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Evaluation of cardio-pulmonary functions of previously healthy adults with moderate-severe COVID-19 pneumonia after discharge

Nuran Günay[1], Şeyma Başlılar[2]

[1]University of Health Sciences, Ümraniye Training and Research Hospital, Department of Cardiology, İstanbul, Turkey
[2]University of Health Sciences, Ümraniye Training and Research Hospital, Department of Pulmonology, İstanbul, Turkey

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ABSTRACT

Aim: Persistent dyspnea is one of the most frequent post-COVID symptoms. We aimed to evaluate the cardiopulmonary functions of COVID-19 survivors with moderate to severe COVID-19 pneumonia without comorbidity, during the first wave of pandemics.

Material and Method: The study was conducted retrospectively in a single center. The electronic data of patients applied with dyspnea one month after hospital discharge, without any comorbidities, and who were evaluated with pulmonary function test (PFT) and echocardiography were included in the study. A total of adult 88 patients who suffered from COVID-19 pneumonia (46 moderate and 42 severe) were enrolled. Results of biochemical, hematological and radiological examinations, PFT parameters and echocardiography were recorded and compared between moderate and severe cases.

Results: The mean age of 88 patients included in the study was 48±13 years. Sixty-seven (74.4%) of the patients were male. Pulmonary thromboembolism was not detected in both groups. PFT parameters performed were similar in the two groups and there was no statistically significant difference**.** Pulmonary function test of the patients with moderate COVID-19 pneumonia revealed mild restriction in 21.7% and moderate restriction in 2% of the patients. In the severe group, 38.1% of the patients had mild and 4.8% of the patients had a moderate restrictive pattern. Small airway obstruction was detected in 37% of the moderate group and in 38.1% of the severe group. Conventional echocardiographic parameters of the two groups were normal. Pulmonary arterial pressures were 22.6±8.3 vs 22.1±6.8; p=0.8 was found. Tricuspid annular plane systolic excursion were within normal limits.

Conclusıon: The persistent dyspnea following COVID-19 pneumonia may be related to disturbances in PFT even in patients without comorbidities. We concluded that; the detailed evaluation of the patients with prolonged respiratory symptoms might help to detect the cardiopulmonary functional disturbances.

Keywords: COVID-19, pneumonia, comorbidity, echocardiography, pulmonary function test

INTRODUCTION

SARS-CoV-2 has affected millions of people to date. It caused mortality and morbidity (1). SARS-CoV-2 is an RNA virus from the same family as severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Although SARS-CoV-2 has a lower mortality (1-7%) than the other two viruses, it is more contagious. The virus can cause asymptomatic infection as well as severe respiratory failure, dysfunction in other organs and death (1-3).

The target organ of the virus is the lung. Apart from the lungs, it can also affect many organs, especially the heart. Male gender, older age, obesity and comorbidities (coronary artery disease, hypertension, diabetes and lung disease) is related to increased morbidity and mortality. But the virus can cause severe pneumonia and death in some patients, even without comorbidity (4,5).

COVID-19 infection can cause cardiovascular complications such as myocarditis, heart failure, cardiac arrest, cardiogenic shock, acute myocardial infarction, arrhythmia, Takotsubo cardiomyopathy and venous thromboembolic disease. The disease can cause complications directly or indirectly (5,6).

Corresponding Author: Nuran Günay, nurangunaydr@gmail.com
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After COVID-19 pneumonia, respiratory physiology deterioration, pulmonary fibrosis and vascular complications may occur (7). Of patients who were treated for COVID-19 pneumonia, impairment of diffusion capacity in PFT was found to be the most common abnormality at the time of discharge (8).

It has been determined that the permanent deterioration in lung function and in the exercise capacity in patients with SARS and MERS infection continues for months or even years (9-11). Long-term studies with SARS and MERS viruses will guide our understanding of the long-term complications of the COVID-19 virus.

In this study, we selected the patients who suffered from COVID-19 pneumonia during the first wave of the pandemic as the morbidity and mortality were more in the first few months of pandemics. The use of intensive corticosteroids and vaccination against SARS CoV-2 resulted in a better prognosis recently (12,13). But the evaluation of patients affected formerly may help us to understand the consequences of the disease in naive cases, as there are still many people against vaccination.

There are few studies addressing cardiac and respiratory functions together after discharge of patients with moderate-to-severe COVID-19 pneumonia. These studies were conducted mainly on patients who have comorbidity. The group we studied, consisted of patients without comorbidities who were unvaccinated and treated with the first treatment protocol in the first wave of the pandemic.

Our study is the first to date in patients with moderate to severe COVID-19 pneumonia without comorbidities.

MATERIAL AND METHOD

The study was approved by the Ministry of Health's Scientific Research Platform, and the study was initiated with the approval of the Ümraniye Training and Research Hospital Clinical Researches Ethics Committee (Date: 11.06.2020, Decision No: B.10.1. TKH.4.34.H.GP.0.01/217). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

The medical records of the adult patients who applied post-COVID outpatient clinic were evaluated retrospectively in a single center between 15 June and 15 August 2020. There were 384 patients who complained of persistent dyspnea on the effort who suffered from moderate and severe COVID-19 pneumonia and applied one month after discharge. The diagnosis of COVID-19 pneumonia was made according to the clinical and radiological definition of the WHO (14). The COVID PCR tests of the patients were positive on admission. All of the patients were evaluated with routine hematological tests and chest X-rays and/or chest computed tomography. The PFT was performed following a negative SARS CoV-2 PCR test. The study was completed with 88 cases with a history of 46 moderate and 42 severe COVID-19 pneumonia.

Patients with severe COVID-19 pneumonia were defined as cases who had one of the following criteria: 1) Peripheral oxygen saturation at rest <93%, 2) Respiratory distress and respiratory rate >30/minute, 3) Partial arterial oxygen pressure/fraction of inspired oxygen < 300 mmHg. Patients who did not undergo invasive mechanical ventilation were included in the study.

Patients with a history of chronic lung disease, coronary artery disease, hypertension, heart failure, atrial fibrillation, right and left bundle branch block, moderate-severe valve pathology, diabetes mellitus, anemia, chronic renal failure, thyroid dysfunction, pulmonary embolism, cancer, rheumatic valve disease, BMI>30 kg/m2 and acute coronary syndrome during hospitalization, myocarditis, patients with pregnancy, chronic infectious and autoimmune diseases, upper airway obstruction, neuromuscular disease alcohol/drug abuse were excluded from the study (**Diagram**).

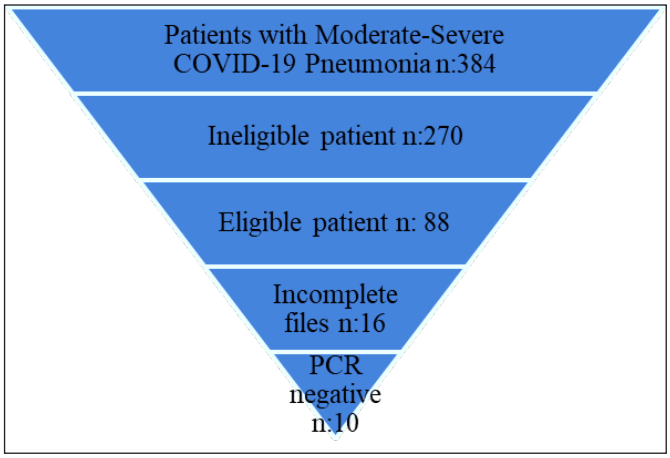

Diagram. Flow-chart of the patient selection

Methods

Routine biochemical examinations, hemograms, D-dimers, troponin values, inflammatory markers, radiological examinations, medications and oxygen treatments given to the patients during hospitalization and one month after discharge were examined. One month after discharge, thorax computed tomography (CT), echocardiography and PFT results were obtained from the system.

The duration of stay in the service and intensive care unit was recorded. The Modified Medical Research Council (mMRC) scale was calculated at the Borg rating of the

perceived exertion scale. Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC, peak expiratory flow (PEF) and forced expiratory flow (25-75%) were recorded from pulmonary function test parameters.

Among the transthoracic echocardiography parameters, left ventricular end-diastolic and end-systolic diameter, interventricular septum, posterior wall and left atrial diameter, right ventricle diastolic diameter, mitral early diastolic and late diastolic maximal flow rates, left ventricular ejection fraction, pulmonary artery systolic pressure, tricuspid S wave, tricuspid annular plane systolic excursions (TAPSE's) were recorded.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) for Windows 26 package program was used for statistical analysis (IBM SPSS 26, New Orchard Road Armonk, Newyork 10504-12722 United States). While evaluating the data, in addition to descriptive statistical methods, the student-t test was used for comparison of quantitative data, the comparison of normally distributed parameters between groups and the Mann Whitney-U test for intergroup comparisons of non-normally distributed parameters. The paired sample-t test was used for in-group comparisons of parameters and Chi-square test was used for the comparison of qualitative data. The results were accepted at the 95% confidence interval and the significance was accepted at the $p<0.05$ level.

RESULTS

Among the 88 patients (46 moderate and 42 severe) included in this study, 67 (74.4%) were male and the mean age was 48±13 years. Their average saturation was 90% during their hospitalization and an average of 98% after discharge from the control saturation. The mean lowest saturation at admission of patients with severe pneumonia was 88% [88 (86-90) vs. 92 (89.7-93.2); p 0.001]. The patients were admitted to the hospital at an average of 4±2 days after the first symptom onset. The time before the admission to the hospital was longer in the severe group, 5±3 days (**Table 1**).

Biochemical tests, hemograms and inflammatory markers of all patients were within normal limits after discharge. The lymphocyte count was statistically significantly lower on the first, third and fifth days of hospitalization of severe patients. CRP level was statistically higher in the severe group on the 1st and 3rd days. LDH value was found to be higher in severe patients. While there was no statistical difference between the two groups in terms of troponin levels during their hospitalization, they were higher in the severe group. The severe group had higher proBNP and D-dimer levels, but there was no statistical difference between the two groups. **Table 2** shows the laboratory findings of the patients.

Patients were treated according to the national COVID-19 treatment guidelines in the first wave of the pandemic. In the severe group, significantly more favipiravir [29 (63%) vs. 37 (88.1%); p 0.007] and tocilizumab [2 (4.3%) vs. 11 (26.2%); p 0.004] was used. The administration of plasma and intravenous steroid in the treatment was low in both groups and there was no statistically significant difference. All patients received oxygen therapy during their hospitalization. 12 patients from the severe group and 4 patients from the moderate group had intensive care admissions. The duration of intensive care and hospital stay was significantly higher in the severe group (**Table 3**).

Table 1. Basic characteristics and vital parameters of the study population

	N (%) / Mean±SD / Median (%25-75)			p
	Total (n:88)	Moderate (n:46)	Severe (n:42)	
Age, years	48±13	48±13	47±10	0.91
Sex, n (%)				0.04
male	67 (74.4%)	31 (67.4%)	36 (85.7%)	
female	21 (23.3%)	15 (32.6%)	6 (14.3%)	
BMI, kg/m^2	28 (26.1-29.3)	28,3 (26,7-29,3)	25.5 (25.9-29.3)	0.12
Tobacco exposure, n (%)				0.67
Never used	59 (67%)	30 (65.2%)	29 (69%)	
Active	3 (3.4%)	1 (2.2%)	2 (4.8%)	
Quit smoking	26 (29.5%)	15 (32.6%)	11 (26.2%)	
SBP, mmHg	120 (110-120)	120 (110-121)	115 (110-120)	0.07
DBP, mmHg	70 (70-80)	70 (70-80)	70 (70-80)	0.30
Heart Rate, beats/min	90.1±13.8	90±14.1	90.2±13.7	0.96
Control Oxygen , Saturation %	98 (96-98)	98 (96-98)	97 (96-98)	0.3
Lowest Oxygen, Saturation %	90 (87-93)	92±(89.7-93.2)	88 (86-90.2)	0.001

*Independent Samples T-Test, chi-square Test, Fisher's Exact Test *p<0.05 statistically significant. Continues variables are reported mean±SD. Categorical variables are reported n(%). Abbreviations: BMI: Body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 2. Laboratory findings of the study population

	N (%) / Mean±SD / Median (%25-75)		p
	Moderate (n:46)	Severe (n:42)	
WBC	5600 (4475-6850)	5850 (4435-7412)	0.46
Neutrophile, count	3350 (2475-4325)	4200 (2982-6025)	0.008
Lymphoctye,count (1st day)	1500 (1200-2100)	1150 (880-1425)	0.000
Lymphoctye, count (3rd day)	1440 (1160-2000)	1100 (830-1380)	0.000
Lymphoctye, count (5th day)	1400 (1000-2100)	1200 (795-1400)	0.015
Hemoglobin, g/dL	14±1.7	13,7±1.2	0.39
Hematocrite	41±5.8	40.3±3.6	0.5
Platelet, count	191500 (170500-219500)	175000 (156500-224000)	0.22
CRP, mg/dL (1st day)	1.85 (0.40-3.95)	4.95 (1.20-10.25)	0.001
CRP mg/dL (3rd day)	4 (1.45-7.00)	6.80 (3.05-12.45)	0.003
CRP, mg/dL (5th day)	5.72±5.70	7.54±5.40	0.13
LDH, U/L (1st day)	280 (228.7-334.5)	332.5 (226.7-444.5)	0.15
LDH, U/L (3rd day)	307.3±88.8	369.9±143	0.019
LDH, U/L (5th day)	339.6±105.6	385.4±194.2	0.21
Troponin, ng/mL (1st day)	0.002 (0.001-0.005)	0.003 (0.002-0.008)	0.54
Troponin, ng/mL (3rd day)	0.003 (0.001-0.007)	0.004 (0.002-0.009)	0.22
Troponin, ng/mL (5th day)	0.002(0.0008-0.0045)	0.002 (0.001-0.006)	0.92
proBNP, pg/ml (1st day)	10.00 (10.00-10.00)	29.00 (29.00-29.00)	0.2
D-dimer, ng/mL (1st day)	550.00 (352-741)	759.50 (467.5-1015)	0.01
D-dimer, ng/mL (3rd day)	582.50 (413.7-922.2)	825.00 (543.5-1417)	0.59
D-dimer, ng/mL (5th day)	860.50 (448-1234.7)	1010.00 (594-1830)	0.2

*Independent Samples T-Test, Mann Whitney-U Test *p<0.05 statistically significant. Continues variables are reported mean±SD. Categorical variables are reported n (%). Abbreviations: WBC: White blood cells; CRP: C-reactive protein; LDH:lactate dehydrogenase; proBNP: pro-brain natriuretic peptide.

Table 3. Inpatient treatment and follow-up.

	N (%) / Mean±SD / Median (%25-75)		p
	Moderate (n:46)	Severe (n:42)	
Plaquenyl, n (%)			0.19
Plaquenyl	3 (6.5%)	8 (19%)	
Plaquenyl+azithromycin	21 (45.7%)	15 (35.7%)	
Plaquenyl+azithromycin+ oseltamivir	22 (47.8%)	19 (45.2%)	
Favipiravir, n (%)	29 (63%)	37 (88.1%)	0.007
Tocilizumab, n (%)	2 (4.3%)	11 (26.2%)	0.004
Plasma, n (%)	3 (6.5%)	6 (14.3%)	0.23
Steroid, n (%)	3 (6.5%)	8 (19%)	0.07
Inhaler usage at discharge, n (%)	1 (2.2%)	0 (0%)	0.33
Oxygen concentrator at discharge, n (%)	0 (0%)	2 (4.8%)	0.13
ICU stay, n	4	12	0.016
ICU duration, days	11.7±7.6	12.3±7.2	0.016
Total time of stay, days	10.3±6.3	15.7±7.5	0.000
mMRC Score	0.24±0.52	0.47±0.74	0.08
Borg Score	0.53±1.10	0.95±1.69	0.17

*Independent Samples T-Test, chi-square Test, Fisher's Exact Test *p<0.05 statistically significant. Continues variables are reported mean±SD. Categorical variables are reported n (%). Abbreviations: ICU: intensive care unit.

Pulmonary thromboembolism was not detected in both groups. Subcutaneous heparin was given to the patients during their hospitalization and discharge. Among the thorax CT findings at admission, consolidation and interstitial septal thickening were seen significantly more frequently in the severe group (**Table 4**).

13 patients from the moderate group and 11 patients from the severe group had a control thorax CT taken 1 month after discharge. It was determined that the ground glass appearance persisted in 8 patients from the severe group and 9 patients from the moderate group. There was nodular appearance in the lungs of 1 patient from the moderate group and 2 patients from the severe group. Reticular/fibrotic appearance was detected in the control CT of 5 patients from the moderate group and 8 patients from the severe group. Interstitial septal thickening and cobblestone appearance were present in 2 patients from the severe group.

88 patients had pulmonary function test results. One patient from the moderate and severe groups each had

obstructive pathology in PFT. In the moderate group, restrictive pattern was mild in 10 patients (21.7%) and moderate in 2 patients (2%). In the severe group, mild restrictive pattern was found in 16 patients (38.1%) and moderate in 2 patients (4.8%). Small airway obstruction was detected in 17 patients (37%) in the moderate group and 16 patients (38.1%) in the severe group (**Table 4**).

33 patients from the severe group and 28 patients from the moderate group had echocardiography in the post-discharge system. Conventional echocardiography parameters of the two groups were normal, there was no statistically significant difference. Left ventricular and right ventricular functions were normal. Right atrial and ventricular sizes were within normal limits, but were larger in the severe group than in the moderate group. Tissue Doppler tricuspid S wave was detected as 13.8 cm/sec in the moderate group and 14.05 cm/sec in the severe group. Pulmonary arterial pressures were 22.6±8.3 vs 22.1±6.8; p=0.8 was detected. TAPSE's were within normal limits, with no statistically significant difference (**Table 5**).

Table 5. Comparison of echocardiographic findings between the groups

	N (%) / Mean±SD / Median (%25-75)		p
	Moderate (n:28)	Severe (n:33)	
LVEDD, cm	4.8 (4.6-5.1)	4.9 (4.6-5.2)	0.97
LVESD, cm	3 (2.7-3.1)	3 (2.8-3.1)	0.8
LVEF %	65.7±2.4	64.5±2.8	0.09
Left Atrium, cm	3.6 (3.5-3.8)	3.7 (3.5-3.8)	0.69
IVS thickness, cm	1 (1-1.1)	1 (1-1.1)	0.4
PW thickness, cm	1 (0.9-1.07)	1	0.4
Aortic root, cm	2.5±0.2	2.4±0.2	0.79
RA Area, mm^2	10.8±3.1	11.9±2.2	0.15
RA mediolateral diameter, cm	3.3±0.2	3.4±0.2	0.16
RA apicobasal diameter, cm	3.6±0.2	3.7±0.2	0.06
RVEDD basal, cm	2.5 (2.4-2.6)	2.6 (2.4-2.7)	0.22
Mitral Inflow E	75.1±12.2	75±16.5	0.98
Mitral Inflow A	72.9±17	67.9±12.9	0.21
Tricuspid Annular S, cm/sn	13.8 (13.3-15.1)	14 (12.7-16.2)	0.67
SPAB, mmHg	22.1±6.8	22.6±8.3	0.8
TAPSE, cm	2.2±0.2	2.3±0.2	0.21

*Independent Samples T-Test, chi-square Test, Fisher's Exact Test, Mann Whitney-U Test *p<0.05 statistically significant. Continues variables are reported mean±SD. Categorical variables are reported n (%). Abbreviations: LVEDD: Left Ventricular End-diastolic Diameter; LVESD; Left Ventricular End-systolic Diameter; LVEF: Left Ventricular Ejection Fraction; IVS; Interventricular Septum; PW: Posterior Wall; RA; Right Atrium; RV: Right Ventricle; RVEDD: Right Ventricular End–diastolic Diameter; SPAB: Systolic Pulmonary Arterial Pressure; TAPSE: Tricuspid Annular Plane Systolic Excursion.

Table 4. Comparison of thorax computed tomography and pulmonary function tests findings between the groups

	N (%) / Mean±SD / Median (%25-75)		p
	Moderate	Severe	
Consolidation, n (%)	18 (39%)	26 (61%)	0.033
Infiltration, n (%)	15 (32%)	12 (28%)	0.68
Reticular fibrosis, n (%)	13 (28%)	9 (21%)	0.46
Pleural effusion, n (%)	1 (2 %)	1 (2.4%)	0.26
Honeycombing, n (%)	45 (97%)	40 (95%)	0.5
Nodule, n (%)	4 (8 %)	2 (4%)	0.46
Interstitial septal thickening, n (%)	7 (15 %)	14 (33%)	0.046
Cobble stone appearance, n (%)	8 (17 %)	11 (26%)	0.31
Pericardial effusion, n (%)	0 (0%)	1 (2%)	0.29
Pulmonary thromboembolism, n (%)	0	0	-
Air bronchogram, n (%)	4 (8%)	4 (9%)	0.89
FVC LT	3±0.8	3.5±0.8	0.41
FVC (%)	87.0±18.4	85.1±16	0.62
FEV 1 LT	3 (2.2-3.7)	3.2 (2.7-3.5)	0.54
FEV 1 (%)	99.5 (86-103.7)	90.5 (82-104)	0.24
FEV 1/FVC (%)	93 (87-96.7)	91.6 (84-96.1)	0.35
PEF LT	6.8±2.5	7±2.6	0.74
PEF (%)	84.8±23.7	85.2±25.8	0.94
FEF 25-75 (%)	117 (94.5-126)	105 (85-123)	0.29
Obstruction on PFT, n (%)	1 (2.2%)	1 (2.4%)	0.94
Restriction on PFT, n (%)			0.21
Mild	10 (21.7%)	16 (38.1%)	
Moderate	2 (4.3%)	2 (4.8%)	
Small Airway Disease on PFT, n (%)	17 (37%)	16 (38.1%)	0.89

*Chi-square Test, Fisher's Exact Test *p<0.05 statistically significant. Continues variables are reported mean±SD). Categorical variables are reported n (%).
Abbreviations: FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume on 1st Second; PEF: Peak Expiratory Flow; FEF 25-75: Maximal mid expiratory flow between 25-75%; PFT: pulmonary function test.

DISCUSSION

The patients included in our study had no comorbidities and were treated for moderate to severe COVID-19 pneumonia. The patients were treated with the treatment protocol in the first wave of the pandemic and they did not have any vaccines. Conventional echocardiography and PFT parameters were similar in the two groups and there was no statistically significant difference. In pulmonary function tests, obstructive type pathology was found in 2 patients, restrictive type pathology was found in 26.4% patients and small airway obstruction was detected in 29% patients.

In the first wave, high mortality rates were seen in the elderly population. With the increase in vaccination studies, the spread of the virus has shifted from the elderly patient group to the younger patient group. COVID-19 vaccines protect against serious illness, hospitalization and death (15,16). Our study has demonstrated the possible level of cardiopulmonary function in unvaccinated healthy individuals with moderate to severe COVID-19 pneumonia in the first month after discharge.

Echocardiography is a cost-effective device used to evaluate cardiac structure and functions. Studies have shown that patients with COVID-19 pneumonia may have right and left ventricular dysfunction and an increase in pulmonary artery pressure (17). In our study, we found that the results of conventional echocardiography of our patients were within normal limits.

COVID-19 infection causes damage to alveolar epithelial cells and endothelium together with fibroproliferation. As a result, it may cause lung fibrosis and pulmonary hypertension in the long term (18,19). In studys conducted in patients with community-acquired pneumonia, it was found that the risk of active cardiovascular disease was significantly increased for several years after hospitalization (20,21). There are still healthy individuals in our society who are not vaccinated. With the removal of pandemic measures, these complications may develop as a result of serious infection in this patient group.

SARS-CoV-2 causes systemic inflammation and coagulopathy (22). In autopsy studies performed on patients who died due to COVID-19 infection, the incidence of micro and macrothrombus was found to be 58% (23). Although some patients received anticoagulant therapy, thromboembolic complications were observed (24,25). Our patients received subcutaneous heparin treatment at admission and at discharge. We did not detect pulmonary thromboembolism in any of the patients but microthrombi may still have formed.

In PFTs performed on patients with COVID-19 pneumonia during their discharge, it was determined that the most common anomaly in lung functions was deterioration in diffusion capacity (8,26). In another study conducted one month after discharge, patients' PFTs also found slight changes in lung function (27). Long follow-up studies of patients with SARS have shown that lung diffusion capacity may remain abnormal within 3 years after recovery in some patients (28). We did not have the data for lung diffusion capacity but we found mild obstructive and restrictive abnormalities in PFTs on first month after discharge. We suggest that the long term evaluations of patients with abnormal PFTs may enlighten whether COVID-19 has a permanent negative effect on pulmonary functions or not.

In the pulmonary function test performed in the 3rd year of 71 patients with SARS pneumonia who received high-dose steroids, restrictive-type pulmonary function test impairment was detected in 22%, while restrictive-type pulmonary dysfunction was not detected in any patient at the 15th year. Mild diffusion capacity deterioration was detected in 1/3 of the patients at 15 years. It was thought that less fibrosis was seen in the patients due to the use of high-dose steroids (29). Our patients did not receive intensive steroid treatment and at the end of the first month, we found restrictive type disorder in 26.4% of their PFTs.

Limitations

The number of patients in our study was small since most hospitalized patients had comorbidities. If the number of patients was more, statistically more significant results could have been obtained. Most of the patients did not have baseline echocardiograms. If they had baseline echocardiograms, we could have the opportunity to compare them with echocardiograms done at one month post-discharge. In addition, if the patients had high-level echocardiographic analyzes and cardiac MRIs, the cardiac involvement of COVID-19 could have been revealed more clearly.

CONCLUSION

The long-term effects of COVID-19 infection are not fully known. We think that especially in the first wave of the pandemic, those who have had a severe illness may be at greater risk for long term efects of COVID-19. Detailed evaluation of the patients with prolonged respiratory symptoms might help to detect the cardiopulmonary functional disturbances. Vaccines are necessary to prevent serious COVID-19 infection, but due to decreased efficacy of vaccines and increased virus variants, effective treatment study must continue.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Ministry of Health's Scientific Research Platform, and the study was initiated with the approval of the Umraniye Training and Research Hospital Clinical Researches Ethics Committee (Date: 11.06.2020, Decision No: B.10 .1.TKH.4.34.H.GP.0.01/217).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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