2%) of the 210 patients in the other group. There was no statistically significant difference between the groups (Fisher's exact test, P=0.727).

When necessary, chest X-rays and/or CT imaging of the thorax were performed at the 1-month follow-up. The results indicated that 169 (77.2%) had complete radiological recovery; however, 38 had not completely recovered. In our study, the control CT imaging results were compared with the PFT results of the patient groups at the 1st month follow-up. A statistically significant decrease was found in the PFT values, especially those for FVC, in the patients with radiological improvement (Table 2).

According to the findings of the first CT (no lung involvement and mild, moderate, and severe lung involvement) performed during emergency admission, the frequencies regarding pathology in the 1-month PFT results were 2 (28.6%), 43 (35.5%), 24 (40%), and 8 (38.1), respectively. However, no statistically significant difference was found between the groups (chi-square test, P=0.904).

Table 2. Comparison of different patient groups according to their pulmonary function tests results at follow-ups.

	Median (25–75%)		p-value
A. Comparison of 1st month and 6th month PFT results in patients with detected PFT pathology in the 1st month (n=80).			
	1st month	**6th month**	
FVC, lt *	3.35 (2.92–3.93)	3.39 (2.74–4.13)	0.646
FVC, % *	88 (75.75–99.5)	84 (73–100)	0.161
FEV1, lt *	3.13 (2.57–3.52)	2.89 (2.38–3.58)	**0.025**
FEV1, % *	95 (84–110.25)	89 (80–103)	**<0.001**
FEV1/FVC, % *	92.90 (88.58–96.08)	89.3 (85.7–95.1)	**0.003**
PEF, lt **	5.73 (4.77–8.88)	4.89 (3.71–6.38)	**<0.001**
PEF, % **	78 (61–126)	60 (47–78)	**<0.001**
FEF 25–75, lt **	3.94 (3.43–5.13)	3.35 (2.67–4.64)	**<0.001**
FEF 25–75, % **	105 (91.5–129)	96 (71–114)	**<0.001**
B. Comparison of patient groups with and without dyspnea in terms of PFT results at the 1st month follow-up.			
	Dyspnea (–)	**Dyspnea (+)**	
FVC, lt *	3.39 (2.93–4.13)	2.84 (2.32–3.63)	**0.001**
FVC, % *	89 (79–101)	81.5 (68.5–95)	**0.027**
FEV1, lt *	3.13 (2.55–3.74)	2.75 (2.22–3.28)	**0.009**
FEV1, % *	97 (86–109)	91.5 (77.5–106.75)	**0.040**
FEV1/FVC, % *	91.5 (86.8–96.2)	95.05 (91.43–100)	**0.004**
PEF, lt **	6.53 (4.97–8.82)	5.14 (4.34–7.33)	**0.024**
PEF, % **	83 (64–103)	71.3 (57.25–95.25)	0.137
FEF 25–75, lt **	3.93 (3.38–5.13)	3.86 (3.43–4.55)	0.445
FEF 25–75, % **	106 (85–125)	104 (91–125.25)	0.962
C. Comparison of PFT results of the patient groups with and without complete radiological improvement at the 1st month follow-up.			
	Radiological improvement (–)	**Radiological improvement (+)**	
FVC, lt *	3.13 (2.3–3.83)	3,32 (2.92–4.13)	**0.033**
FVC, % *	81 (71.5–94)	89 (81–89)	**0.041**
FEV1, lt *	2.85 (2.15–3.52)	3.13 (2.52–3.68)	0.112
FEV1, % *	89 (80.5–107.5)	98 (87–109)	0.051
FEV1/FVC, % *	93.2 (90.5–97)	91.7 (86.5–96.15)	0.095
PEF, lt **	6.67 (4.98–9.15)	6.17 (4.73–8.36)	0.630
PEF, % **	91 (63.5–105)	78.5 (61–100.75)	0.266
FEF 25–75, lt **	3.88 (3.42–5.38)	3.93 (3.38–4.76)	0.787
FEF 25–75, % **	111 (93.5–133.5)	105 (87–122)	0.123

*These values are for all patients for whom 1st and 6th month PFT results are available (80 patients). **These values are the data of 78 patients who were able to comply with the test performed. Bold values indicate statistically significance.

The 1-month PFT results in terms of the mMRC and Borg scale results indicated that there was no statistically significant difference between the patients with pathology and those without (Mann–Whitney *U*-test: P=0.986 and 0.820, respectively). In addition, no statistically significant difference was found between the groups with and without pathology in the 6-month follow-up PFT results in terms of the mMRC and Borg scale results that were applied during the 1st month (Mann–Whitney *U*-test: P=0.795, P=0.611, respectively).

When the patients were dichotomized into the severe COVID-19 and other groups on the basis of their initial CT results, the median mMRC score of those with severe lung involvement was 0 (0–0). For those in the other group, it was 0 (0–1). There was no statistically significant difference between the groups (Mann–Whitney *U*-test, P=0.075). The median Borg scale scores were 0 (0–1) for the patients with severe COVID-19 and 0 (0–1.5) for the other patients. No statistically significant difference was found between the groups (Mann–Whitney *U*-test, P=0.314).

There was no statistically significant difference in the mMRC scores of the obstructive lung disease groups (mild, moderate, and severe), which were established on the basis of the PFT results (Kruskal–Wallis test, P=0.892). Again, no statistically significant difference was found in the scores of the restrictive lung disease groups (mild, moderate, and severe), which were established on the basis of the PFT results in terms of the mMRC and Borg scale scores (Kruskal–Wallis test, P=0.764). There was no statistically significant difference in the mMRC scores of the groups with and without small-airway obstruction, as determined by the PFT results (median mMRC scores = 0 [0–0], 0 [0–0], respectively; Mann–Whitney *U*-test, P=0.119). There were significant differences in the Borg scale scores of the groups (median scores= 0 [0–1], 0 [0–1], respectively; Mann–Whitney *U*-test, P=0.016).

The results of the univariate analysis indicated that only oseltamivir use and systolic arterial blood pressure (sBP) variables were predictive of the presence of pathology in the 1-month PFT. The logistic regression analysis included oseltamivir and sBP with the following variables, which did not show a significant difference in the univariate analysis, but with a p-value less than 0.2: cough, malaise, presence of diabetes mellitus, and consolidation characterized by CT showed a statistically significant difference. The regression analysis indicated that only the use of oseltamivir detected the presence of pathology in the PFTs in the 1st month (Table 3).

Table 3. Univariate and multivariate analysis of variables for COVID-19 patients' presence of pathology in the 1st month pulmonary function test prediction.

Variables	Abnormal PFT	Normal PFT	Univariate		Multivariate	
	N (%)/ Median (IQR)	N (%)/ Median (IQR)	HR (95%CI)	p-value	HR (95%CI)	p-value
Age, years	47 (40.75–57.5)	51 (45–54)	–	0.735	–	–
Sex (female)	32 (36.8)	55 (63.2)	1.02 (0.58–1.79)	0.950	–	–
BMI>30	26 (34.7)	49 (65.3)	0.88 (0.49–1.58)	0.679	–	–
Symptoms						
Temperature ≥38°C	34 (36.6)	59 (63.4)	1 (0.57–1.75)	0.977	–	–
Cough	37 (42.5)	50 (23.3)	1.52 (0.86–2.66)	**0.147**	1.63 (0.81–3.26)	0.170
Dyspnea	14 (41.2)	20 (58.8)	1.26 (0.6–2.66)	0.544	–	–
Hemoptysis	1 (100)	0 (0)	5.26 (0.21–130.56)	0.366	–	–
Fatigue	40 (41.2)	57 (58.8)	1.44 (0.83–2.51)	**0.199**	1.87 (0.92–3.77)	0.082
Other symptoms	43 (35)	80 (65)	0.85 (0.49–1.49)	0.571	–	–
Comorbid diseases						
Hypertension	15 (37.5)	25 (62.5)	1.03 (0.51–2.1)	0.927	–	–
Diabetes mellitus	14 (51.9)	13 (48.1)	2.02 (0.9–4.56)	**0.085**	1.8 (0.69–4.72)	0.233
Coronary artery disease	4 (36.4)	7 (63.6)	0.98 (0.28–3.45)	1	–	–

Continue...

Table 3. Continuation.

Variables	Abnormal PFT	Normal PFT	Univariate		Multivariate	
	N (%)/ Median (IQR)	N (%)/ Median (IQR)	HR (95%CI)	p-value	HR (95%CI)	p-value
Congestive heart failure	2 (66.7)	1 (33.3)	0.31–39.08)	0.556	–	–
Thyroid disorder	1 (14.3)	6 (85.7)	0.28 (0.03–2.35)	0.265	–	–
Chronic renal failure	3 (60)	2 (40)	2.63 (0.43–16.09)	0.360	–	–
Cigarette smoker (current smoker or quitted)	6 (37.5)	10 (62.5)	1.05 (0.37–2.99)	0.933	–	–
Pack/year ratio in smoking patients	10 (3–20)	14.5 (5.75–20)	–	0.231	–	–
Occupational exposure	3 (42.9)	4 (57.1)	1.32 (0.29–6.03)	0.708	–	–
Medication						
Hydroxychloroquine	78 (37.3)	131 (62.7)	1.19 (0.11–13.35)	1	–	–
Oseltamivir	53 (43.1)	70 (56.9)	1.84 (1.03–3.28)	**0.039**	**2.26 (1.05–4.84)**	**0.037**
Azithromycin	59 (38.6)	94 (61.4)	1.14 (0.76–1.71)	0.529	–	–
Ceftriaxone	22 (37.3)	37 (62.7)	1 (0.68–1.48)	0.996	–	–
Other antibiotics (clarithromycin, meropenem, tazocin, moxifloxacin)	11 (47.8)	12 (52.2)	1.63 (0.68–3.90)	0.271	–	–
Favipiravir	16 (36.4)	28 (63.6)	0.97 (0.49–1.93)	0.926	–	–
Enoxaparine	36 (32.7)	74 (67.3)	0.72 (0.58–1.15)	0.156	–	–
Vital signs						
Heart rate, beats per minute	84.5 (78.8–100.3)	84 (78–92)	–	0.414	–	–
Systolic blood pressure, mmHg	110 (100–120)	110 (110–120)	–	**0.031**	0.98 (0.95–1)	0.090
Diastolic blood pressure, mmHg	70 (65.5–80)	70 (64–80)	–	0.422	–	–
Pulse O_2 saturation, %	97 (94.75–98)	96 (94–98)	–	0.785	–	–
Laboratory results						
Elevated liver enzymes	3 (25)	9 (75)	0.55 (1.15–2.12)	0.540	–	–
Impaired kidney function tests	1 (25)	3 (75)	0.575 (0.06–5.64)	1	–	–
Lymphocyte, $10^3/\mu L$	1.64 (1.27–2.1)	1.45 (1.06–1.94)	–	0.323	–	–
CRP mg/L	1.4 (0.275–5.85)	1.7 (0.3–6.5)	–	0.378	–	–
D-Dimer	522 (348.5–800)	530 (410–890)	–	0.388	–	–
Thorax computed tomography results						
Severe distribution	8 (38.1)	13 (61.9)	1.06 (0.42–2.69)	0.900	–	–
Ground glass opacification	71 (37.4)	119 (62.6)	1.29 (0.47–3.55)	0.618	–	–
Consolidation	37 (32.7)	76 (67.3)	0.68 (0.39–1.2)	0.183	0.80 (0.39–1.64)	0.540
Bilateral distribution	57 (34.8)	107 (65.2)	0.67 (0.34–1.3)	0.233	–	–
Hospital length of stay, days	7 (5–11)	7 (5–12)	–	0.449	–	–
Total time of treatment, days	11.5 (0–19)	11 (6–18)	–	0.563	–	–

Bold values indicate statistically significance.

DISCUSSION

A majority of patients are considered to have recovered from COVID-19. However, residual lung abnormalities have been found 1–3 months after discharge from the hospital[5,6]. Currently, the mechanisms in the long-term effects are considered to be hypoxia or mechanical ventilation-related damage, uncontrolled cytokine release and immune system activation-associated tissue destruction, angiotensin-converting enzyme 2-mediated viral invasion associated direct pneumocyte apoptosis, surfactant inactivation, microvascular or thrombotic disease, and endothelial dysfunction[2,7].

The findings of this study regarding the presence of residual lung abnormalities at follow-up are important. A statistically significant increase in lung dysfunction was observed in the patients who underwent PFTs in both follow-ups (1st and 6th month). The results suggest that all patients with COVID-19 pneumonia should be evaluated for an indication of PFT in the 1-month post-discharge follow-up for residual lung injury. The study also found two issues that influence the need for PFTs. One is a complaint of ongoing dyspnea since the onset of COVID-19 pneumonia. The other is the presence of pathology in the 1-month post-discharge imaging.

Recent studies have reported that restrictive disorders, reduced diffusing capacity, and small-airway obstruction may develop within the first 12 weeks after discharge. Fibrotic changes, including lung fibrosis, have been detected 3 weeks after symptom onset regardless of the severity of the acute illness[2]. Similarly, restrictive disorders and small-airway obstruction were more prevalent in this study. However, some patients also exhibited obstruction of the large airways.

Zhao et al. evaluated recovered patients who were initially admitted with CT abnormalities. They found that 70.91% had radiological abnormalities and 25.45% had lung function abnormalities 3 months after discharge[8]. In this study, 21% of the patients had lung function abnormalities 6 months after COVID-19 pneumonia.

In a recently published study, Guler et al. found lower lung volumes in patients 4 months after severe or critical COVID-19 disease[9]. In this study, no statistically significant respiratory function loss was detected in the 1- and 6-month PFT results of the patients who were considered clinically critically ill during the acute illness period. However, these results might have been influenced by relatively low number of patients in intensive care unit in the study. The statistical analysis indicated a lack of correlation between the severity of the radiologically calculated lung involvement during the acute illness period and the PFT findings. However, FVC and FEV1 were more significantly affected in patients with respiratory distress complaints at the end of the 1st month than in those who did not have these complaints. Again, the negative effects on FVC were evident in those who did not exhibit radiological improvement at the 1-month evaluation.

Another important finding that should be investigated further is the statistically significant lung dysfunction determined in patients whose COVID-19 pneumonia treatment included oseltamivir. The reason might be the use of oseltamivir in combination with other drugs in patients diagnosed as critically ill. However, this could also be a coincidence. Thus, more research is needed.

Limitations

The possibility of underlying asymptomatic chronic lung disease in the patients in the study cannot be completely excluded. In addition, individuals with a body mass index higher than 26.4 have been found to have lower FEV1 and FVC[10]. Due to the small number of obese patients in the current study, subgroup analyses of specific PFT parameters could not be performed.

It is very important that follow-up be done with a higher number of intensive care unit patients. Although our study included a significant number of patients, the number of patients with a history of intensive care hospitalization was relatively low. However, studies have indicated that 80% of patients hospitalized with COVID-19 and 60% of those admitted to intensive care units survive[11]. Perhaps, compared with those who died, the number of patients who were treated in the intensive care unit and discharged from the hospital was relatively low in our study period. Since the number of these patients was not recorded, a clear interpretation could not be made.

The single-center design of the study was also an influential factor in the number of patients with a history of intensive care hospitalization.

CONCLUSIONS

This study indicates the significant role of PFTs in follow-up studies of COVID-19 pneumonia. PFTs can reveal reduced lung function even after the noncritical course of the disease. In summary, patients should participate in follow-ups 1 month after the end of COVID-19 pneumonia treatment. PFTs should be applied to those with sequelae and/or radiological abnormalities of the respiratory tract during these follow-ups. Those with abnormal PFT results should undergo a 6-month follow-up and begin medical management. In addition, the relationship between oseltamivir use and lung damage should be explored in future studies.

AUTHORS' CONTRIBUTIONS

SEE: data curation, formal analysis, investigation, methodology project administration, resources, and supervision, and writing. **SB:** resources, visualization, and roles/writing. **GA:** validation, visualization, and roles/writing. **AE:** resources and writing. **AA:** visualization and writing – review. **MMI:** writing. **SO:** writing.

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