Evaluation of the Pulmonary Function Test (PFT) in Patients Affected by Severe COVID-19 Pneumonia: 6 to 12 Weeks After Discharge

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Abstract- The most lethal adverse effect of COVID-19 is acute respiratory distress syndrome, which can lead to rapid death. This symptom even causes concern for patients who have recovered and have been discharged. Therefore, it is obligatory to test and monitor variations in their lungs' function after recovery. In this study, we evaluated the pulmonary function of 64 patients with severe COVID-19, six weeks to 3 months after discharge. Pulmonary function parameters were measured by spirometry and body box according to the criteria of the American Thoracic Society and under the supervision of an adult pulmonologist. According to the forced expiratory volume (FEV1)/forced vital capacity (FVC) ratio and total lung capacity (TLC) values, it was found that 3.1% of people had an obstructive pattern, 40.63% of patients had the restrictive pattern, and 6.25% of improved individuals showed a mixed pattern. Furthermore, the study of diffusion capacity of carbon monoxide (DLCO) index revealed that 13.3%, 25%, and 53% of cases had mild, moderate, and severe disorders of gas exchange, respectively. In addition, determining the maximum amount of inspiratory muscles (PI max) and expiratory muscles (PE max) disclosed that the rate of these two indicators in 62.5% and 71.88% of the subjects were less than 50%, respectively. In general, the results of the present study suggest that pulmonary function test and follow-up of patients' condition are not only recommended but seems to be essential after recovery due to the large percentage of patients with the restricted pattern a few weeks after recovery.

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Introduction

Respiratory infections are major reasons for demise that lead to the death of about 7 million people all around the world annually (1). Different types of viruses are responsible for these epidemics (2). COVID-19 is an example of those infections mentioned above that it is an emerging infectious disease caused by a virus called acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (3,4). The World Health Organization (WHO) (3,5) declared the outbreak of SARS-CoV-2 in March 2020 as a pandemic. Although research is still ongoing on the routes of transmission of this disease, various studies have shown that the main ways of transmission are through respiratory droplets and person-to-person contact (3,6). These respiratory droplets are airborne and spread to others via breathing, talking, sneezing, and coughing (7).

The most common symptoms associated with SARS-CoV-2 include fever, weakness, cough, and diarrhea.

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More than half of the patients report shortness of breath. Additionally, a small number of them have acute respiratory distress syndrome (ARDS). On the other hand, in many cases, this disease causes severe involvement of the respiratory system and has caused major complications in patients (6). Although most people with COVID-19 demonstrate mild symptoms, in 19% of cases the patient develops pneumonia, shortness of breath, infectious shock and even failure of other organs (8).

The lung is the most pivotal organ in respiratory diseases, especially COVID-19, which is affected by pollutants and infectious agents (9,10). The most important effects consist of destruction of the air sac epithelium, hyaline membrane formation, bleeding and capillary damage and increased fibrosis of the air sac wall, which eventually leads to fibrosis and increased pulmonary blood pressure (9). These clinical manifestations and findings even cause concern for patients who have recovered and have been discharged. Some patients may even experience lung disorders for several weeks or even years after discharge. Therefore, it is necessary to test and monitor changes in lung function after recovery.

Spirometry is one of the most vital and mutual tools used by pulmonologists in recent decades to screen patients and pulmonary function test (PFT) (11). In spirometry, important criteria of pulmonary function such as forced expiratory volume (FEV1), forced vital capacity (FVC) and FEV1/FVC, etc. are examined. In addition, by looking closely at the parameters and ratios obtained in spirometric and plethysmographic experiments, the main patterns of lung ventilation function can be identified, including natural, obstructive, restrictive and mixed patterns. Because PFT plays a vital role in determining the condition of the lungs and diagnosing various diseases such as asthma, chronic obstructive pulmonary disease (COPD) and chronic respiratory failure, in the present study the pulmonary function of patients with severe COVID-19, 6 to 12 weeks after recovery and discharge from the hospital has been thoroughly evaluated. Besides, the important spirometry indices mentioned above, the parameters of maximum inspiratory pressure (PI max) and maximum expiratory pressure (PE max), diffusion capacity of carbon monoxide (DLCO), residual volume (RV), total lung capacity (TLC), RV/TLC, COPD assessment test (CAT) score, MRC score, airway obstruction pressure (*P*:0.1) and oxygen saturation percentage were also examined.

Given the limited information on the pulmonary function in patients affected by severe COVID-19 pneumonia after recovery, in this study, we intend to review the results of PFT and patterns of lung involvement after discharge in patients with COVID-19 pneumonia.

Materials and Methods

Study design and patients

This descriptive cross-sectional study was conducted in collaboration with Hajar and Shahid Labbafinejad hospitals in 2020. Written informed consent was obtained from all participants, and they were completely informed about the procedure. The confirmed 64 patients who were hospitalized due to COVID-19 and severe lung involvement (patients whose lung involvement was at least 30%), six weeks to 3 months after discharge, were enrolled in this study. All participants received oral and written information concerning the study and gave oral and written informed consent before the interviews were conducted. This study follows the ethical principles of the Declaration of Helsinki.

Measurements

Patients' demographic information was collected by a standard questionnaire. Pulmonary function parameters were measured by spirometry (ZAN-GPI 300) and body box (ZAN 500 USB Body) according to the criteria of the American Thoracic Society and under the supervision of an adult pulmonologist. It should be noted that the subjects under study were non-smokers and were not employed in industries or occupations related to chemical agents, particulate matter, or other compounds that cause lung diseases.

Statistical analysis

After completing the questionnaires and performing spirometry, body box, and DLCO tests, the collected results were analyzed using SPSS software version 22 with Pearson correlation test at a significant level of 5%. Mean, standard deviation, maximum and minimum were also used to describe the data. In addition, the Excel environment is used to draw graphs.

Results

It should be noted that in the present study, 64 cured patients with COVID-19 pneumonia were examined within a period of 6 weeks to 3 months after discharge from the hospital. Of the 64 patients studied in this study, 12 were female, and the rest were male. The mean age of the subjects was 59.38 years. The minimum and

maximum ages of the participants were 41 and 90 years, respectively.

The mean maximal inspiratory pressure (PI max) and expiratory pressure (PE max), which indicate the strength of the respiratory muscles, were 42.7% and 41.7%, respectively (Table 1). One of the important parameters that was examined in this study was *P*:0.1. This index is used in acute respiratory failure to assess respiratory capacity and measure airway obstruction pressure. The minimum and maximum of this index in the study population were 40 and 216, respectively (Table 1). In addition to the above, in the present study, the DLCO index was used to assess the ability and function of the lungs to transfer gases into the bloodstream, which is estimated at an average of 118.5% (Table 1). Also, as shown in Table 1, in the present study, the levels of saturated oxygen, total lung capacity (TLC), the ratio of residual volume to total lung capacity and the CAT score and MRC score indices were examined for more accurate assessment of lung function. Among the mentioned parameters, the Global Initiative Group for Chronic Obstructive Pulmonary Disease (GOLD) has recommended two indicators, CAT score and MRC score, for the evaluation, diagnosis, and treatment of COPD, because pulmonary function alone is unable to describe various aspects of COPD. Therefore, GOLD recommends the use of CAT score and MRC score to evaluate the symptoms. The CAT score parameter is a tool for assessing and quantifying the quality of life-related to the health and burden of COPD patients, which is scored from 0-40. In this index, the ranges of 10-0, 20-11, 30-21, and 40-31 indicate mild, moderate, severe, and very severe clinical effects, respectively. In addition, the MRC score is scored between 4-0 due to the severity of shortness of breath. Therefore, as can be seen, the mean CAT score and MRC score in this study were scored 4±5.9 and 0.7±1.1, respectively, which shows that the situation of the study population in the present study was appropriate in terms of these parameters. In the present study, a strong significant direct relationship was observed between these two indicators ($P<0.05$).

Table 1. Mean age of the subjects along with statistical analysis of PFT parameters

Minimum	Maximum	Standard deviation±Average	Variable
41	90	11±59.38	Age
56	110	12.8 ±85.4	FEV1**%**
48	117	15.3 ±80.6	FVC**%**
65	90	5.5±79.7	FEV1/FVC**%**
15	72	15.5±42.7	PI max**%**
14	65	12.9±41.7	PE max**%**
40	216	49.6±102.8	*P*:0/1**%**
30	176	27.3±98.5	D_{LCO}**%**
60	287	50.6±118.52	RV**%**
54	130	19.7±84.8	TLC**%**
75	194	21.8±119.3	RV/TLC**%**
88	98	2.5±94.3	O2 saturation**%**
0	14	4±5.9	CAT score
0	3	0.7±1.1	MRC score

As can be seen in Table 1, the mean of FEV1 and FVC parameters, which are the most important parameters of volume and pulmonary dynamics, in the study population in this study were 85.4 and 80.6. One of the most important parameters to be examined in PFT is the FEV1/FVC ratio. The results of this study display that the maximum ratio was 90 and the minimum was 65, while the average ratio was 80%. Therefore, according to the results of this study and as seen in Figure. 1, 3.1% of people had the obstructive pattern, which means that in these cases, the FEV1 / FVC ratio was below 0.7 and TLC above 0.8.

In addition, because in 40.63% of people, the TLC was <0.8 and the FEV1/FVC ratio>0.7, it can be concluded that these people have a restrictive pattern. In addition, according to Figure. 1, in 25.6 % of people with TLC <0.8 and FEV1/FVC ratio <0.7, which indicates that these people have a mixed pattern.

In addition, as shown in Figure. 2, in 53% of patients, because the diffusion capacity of carbon monoxide

(DLCO) was below 80%, it indicates that these individuals have a mild gas exchange disorder in their lungs. DLCO in 25% of people was in the range of 80-60%, and in 13.3% of people was less than 40%, and therefore the gas exchange disorder is moderate and severe in them, respectively.

As the clinical symptoms of COVID-19 are very wide and different, one of the strengths of this study was to know the values of PI max and PE max in people hospitalized for COVID-19, 6 to 12 weeks after discharge. According to Figure. 3, 62.5% and 71.88% of the subjects had PI max and PE max below 50%, respectively. The results of the present study showed that there was a strong direct correlation between PE max index and two indices, MRC score and CAT score (P<0.05).

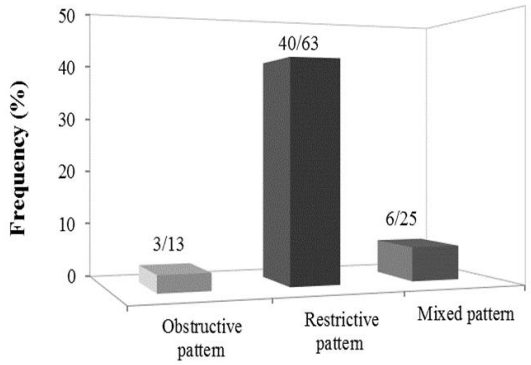

Figure 1. Percentage of spirometry disorders in patients admitted for COVID-19, 6 to 12 weeks after discharge

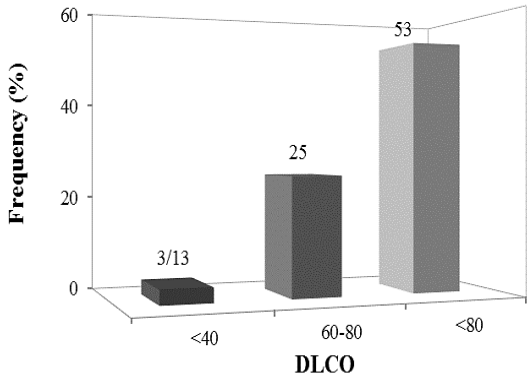

Figure 2. Percentage of DLCO in COVID-19 patients 6 to 12 weeks after discharge

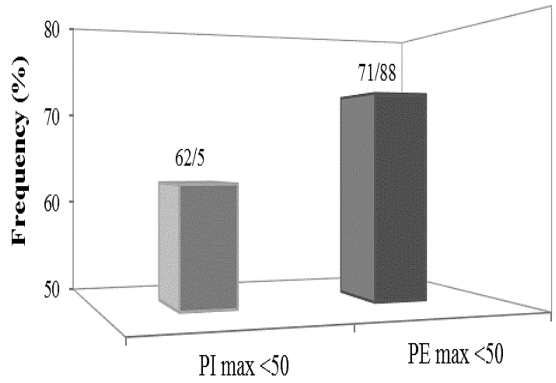

Figure 3. Status of PE max and PI max in patients admitted for COVID-19, 6 to 12 weeks after discharge

Discussion

How long PFT has been accomplished worldwide after discharge can affect how the results are performed. Most studies in the world examine patients' lung function one month after discharge, while the British Thoracic Society recommends three months after discharge to assess lung function (9). Therefore, in this study, the mentioned time period has been considered.

In the current study, the mean CAT score and MRC score showed that the situation of the study population was appropriate. A study conducted by Cheng *et al*., in 2019 showed that there is no significant relationship between these two indicators, but the CAT score is more appropriate and more sensitive than the MRC score for assessing the status and evaluation of COPD symptoms in patients (12). In the present study, a strong significant direct relationship was observed between these two indicators ($P<0.05$).

One of the most important parameters to be examined in PFT is the FEV1/FVC ratio. By evaluating the TLC values in individuals, the pattern of lung ventilation function can be obtained (9). In this study, 3.1% of people had the obstructive pattern, which means that in these cases the FEV1/FVC ratio was below 0.7 and TLC above 0.8. In contrast, in the study of Frija-Masson *et al*., (2020), only two people had an obstructive pattern, which was found to have underlying diseases such as asthma and sarcoidosis (13).

In addition, 40.63% of patients in our study had a restrictive pattern. In this model, the lung volumes, especially the FVC or the same volume of air that can be removed from the lungs with maximum power after a deep breath, is reduced. In this pattern, which is more common in people with severe pulmonary fibrosis, such as patients with asbestosis, the function of the pulmonary vesicles is mainly affected (14).

The results of this study revealed that the change in lung emission capacity is one of the most important complications of COVID-19, which continues even after recovery in some people. In the Frija-Mason study conducted in 2020, the functional characteristics of the lungs of 50 patients were evaluated 30 days after the onset of the disease, which, like the present study, showed the prevalence of DLCO changes in the relevant patients (13). In this regard, a study by Yao *et al*., (2020) on the autopsy of COVID-19 patients found that in addition to the destruction of the air sac structure that occurs to varying degrees in these patients, pulmonary fibrosis also could be expected. Therefore, these pathological changes can be the main cause of defects in carbon monoxide emissions in these patients even after recovery (15). In addition, the study by Bao *et al*., (2020), which studied the lung manifestations of COVID-19 patients through computer tomography (CT) scan findings, confirmed the lung damage caused by the disease, and the need to monitor the lung status of patients was emphasized after discharge (16). Furthermore, in the study of Klok *et al*., (2020), it is recommended to follow the pulmonary condition of patients after discharge, especially those patients who have slowly recovered or whose recovery was incomplete (17).

Another important factor in assessing lung function in determining the maximum amount of inspiratory (PI max) and expiratory (PE max) muscle force. These factors are used in the evaluation of patients with neuromuscular dysfunction or COPD (18). Therefore, in common neuromuscular diseases (such as amyotrophic lateral sclerosis) or poor motor function, both PE max and PI max indices are reduced. The PI max index decreases selectively with diaphragmatic impairment. In addition, patients with spinal cord injuries but healthy phrenic nerves also have low MRPs, which mainly affect PE max. Therefore, having information in this field is very important to determine the causes of respiratory symptoms, diagnosis, and prognosis of the disease (19).

To be concluded, a large percentage of patients with COVID-19 have a restricted pattern a few weeks after recovery. Additionally, the lungs of more than half of the subjects have problems in gas exchange after discharge. Therefore, monitoring the status of patients with various methods such as PFT is not only recommended but also seems to be necessary. Therefore, due to the different clinical manifestations from the onset of this pandemic until now, the need for similar studies with a larger statistical population and in an integrated manner, as well as regular PFT are strongly suggested to help specialists and other decision-makers in the treatment of the disease as well as post-discharge care strategy making.

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