Evaluation of Lung Function Tests in the Follow-up of COVID-19 Patients Discharged From Razi Hospital in Rasht, Iran

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Abstract

Background: The COVID-19 pandemic has been a significant concern for the global health community since its onset. This study aimed to evaluate lung function tests in the follow-up of COVID-19 patients discharged from Razi Hospital in Rasht, Iran, in 2020.

Materials and Methods: This cross-sectional study evaluated lung functional tests, including spirometry and the six-minute walking test (6MWT), in the follow-up of 239 hospitalized COVID-19 cases. All demographical and clinical data, along with the lung performance test results of the patients, were recorded, and statistical data were analyzed using SPSS, version 24.

Results: The mean age of the patients was 51.69 ± 13.98 years, and most of them were females. About 60.25% of patients had underlying diseases. The frequency of positive 6MWT tests during the first three, six, and nine months after discharge was 7.96%, 8.70%, and 14.29%, respectively. In the first trimester after discharge, the 6MWT test was more positive among females. In addition, forced expiratory volume (FEV1)/forced vital capacity (FVC) showed a significant positive relationship with diastolic blood pressure (DBP) and heart rate (HR). After six months, positive 6MWT results were significantly associated with older ages and underlying diseases. The amount of FVC was positively associated with DBP, distance traveled in the 6MWT test, and HR, but it was negatively related to age.

Conclusion: The findings revealed that older age, female gender, and underlying diseases were associated with positive 6MWT results, decreased pulmonary function, and higher DBP and HR.

Keywords: COVID-19, Lung function, Six-minute walking test

Introduction

Coronaviruses are a group of viruses with symptoms of infection ranging from the common cold to life-threatening acute respiratory syndrome. In the last two decades, two types of coronavirus, severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome-CoV, have been responsible for two significant epidemics. This pathogen has caused the COVID-19 pandemic, which was warned of in February 2020 (1). This acute respiratory tract infection is mainly transmitted through the airway. Although some patients may have no symptoms, studies indicate that most patients have a history of contact with a suspected or definite case of COVID-19. Fever, cough, fatigue, and shortness of breath are some of its symptoms (2-5).

The initial diagnosis of COVID-19 disease is based on clinical signs, laboratory evidence, and a computed tomography (CT) scan of the lungs and is finally confirmed by polymerase chain reaction. Extrapulmonary manifestations, such as the kidneys and heart, are associated with an increased risk of threatening vascular events (6-9). The most common CT findings reported in COVID-19 pneumonia are bilateral, multi-lobar, and subpleural areas of ground glass opacity with or without consolidations affecting the lower lobes (10-13). SARS-CoV-2 infection can occur in all age groups. However, the risk of disease, complications, and even death is higher in older people and men. In addition, studies have demonstrated that diabetes mellitus, hypertension (HTN), and lung diseases are mostly associated with morbidity and mortality. However, many patients are healthy young people with no history of underlying
Although various risk assessment protocols have been developed around the world for the rapid diagnosis of patients, none of them can detect latent hypoxia. Nonetheless, a simple 6-minute walk test (6MWT) can easily predict arterial blood oxygen depletion (17-19). Generally, it has been used to measure the response to medical interventions in patients with moderate-to-severe heart and lung diseases. The 6MWT also reflects the onset of the anaerobic metabolism due to secondary hypoxia and inadequate oxygen delivery (17, 20-23). In this study, lung functional tests, including spirometry and 6MWT, were evaluated in the follow-up of patients diagnosed with COVID-19 after discharge from Razi Hospital in Rasht, Guilan Province, Iran, in 2020.

Materials and Methods

Study Design and Patients

The present cross-sectional study included 266 hospitalized COVID-19 patients discharged from Razi Hospital, Rasht, in 2020. The 6MWT and spirometry tests were performed for all patients under the same condition. For the 6MWT, patients’ vital signs and blood oxygen saturation were measured by a pulse oximeter. Then, they were asked to walk a certain distance as much as possible, and the best practical walking time was estimated to be six minutes. At the end of the six minutes, arterial oxygen saturation was measured again. In case of oxygen saturation, a decrease of more than 3% of the baseline, or an oxygen saturation level of 94%, was considered positive. If the patient had symptoms such as lightheadedness, chest discomfort, fatigue, or shortness of breath, the test was stopped, an oxygen saturation check was performed, and the patient was asked to rest for a while. Further, for patients over 60 years of age, an oxygen relief check was performed at the end of three minutes, and if the conditions were expected, the test would be resumed. In addition, data such as age, gender, comorbidity, number of visits, walking length, remaining clinical symptoms, and stopping reasons for incomplete tests were recorded, along with vital signs and oxygen saturation before and after tests. These data were recorded in the second and third follow-ups. All patients with COVID-19 who were discharged from September 2020 to December 2020 were included in the study, and the coexistence of other respiratory diseases was considered an exclusion criterion.

Statistical Analysis

The statistical data were reported as numbers and percentages, means and standard divisions (SD), as well as medians and maximum and minimum levels by considering a confidence interval of 95%. Mann-Whitney U, Pearson chi-square, and Fisher’s exact tests were applied to evaluate the association between the variables. Data were analyzed with SPSS software (version 24) using repeated measures tests, and a significant level was considered less than 0.05.

Results

The mean age of 239 patients with COVID-19 was 51.69 ± 13.98 (18-85) years, and about 51.5% of them were females. Approximately 60.25% of patients suffered from comorbidities. Diabetes (35.42%) and HTN (23.61%) were the most frequent underlying diseases. The data related to the oxygen saturation data, heart rate (HR), and blood pressure (BP) are presented in Table 1.

The results of the 6MWT were positive in 7.96% of patients. This value was 8.70% and 14.29% in the second and third referrals, respectively (Table 2).

Nearly 12.88% of patients stopped the 6MWT test after the first visit. This increased to 13.04% and 14.29% in the second and third visits. Skeletal pain was the most common reason for stopping the test. Poor cardiac outputs and an extensive decrease in pulmonary capacity due to the inflammation of COVID-19 pneumonia or microthrombosis of the alveolus were the most important reasons for the 6MWT positive results. The average oxygen saturation in all three visits was about 97%. The 6MWT test did not stop due to the decrease in oxygen saturation to less than 94%. The patient’s HR during the 6MWT test in the two first visits was almost the same and varied from 84 beats per minute at the beginning to 96 beats per minute at the end. The amplitude of these changes was less in the third visit. Mean BP values increased significantly from the first to the third visit. However, it should be noted that the number of patients referred in the third round was much less than in the previous two rounds.

Based on the results of the present study, 7.96% of the cases failed to complete the first 6MWT and were considered positive. The result of this test was positive in 8.70% and 14.29% of cases in the second and third visits, respectively. Skeletal pain was the most common reason for stopping the 6MWT. Around 36.67%, 50%, and 100% of tests were stopped in each referral due to skeletal pain, respectively. The mean first forced expiratory volume (FEV1) was 104 ± 26.2, 99.08 ± 27.18, and 100.88 ± 31.74 L in the first, second, and third visits, respectively. In the first, second, and third visits, the mean forced vital capacity (FVC) values were 97.88 ± 29.2, 94.40 ± 30.14, and 90.29 ± 58.28 L, respectively. The mean FEV1/FVC was 94.77 ± 26.54, 87.57 ± 15.94, and 86.29 ± 12.42 in the first, second, and third visits, respectively. The mean walked distance during the first, second, and third visits was 412.48, 412.51, and 343.57 meters. The most frequent clinical symptom was shortness of breath, with 30.13%, 26.67%, and 11.76% in the first, second, and third visits, respectively. Although patients experience various symptoms, such as coughing and shortness of breath,
they often perform well on lung tests.

The number of positive 6MWT results in the first visit was significantly higher among women (88.89%, \( P < 0.05 \)). The association between age and the 6MWT results was insignificant in the second visit (\( P > 0.05 \)), and about 75% of patients with positive results were 61 years old or older. In the second visit, all patients with positive tests had underlying diseases, and there was no significant association between the results of 6MWT with oxygen saturation and HR (\( P > 0.05 \), Table 3).

There was a significant association between age and measured FVC in the second visit and six months after discharge. The average FVC decreased with an increase in age (\( r = -0.320, P = 0.001 \)). Moreover, there was a significant relationship between the distance traveled in the 6MWT test and the amount of FVC, implying that patients with higher FVC passed longer distances in the 6MWT test (\( r = 0.227, P = 0.043 \)).

**Discussion**

A total of 239 cases of COVID-19 patients were followed in three stages. The age average was 51.69 years old, and most patients were females. The most common underlying diseases were diabetes and HTN. The mean oxygen saturation was 97% before and after the 6MWT test in all three visits. The frequency of 6MWT positive tests during three, six, and nine months after discharge was 7.96%, 8.70%, and 14.29%, respectively. Frija-Masson et al performed pulmonary function tests in COVID-19 patients with a mean age of 54 years, 30 days after the first symptoms, of whom about 56% of patients expired. They reported that the most common comorbidities were
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Table 3. Frequency of 6MWT According to Demographical Data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Positive No. (%)</th>
<th>Negative No. (%)</th>
<th>P Value</th>
</tr>
</thead>
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<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>&lt;60 years</td>
<td>2 (11.1)</td>
<td>108 (51.92)</td>
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<tr>
<td>&gt;60 years</td>
<td>16 (88.89)</td>
<td>100 (48.08)</td>
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</tr>
<tr>
<td>Age</td>
<td>9 (50.0)</td>
<td>16 (76.92)</td>
<td>0.013</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>9 (50.0)</td>
<td>48 (23.08)</td>
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</tr>
<tr>
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<td>No</td>
<td></td>
</tr>
<tr>
<td>&lt;60 years</td>
<td>14 (77.78)</td>
<td>121 (58.17)</td>
<td>0.104</td>
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<tr>
<td>&gt;60 years</td>
<td>4 (22.22)</td>
<td>87 (41.83)</td>
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<tr>
<td>Gender</td>
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<td>Female</td>
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<td>&lt;60 years</td>
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<tr>
<td>&gt;60 years</td>
<td>2 (25.0)</td>
<td>63 (75.0)</td>
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<tr>
<td>Underlying disease</td>
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<td>No</td>
<td></td>
</tr>
<tr>
<td>&lt;60 years</td>
<td>5 (100.0)</td>
<td>55 (65.48)</td>
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<td>&gt;60 years</td>
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<td>29 (34.52)</td>
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<tr>
<td>Gender</td>
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<td>Female</td>
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<tr>
<td>&lt;60 years</td>
<td>0 (0.0)</td>
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<tr>
<td>Underlying disease</td>
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<td>No</td>
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</tr>
<tr>
<td>&lt;60 years</td>
<td>1 (100.0)</td>
<td>5 (83.33)</td>
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<tr>
<td>&gt;60 years</td>
<td>0 (0.0)</td>
<td>1 (16.67)</td>
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</tbody>
</table>

Note: 6MWT: Six-minute walk test.

HTN (45%) and diabetes mellitus (16%), respectively (24). Huang et al studied lung function tests 30 days after discharge. In their study, the mean age of patients was 46.72 ± 13.78 years, and 54.4% were females. In general, 36.8% of the cases had at least one underlying disease. The most common of which were HTN (19%) and diabetes mellitus (7%), respectively (25).

Fumagalli et al assessed clinical signs and respiratory tests in COVID-19 patients up to six weeks after discharge. The mean age of the patients was 57.8 ± 10 years, and the prevalence of HTN and diabetes was 23% and 7.7%, respectively. The most common reason for stopping the test was skeletal pain. Fumagalli et al reported dyspnea and fatigue as the most common symptoms after the 6MWT test (26). Over time, the traveled distance decreased, and the number of asymptomatic patients increased. The most common complaint of patients was shortness of breath in the first nine months. In the first trimester after discharge, more women were positive for 6MWT. After six months, patients aged 61 years or older with underlying diseases had positive 6MWT results. COVID-19 can also cause neuromuscular weakness, which reduces the lungs' ability to open. Accordingly, the results of the 6MWT test did not improve significantly between three and nine months after discharge. No significant correlation was observed between spirometry values and gender, oxygen saturation, or underlying diseases. FEV1/FVC had a significant positive relationship with diastolic blood pressure (DBP) and HR in the first three months after discharge.

Conclusion
According to the findings, pulmonary rehabilitation and respiratory physiotherapy for hospitalized patients diagnosed with COVID-19, even after discharge, can reduce the incidence of irreversible pulmonary complications such as pulmonary fibrosis.

Competing Interests
There are no conflicts of interests.

Ethical Approval
The study was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1399.498).

References
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