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Clinical, radiological outcomes and pulmonary function tests in patients recovered from COVID-19 in a three-month follow-up

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Abstract

Introduction: Long-term pulmonary consequences of coronavirus disease 2019 (COVID-19) are unknown.
Objectives: The aim of this study was the clinical and radiologic consequences and pulmonary function test in the cured COVID-19 patients in a three-month follow-up.
Patients and Methods: Patients with laboratory-confirmed COVID-19 infection by a reverse transcription polymerase chain reaction (RT-PCR) assay were recruited in this prospective descriptive epidemiological study. Computerized tomography (CT) scan and blood oxygen measurement were performed before and three months after discharge for all the patients. Spirometry test and 6-minute walk test (6MWT) were conducted to determine the levels of dyspnea and persistent respiratory symptoms.
Results: Eighty patients were recruited in this study. At the 3-month follow-up, oxygen saturation was higher than the time of discharge from the hospital. Chest CT scan showed abnormal results in 66.3% of patients. The pulmonary function test results indicated that only 27 (35.75%) of patients had abnormal test. The median distance in the 6MWT was 325 meters (interquartile range, 96-480 m).
Conclusion: Follow-up of COVID-19 patients revealed radiological abnormalities in most cured COVID-19 patients, indicating the need for more extended follow-up periods for investigating the long-term consequences of COVID-19.

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Introduction

Novel coronavirus occurred in viral pneumonia cases in Wuhan, Hubei province in 2019. It received the official name of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the World Health Organization (WHO). SARS-CoV-2 was quickly spread in and out of Hubei province and other countries in the world and tremendously increased the infected cases across the world (1). In diagnosing patients with COVID-19, the chest computerized tomography (CT) scan had higher sensitivity than Chinese test kits. Common chest CT scan finding, including ground glass opacity, multifocal patch consolidation, and interstitial changes with peripheral distribution (2). It should be mentioned that the novel coronavirus may lead to complications in each system of the body. Respiratory complications are the most known one, influencing disease progression and patient prognosis. Various studies have reported the involvement of the cardiovascular system, which can appear as arrhythmia, pericarditis, cardiomyopathy, emboli and even shock (3).

Key point

In a study on 80 COVID-19 patients with a three-month follow-up, we found radiological abnormalities cured in most of the patients.

In the acute phase of the disease and during the first days, ground-glass opacity (GGO), as the dominant finding, can be observed in chest CT scans. During the second week of the disease, the GGO index directs toward consolidation that decreases again with the onset of recovery. Finally, parenchymal changes in lungs are eliminated in some patients completely. Although the virus eradicates in the cured patients, mechanisms underlying fibrosis still remain active and may result in progressive and irrevocable changes in very few patients. Even a little non-progressive fibrosis can increase side-effects and mortality rate, particularly in elderly patients and those

with a prior history of cardiovascular disease. Secondary infections following viral pulmonary infection include a major known side-effect caused by the facilitation of colonization and proliferation of bacteria in the respiratory tracts (4,5). Accordingly, secondary infections are reported after COVID-19 (6). In addition to secondary bacterial infection, fungal infections, such as various verities of aspergillus, especially aspergillus fumigatus, can affect the disease process (7). Acute respiratory distress syndrome (ARDS) is a major common side-effect of COVID-19, which is observed in 20-40% of patients with severe respiratory symptoms (8). Pulmonary cavity is not considered the common radiologic findings of the COVID-19 index and even based on the Radiological Society of North America (RSNA) criteria, cavitary lung lesions make other differential diagnoses more likely than COVID-19 (3).

The COVID-19 patients are susceptible to the development of pneumothorax and pneumomediastinum. These side-effects are particularly more prevalent among patients with underlying diseases, such as chronic obstructive pulmonary disease (COPD) or those treated with an artificial respiration device, which might be caused by the reduced capacity of the involved lung and susceptibility to barotrauma due to artificial respiration. Timely diagnosis and appropriate treatment of such side effects significantly decrease morbidity and mortality rates (9).

Objectives

Although in many patients, complete recovery of pulmonary findings is observed; however, complications from COVID-19 are seen in some patients as well. Respiratory complications are one of the most well-known manifestations that can affect the course of the disease and the patient's prognosis. Therefore, this study aimed to investigate the clinical and radiological consequences and pulmonary function tests in cured COVID-19 patients in a three-month follow-up after treatment in Ahvaz.

Patients and Methods

Study design

The present study was a prospective descriptive epidemiological study. The subjects included patients with COVID-19 who were referred to Ahvaz Jundishapur University of Medical Sciences teaching hospitals in 2021 and then to pulmonary clinic for follow-up three months later. Data collection instrument was a questionnaire which demographic information including age, gender, patient's clinical information, and the results of radiography images of pulmonary involvement were recorded.

Chest CT scan

All the patients underwent basic and controlled chest CT scans before and three months after discharge. According to the CT scan images, chest CT severity score was also calculated based on the degree of involvement of the lung lobes as 0%, 1-25%, 26-50%, 51-75%, and 76-100% (10).

Spirometry and pulmonary function tests

For all the participants pulmonary function test was measured at the end of the three months. Spirometry included the measurement of FEV1 (forced expiratory volume in 1 second), FVC (forced vital capacity), FEV1/FVC and forced mid-expiratory flow (FEF25-75%)

The patients' saturation pulse O_2 (SpO_2) was examined and recorded both at time of discharge and three-month after discharge. Six-minute walking distance test, was employed to investigate dyspnea level, persistent respiratory symptoms, and activity limitation three months later. Parameters such as heart rate, oxygen level (SpO_2 and heart rate) and distance were examined at the end of six minutes walking test.

Statistical analysis

The findings were reported based on frequency, frequency percentage or mean, and standard deviation. The *t* test and repeated measures were used to compare the two groups. SPSS statistics version 16 was employed to analyze the data. The significance level was considered less than 0.05.

Results

A total of 80 patients (34 women and 46 men) participated in the study**.** The average age of the patients was 59.1±11.9 years. Around 56.2% of patients had no underlying diseases. About 26.2% of the patients suffered diabetes, 11.2% had hypertension, and 6.2% had history of pulmonary diseases. The average level of O_2 saturation at the time of discharge and three months later were 92% and 96.4%, respectively. Data analysis showed that levels of O_2 saturation was significantly different between them ($P=0.02$; Table 1).

Chest CT scan findings at discharge time and three months later were shown in Table 2. At discharge time, 61.25% of patients had pulmonary involvement of 26%-50%. Moreover, 25% of them had 51%-75% of pulmonary involvement; 7.5% were with more than 75% and the least frequency (6.25%) related to 1%-25% of pulmonary involvement. Chest CT scan findings three months after discharge showed that 27 participants (33.7%) had normal CT scan. In 41 individuals (51.3%), pulmonary involvement was 1%-25% and eight individuals (10%) had 26%-50% of lung involvement. The highest degree of involvement was seen in four patients with more than 50% pulmonary involvement (Table 2). The CT results showed a decrease in ground glass opacities, whereas fibrosis gradually increased in the form of sub-pleural line, fibrous stripes and partially traction bronchiectasis.

Accordingly, pulmonary function test was conducted for patients. The test results showed that 66.25% of the patients had normal spirometry and only 27 patients (33.75%) had abnormal spirometry. The levels of FEV1,

Table 1. Patients' blood oxygen saturation in discharge and three-month later

Variables	Lowest	Highest	Mean	SD	*P* value
Blood oxygen at discharge (%)	87%	96%	92.08%	2.02	0.02
Blood oxygen 3 months after discharge (%)	88%	99%	96.41%	1.66	

FEV1/ FVC and FVC in these 27 patients (patients with abnormal pulmonary function test results were shown in (Table 3).

After three months of discharge, 6-minute walk test (6-MWT) was conducted. The minimum and maximum results of distance were 96 and 481 meter in this study. The mean distance was 325.4 ±106.2 meter. Moreover 22 patients (27.5%) had distance more than 400 meter and three patients showed decreased O_2pulse saturation <90%. Heart rate level before and after the 6MW test was shown in Table 4.

Discussion

The present study aimed to evaluate the clinical and radiological consequences and pulmonary function tests in the cured COVID-19 patients in a three-month follow-up after treatment. A total of 80 patients were examined in this study.

Concerning the underlying diseases, the analysis revealed that 56.25% of patients did not have any underlying diseases, 26.25% suffered from diabetes, 11.25% had hypertension and 6.25% had underlying respiratory disease. In 2020, a meta-analysis on the prevalence of underlying diseases among COVID-19 patients demonstrated that the most common underlying diseases in these patients were hypertension , cardiovascular disease and diabetes (11).

Chest CT scan was carried out for all the patients in the present study before and three months after discharge. At the time of discharge, 61.25% of the patients had 26%-50% pulmonary involvement, 32.5% more than 50%, and the rest of them (6.25%) had 1%-25%. We found that 33.7% of the patients had normal CT scan results three months after discharge. Pulmonary involvement was observed in the rest of the patients. The degree of this involvement was varied. The highest degree of involvement was observed in only four patients with more than 50% pulmonary involvement. Furthermore, 41 patients (51.3%) had 1%-25%, 8 patients (10%) 26%-49% pulmonary involvement. The results of our study revealed that radiographic images have improved with quarterly follow-up; however, this time is not enough for everyone. Besides, more severe pulmonary involvements were more prone to have pulmonary residuals in chest CT scan. In spite of the residual involvement in the CT scan of 66.3% of patients, the pulmonary function test (spirometry) was abnormal in just 27 patients (33.75%).

Table 2. The results of patient CT scan three months after discharge

Chest CT scan findings	At discharge time No. (%)	After three months later No. (%)
Normal	0 (0)	27 (33.7)
1-25%	5 (6.25)	41(51.3)
26-50%	49 (61.25)	8 (10)
51-75%	20 (25)	4 (5)
>75%	6 (7.5%)	0

Table 3. Pulmonary function test results in patients with abnormal spirometry

Variables	Lowest	Highest	Mean	SD
FEV1 (%)	44	85	64.52	11.27
FEV1/FVC	67	131	84.21	14.75
FVC (%)	40	112	63.92	14.59

FEV1, Forced expiratory volume in 1 second; FVC, forced vital capacity.

Lerum et al in Norway, in a three-month follow-up of 113 COVID-19 patients, sowed the mMRC (Modified Medical Research Council) Dyspnea Scale was >0 in 54% and >1 in 19% of the participants. Moreover, FEV1 and FVC of the patients were in a normal range, while diffusing capacity for carbon monoxide (DLCO) was reduced in 24% of participants. Ground-glass opacities with >10% distribution in at least one of four pulmonary zones were present in 25% of participants, while 19% had parenchymal bands on chest CT. However, intensive care unit (ICU) survivors had more CT scan abnormalities and lower performance to do daily activities three months after discharge (12). The finding of the above study is in line with the present study.

Moreover, another study by Fan et al, which examined twelve patients with severe pulmonary involvement who needed to be hospitalized in ICU. The average time of investigating radiologic findings in these patients was about 56 days after the onset of symptoms. According to the lung CT scan after three months, despite relative healing of lesions of the acute phase, such as GGO and consolidation, lung parenchymal changes were still observable mostly as fibrotic findings (13). This finding is in line with our study.

Daher et al have examined 33 COVID-19 patients six weeks after discharge who were hospitalized without need

Table 4. Heart rate level before and after the 6MW test

Variables	Lowest	Highest	Mean	SD	*P* value
HR Before (6-MWT) test	60	117	86.06	13.97	0.001
HR After (6-MWT) test	68	132	99.00	15.52	

HR, Heart rate; 6-MWT, 6-Minute walk test.

for mechanical ventilator. Body plethysmography, DLCO, analysis of blood gas (ABG), and 6MWT, echocardiography and laboratory tests were also conducted. Follow-ups after discharge showed no thromboembolic complications in the patients. Eleven patients (33%) suffered from dyspnea, eleven (33%) patients had coughs and fifteen patients (45%) suffered from fatigue. Pulmonary function test revealed no limitation except partially decreased in DLCO. There were no echocardiographic disorders and 6MWT decreased in the majority of the patients without oxygen desaturation (14). Another study has also been performed by Strumiliene et al on the pulmonary function, exercise capacity and the remained radiologic changes in a two-month follow-up of cured COVID-19 patients. Patients' follow-up detected the impairment of lung function in 24 patients (47.2%). Reduction of lung volume and DLCO was observed in fifteen patients (29.4%) and obstruction was observed in only one patient. Twelve out of 51 patients (27.3%) showed functional limitation in 6MWT and 9.1% revealed saturation with SO_2<90. During follow-up, the chest CT scan demonstrated various levels of abnormalities in 96.1% of the patients (15) .

Post-COVID-19 pneumonia changes are mainly consistent with severity pulmonary involvement. "Fibrotic-like" changes are potential precursors of fibrosis; however, there is a high probability that these will resolve over time. Imaging follow-up should be conducted after a delay to allow resolution of the reversible inflammatory process (16).

Most of the patients who overcome the SARS-CoV-2 infection do not present complications and do not require a specific follow-up especially mild to moderate form of diseases, nevertheless a significant proportion especially those who were admitted to hospital require clinical and radiological follow-up.

Our study had several limitations. Evaluation of other pulmonary function tests such as DLCO was not possible. The relationships between functional impairment and residual fibrotic changes remain unknown. The follow-up time in this study is short and further studies are warranted to clarify whether pulmonary abnormalities persist in the longer term.

Conclusion

In the present, follow-up of cured COVID-19 patients indicated that radiologic abnormalities persist in many cured COVID-19 patients. Thus, the follow-up of COVID-19 patients is essential to properly manage any long-term or emerging consequences. Various imaging methods, particularly chest CT scan, play a significant role in the primary diagnosis of the disease. Chest CT scan has multiple functions in the follow-up of the healing process and diagnosis of the possible secondary side-effects. Reducing or halting pulmonary side effects following COVID-19 infection is significant in improving the cured patients' quality of life.

Limitations of the study

Considering the limitations such as the non-cooperation of the patients in the follow-up and re-doing the breathing test on time, the low sample volume and the large drop in the sample collection, it is suggested that the study with a larger sample volume and a longer treatment period in order to give enough time for the emergence of therapeutic effect should be conducted.

Authors' contribution

Conceptualization: Hanieh Raji, Zahra Mehraban, Sahar Azizi Moghadam.
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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The institutional ethical committee at Ahvaz Jundishapur University of Medical Sciences approved all study protocols (IR.AJUMS.HGOLESTAN.REC.1399.139). Accordingly, written informed consent was taken from all participants before any intervention. This paper was extracted from the M.D., thesis of Sahar Azizi Moghadam (thesis #4297) at the department of internal medicine department. Besides, ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors.

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