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Post-recovery pulmonary function test and thorax CT correlations in COVID-19 survivors

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Abstract

Aim: Long-COVID has been described as persistent symptoms involving multiorgan systems in COVID-19 survivors. This single-centred study investigated the correlation between pulmonary function test (PFT) and thorax computed tomography (CT) results in COVID-19 survivors after six months of follow-up period.

Material and Methods: Patients recovered from COVID-19 aged between 18 and 50 years were included in this study and divided into two groups according to PFT results as patients with normal PFT results (PFT normal; n = 74) and with PFT results with restrictive pattern (PFT restrictive; n = 12). The primary aim of this study was to try to predict the prognosis of long-term chronic pulmonary system diseases using pulmonary function test, thorax CT and laboratory findings in the sixth month after recovery.

Results: There were no significant differences between the patients in PFT normal and PFT restrictive groups in terms of symptoms and CT findings at admission. On the other hand, the rate of dyspnoea and exertional dyspnoea was significantly more pronounced in patients in PFT restrictive group, while there were no significant differences between CT findings. Both univariate and multivariate regression analyses showed that percent forced expiratory volume in one second (%FEV1) and percent forced vital capacity (%FVC) results are associated factors in discriminating normal and PFT results with restrictive pattern in COVID-19 survivors.

Discussion: PFTs should be included in follow-up evaluations of COVID-19 patients in order to elucidate the post-COVID-19 pulmonary abnormalities.

Keywords

Computed Tomography, COVID-19, Long-COVID, Pulmonary Function Test

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Introduction

Coronavirus Disease 2019 (COVID-19), caused by the novel severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2), emerged from China in December 2019 and has continued to affect the humanity worldwide as an exceptional challenge [1]. The route of infection of the virus is mainly via air droplets and aerosol [2]. Its presentations include symptoms of respiratory illness together with other symptoms including fever, cough, myalgia, shortness of breath, loss of taste / smell in symptomatic individuals [3, 4], while substantial number of individuals were reported as asymptomatic COVID-19 cases [5]. Since its emergence, a remarkable effort has been made for the diagnosis, management, treatment, and prevention of the disease. However, chronic impacts of the disease on the patients still remain elusive. Long-lasting symptoms may be present in patients after recovery from severe or moderate COVID-19 [6], however, individuals showing "mild" symptoms who were stated to require care at home and isolation with the expectation of the recovery from infection also had post-COVID-19 syndrome (Long COVID) [7, 8]. The term of long COVID is used to describe persistent symptoms with the involvement of multiorgan systems after recovery from the acute infection [9, 10].

Many individuals that were recovered from COVID-19 shared their experiences through social media, blogs, and traditional media. Aside from these anecdotal indications, several studies about long COVID were published. However, more studies regarding the long-lasting effects of COVID-19 are needed. The primary aim of this study was to try to predict the prognosis of long-term chronic pulmonary system diseases in patients that were diagnosed with COVID-19 before May 2020 in the emergency room (ER) of a tertiary Education and Research Hospital emergency service serving as Pandemic Hospital and recovered after treatment by analysing the pulmonary function test, tomography, and laboratory findings on the sixth month after recovery. The secondary aim of this study was to identify the symptoms that affect the quality of life of patients to take early measures for chronic diseases that may arise in the future.

Material and Methods

Study group and design

The single-centred study was conducted between 01/01/2021 and 01/02/2021 after approval of the local Clinical Research Ethics Committee (date: 22.12.2020, number: 3072). All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments. Authors have complied with the international guidelines, the "Regulations on Pharmaceutical Research," enforced by The Ministry of Health of Turkey published in the 27089 numbered Official Journal dated 23 December 2008 and also with other regulations published at a later date. Our study included a total of 86 patients who admitted to ER in our hospital, which served as a pandemic hospital. The inclusion criteria were being aged between 18 and 50 years, having a positive COVID-19 polymerase chain reaction (PCR) test result before May 2020, having no known pulmonary and / or neurological and / or neuropsychiatric disorders, being non-smoker and having a complete medical record. Patients who were younger than 18 years or older than 50 years, with negative PCR test result, without complete medical record, with known pulmonary and / or neurological and / or neuropsychiatric disorders and smokers were excluded from the study. All patients included in this study were either transferred from ER to the service or discharged and none of the patients were hospitalized in the intensive care unit (ICU).

Patients' information was accessed from the hospital electronic information system. Medical records of the volunteers after the first admission, before May 2020, including complete blood counts, comorbidity, laboratory parameters, computed tomography (CT) results and demographical characteristics were also accessed and investigated. The patient group who met the inclusion criteria were contacted by phone and informed about the study, and the tests and analyses to be performed were explained in detail. Patients who volunteered to participate in the study were invited to the hospital during the weekdays with a maximum of five patients for each day with an appointment. Written informed consents of the patients were obtained on arrival to the hospital for their anonymized information to be published in this article.

Patients' demographical characteristics (age, gender and whether they were healthcare workers or not), complaints present at the first admission, treatment that they received were recorded. Moreover, complete blood count, blood biochemistry (glucose, urea, creatinine, lactate dehydrogenase (LDH), C-reactive protein (CRP)), d-dimer, ferritin, troponin, arterial blood gas measurements (pH, CO2 and SO2) were performed at the first admission and six-months follow-up. Thorax CT results obtained at the first admission and six-months follow-up were compared. Symptoms that patients experienced within six months after recovery were also recorded.

Pulmonary function test (PFT) was performed on the patients at the first admission and six-months follow-up by an experienced technician using the device Spirolab III with Colour LCD (MIR; Rome, Italy). Patients were evaluated based on the percent predicted forced expiratory volume in one second (FEV1%), percent predicted forced vital capacity (FVC%), FEV1/FVC and forced expiratory flow at 25-75% of the pulmonary volume (FEF25-75) according to the guidelines published by American Thoracic Society [11], and were required to have FEV1/FVC > 70% to eliminate any obstructive lung disease. PFTs were conducted triplicates and the most accurate tests were used for the analysis.

Statistical Analysis

Statistical analyses were conducted using SPSS version 27.0 (IBM, USA). In descriptive statistics, mean, standard deviation (SD), median, minimum and maximum values, frequency and ratio were used. The Kolmogorov-Smirnov test was used to evaluate the distribution of the data. Quantitative independent data were analysed using an unpaired t-test in case the normal distribution criteria were met, or the Mann-Whitney U test in case they were not normally distributed. Qualitative independent data were analysed using the Chi-square test, and when the conditions for the Chi-square test were not met, Fischer's exact test was used. Univariate or multivariate logistic regression analyses were performed to investigate the level of effect.

Results

The mean age of the patients was 36.9 ± 9.1 years and most of the patients admitted to the ER were females (57%; Table 1). Cough was the most pronounced symptom at the admission (62%) and this was followed by fever (57%) and dyspnoea (43%; Table 1). The other symptoms are weakness-myalgia (36%), throat pain-headache (16%), sputum (7%), diarrhea (6%) and loss of odour-taste (6%). The general condition of the most of the patients at the admission were good (Table 1), while CT findings of the patients were found as severe (43%) and moderate (42%; Table 1; Figure 1 and 2). Most of the patients admitted to ER were outside of the healthcare sector (76%; Table 1). Treatment of the 48 patients continued in the clinics after discharge from ER (Table 1). The mean duration of the hospital stay was 3.6 ± 3.6 days (Table 1).

In the group of PFT restrictive, FEV1% and FVC% values were significantly lower than the group with PFT normal ($p<0.05$), while FEV1/FVC and FEF25-75 values did not differ ($p>0.05$) (Table 2). The ratio of male patients in the group of PFT restrictive was significantly higher than the group of PFT normal ($p<0.05$). There were no differences in age between the two groups ($p>0.05$). On the other hand, other parameters such as symptom at the admission, general condition at ER admission, CT findings at the admission (Figure 1a, c and Figure 2a), duration of the hospital stay, and medical treatment of the patients did not differ between the groups. On the other hand, there were no differences between two groups with regards to complete blood count, blood biochemistry, d-dimer, ferritin, troponin, and arterial blood gas measurements at the first admission and six-months follow-up ($p>0.05$).

Persistent symptoms were observed in 28 patients (32.5%). In the PFT restrictive group, the rate of persisting symptoms was significantly higher than in the group with PFT normal group six months after the first admission ($p<0.05$; Table 2). Among persistent symptoms, rates of dyspnoea on exertion and dyspnoea were significantly higher in PFT restrictive group than in the normal PFT group found at month six of the follow-up ($p<0.05$), however, rates of other persisting symptoms including diarrhea, loss of odour-taste and cough investigated on the follow-up examination did not differ between the groups ($p>0.05$; Table 2). On the other hand, the presence of abnormal CT findings (fibrosis, small nodule, atelectasis, pleural thickening, attenuation, emphysema, traction bronchiectasis, interlobular thickening) as well as the type of the abnormality when examined six months after the first admission did not differ between the groups ($p>0.05$; Figure 1b, d and Figure 2b). The level of effects of gender, FEV1%, FVC%, persistent symptom six months after the first admission and dyspnoea on exertion six months after the first admission were investigated using both univariate and multivariate logistic regression models. In the univariate model, significant effects of gender, FEV1%, FVC%, persistent symptoms six months after the first admission and dyspnoea on exertion six months after first admission ($p<0.05$) were observed in the differentiation of group of patients in PFT normal and PFT restrictive (Table 3). On the other hand, in the multivariate model, FEV1% and FVC% were found to be significant and independently effective in the differentiation of patients in PFT normal and PFT restrictive

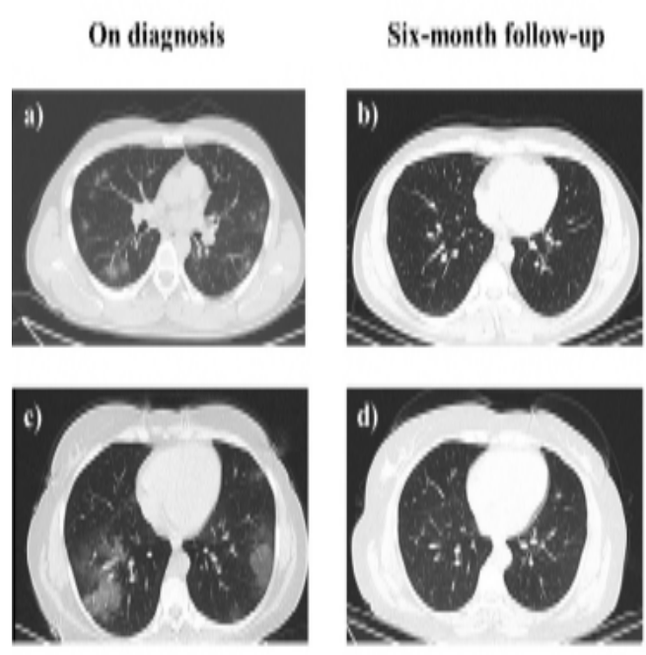


Figure 1. Representative CT images of two patients with normal PFT results. (a and b) CT image of a 27-year-old female patient obtained on arrival and on a six-month follow-up examination. (a) Subpleural scattered ground-glass areas were observed in both middle lobes and basal parts of the lungs and it was compatible with alveolar infiltration and (b) when compared with the CT image on the diagnosis, it was noted that all of the ground glass-dominated pneumonic infiltrates thought to be associated with COVID-19 in both lungs were

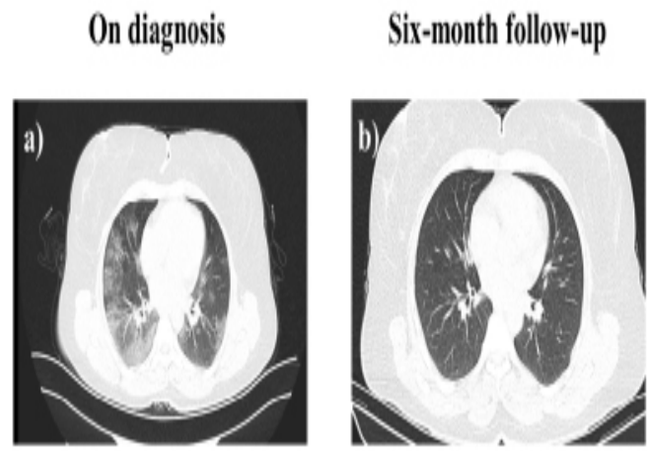


Figure 2. Representative CT images of a patient with PFT results with restrictive pattern. CT image of a 37-year-old female patient obtained on arrival and on a six-month follow-up examination. (a) In the bilateral lung parenchyma, areas of alveolar infiltration with multilobar patchy ground-glass density were observed. Findings were consistent with typical viral pneumonia. (b) When compared with the CT image obtained on diagnosis, ground-glass-dominated pneumonic infiltrates thought to be associated with COVID-19 in both lungs were regressed.

Table 1. Patient characteristics at the admission to ER and medical treatment that the patients received.

		Min - Max	Median	Mean ± SD /n (%)
Age		18.0 -52.0	37.0	36.6 ± 9.1
Gender	Male			37 (43)
	Female			49 (57)
Symptom at admission				
Cough				53 (62)
Fever				49 (57)
Dyspnoea				37 (43)
General Condition at ER Admission	Good			84 (98)
	Moderate			2 (2)
CT findings at the admission	Severe			37 (43)
	Moderate			36 (42)
	Mild			13 (15)
Healthcare employee	Yes			21 (24)
	No			65 (76)
Reason of Hospitalization Termination from ER	Discharge			38 (44)
	Transfer to the clinics			48 (56)
Duration of hospital stay (Days)		0.0 -15.0	5.0	3.6 ± 3.6

CT: Computed tomography; ER: Emergency room.

groups (p <0.05; Table 3).

Discussion

Long COVID has been reported in patients recovered from COVID-19. In the present study, we investigated the pulmonary function and long-lasting symptoms in COVID-19 patients six months after recovery. Although the condition of the patients was generally improved, patients with PFT results with restrictive patterns at the evaluation still had dyspnoea and dyspnoea on exertion at a significantly higher rate than the patients with normal PFT results six months after recovery. Moreover, FEV1% and FVC% were found to be effective in the differentiation of post-COVID patients in PFT normal and PFT restrictive groups in both univariate and multivariate logistic regression models.

In this study, around one-third of the patients showed long-lasting symptoms that was consistent with previous studies [12, 13]. Although fatigue was the most common persistent symptom after recovery from COVID-19 in previous studies [12-15], in our study, participants did not report fatigue as long-lasting symptoms in both PFT normal and PFT restrictive groups. On the other hand, most common long-lasting symptom was dyspnoea on exertion in both groups in our study group

Table 2. After six months of follow-up, PFT results and characteristics of the patients at admission, as well as persistent symptoms and CT findings, according to PFT results.

PFT Results						
		Normal		Restrictive		P value
		Mean ± SD / n (%)	Median	Mean ± SD / n (%)	Median	
FEV1%		93.6 ± 8.6	93.0	79.0 ± 6.0	79.0	0.000 [t]
FVC%		94.6 ± 9.1	93.0	78.8 ± 4.9	79.0	0.000 [t]
Symptom at admission						
Cough		46 (62.2)		7 (58.3)		0.731 [X²]
Fever		42 (56.8)		7 (58.3)		0.919 [X²]
		Normal		Restrictive		P value
Presence of persisting symptoms after six months	Absent	60 (81.1)		3 (25.0)		0.000 [X²]
	Present	14 (18.9%)		9 (75.0)		
Persisting symptoms after six months						
Dyspnoea on exertion		7 (50)		7 (78)		0.000 [X²]
Dyspnoea		0 (0)		3 (33)		0.002 [X²]
Control CT at month six	Normal	37 (50)		4 (33)		0.284 [X²]
	Other	37 (50)		8 (67)		
Control CT findings at month six						
Fibrosis		21 (57)		4 (50.0)		0.726 [X²]
Small Nodule		14 (38)		5 (62.5)		0.078 [X²]

CT: Computed tomography; ER: Emergency room; FEV1%: Percent forced expiratory volume in one second; FVC%: Percent forced vital capacity; PFT: Pulmonary Function Test. (Statistical analyses: t: Student's t test; m: Mann-Whitney U test; X^2: Chi-Square test)

Table 3. Results of logistic regression analysis

	Univariate model			Multivariate model		
	OR	%95 CI	P value	OR	%95 CI	P value
Gender	0.20	0.05 - 0.81	0.024			
FEV1%	0.57	0.40 - 0.83	0.003	0.67	0.44 - 0.98	0.037
FVC%	0.54	0.36 - 0.79	0.002	0.58	0.37 - 0.91	0.018
Persistent symptoms six months after the first admission	Ara.86	3.08 - 53.74	0.000			
Dyspnoea on exertion six months after first admission	13.40	3.35 - 53.63	0.000			

FEV1%: Percent forced expiratory volume in one second; FVC%: Percent forced vital capacity.

and dyspnoea and dyspnoea on exertion was found to be significantly higher in the PFT restrictive group. Dyspnoea has been implicated to affect the quality of life of the patients after recovery from COVID-19 [16]. Moreover, in several other studies, patients reported declined quality of life [12, 17].

One of the limitations of our study was the relatively small sample size of the single-centre cohort. Moreover, performing baseline PFTs, such as PFT on the day before discharge, might have been relevant to observe the recovery of the patients within the follow-up period. Longer- term studies are required to assess the pulmonary sequelae in COVID-19 survivors.

In our study, we observed that CT results in both PFT normal and PFT restrictive groups did not differ. On the other hand, we observed that FEV1% and FVC% were associated with the long-term complications of COVID-19 after recovery. Studies highlighting the PFT data have been very limited in post-COVID-19 patients [17-19]. As previously suggested [17], our study suggests that PFT can be performed in patients recovered from COVID-19 and should be included in the follow-up procedures of the patients in order to elucidate the post-COVID-19 pulmonary abnormalities.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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