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Six Minute Walk Test in Covid 19 Recovery Patients

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ABSTRACT

Introduction: COVID-19 pneumonia is a respiratory disease caused by a novel and terrible coronavirus, which usually presents with lung involvement and symptoms range from cough , shortness of breath to respiratory distress syndrome and hypoxemia .Some persistent symptoms such as dyspnea and fatigue represented in covid 19 patients following disease improvement. In the current study, we evaluated the pulmonary status of COVID-19 patients who had lung involvement after 3 months relief ,utilizing a 6-minute walking test (6MWT).

Method: In this single center cross-sectional study, we recruited 60 COVID-19 confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR)), patients who were cured three months ago and collected their demographic information, modified medical research council (MMRC)questionnaire , pulmonary involvement percentage (based on CT-scan reports), 6MWT, heart rate, gender, height, weight, body mass index (BMI), and saturation of O2 (SPO2)% before and after 6MWT. The study used frequency tests to describe qualitative variables and mean ± standard deviation (SD) for quantitative variables. Data analysis included t-tests, chi-squares, and ANOVA. SPSS 26 is used for all analytic processes.

Result: The participants had mean age 44.27± 11.5 years included 32 men (53.3%) , 28 women (46.7%). The mean 6MWTdistance was 454.97±95.32 meters(range:219-620 meters). The CT scan score was 6.58±2.60 (3-13)out of 24. Age and functional dyspnea showed a significant reverse association with 6MWT, although SPO2% before and after 6MWT showed a straight association (p-value< 0.05). There was no significant association between 6MWT and BMI, heart rate, gender, or score of pulmonary involvement CT scan(p-value > 0.05) .

Conclusion: 6MWT is a simple and benefit tool for prediction physical pulmonary function. Exertional dyspnea and Spo2% showed adverse effect before and after walking in 6MWT in Covid 19 patients recovery .

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Introduction

Coronavirus 19 disease pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is one of the most serious challenges the global society has ever endured, Reaching hundreds of millions causing deaths (1). In addition to mortality, inability to function and reduced physical energy reserves are important problems in post-COVID recovery patients. Covid 19 diseases associated with a high level of

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morbidities burden . Respiratory complaints and pneumonia are outstanding and common involvement of Covid 19 disease (2). Since, there is a considerable evidence that the persistence symptoms in patients recovering from COVID-19 is raising new concerns in the healthcare community.

A study on this matter found that 43% of recovering covid-19 patients suffer from long-term complications . Declined lung reserved and compliance lead to adverse lung function in Covid19 patients after improvement (3,4). Lopez L S et al reported that fatigue (58%) and dyspnea(24.4%) have been known to be the most common symptoms remaining in post-COVID-19 patients (5). The incidence of chronic respiratory symptoms were higher in hospitalized patients discharged than in non-hospitalized cases (6).Several COVID 19 patients recovery report feeling drained of energy and unable to completely engage in previous activities. The 6 minute walk test (6MWT) is a commonly used for the objective evaluation of functional exercise capacity for the management of patients with pulmonary disease (7). Assessment of the pulmonary functional capacity by determining the distance walking in 6 minutes, along with measuring parameters such as heart rate, blood pressure, Spo2%, and evaluating fatigue and shortness of breath are among the benefits index of 6MWT (8). Several studies on post-COVID-19 patients have performed to evaluate the functional capacity of recuperating patients (9). We aimed to determine the factors affecting the functional capacity in patients recovering from covid-19 patients recovery with 6MWT.

Materials and Methods

Study design and participation

We conducted a single-center cross-sectional study on 60 COVID-19 patients for active follow up at Imam Reza hospital, Mashhad university of Medical sciences from October 2021 to December 2021 . The sample size was obtained according to the formula and the study of Curci (10) number of 60 patients.

P1= 0.5
P2= 0.82
α= 0.05
β= 0.2, n=2(Z1-α/2+Z1-β)^(2/pq)/(P1-P2)^2
Z= 1.96
Attrition= 0.1
n= 60

All patients who had been infected with SARS-CoV-2 for three months recovery ago , confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR) at first, according to the information recorded in the patient's hospital profile, were included in the study. Patients' pulmonary involvement was mild, moderate to severe based on a lung CT scan at the time of infection according to lung CT scan Score (11). Patients who have been diagnosed with myocardial infarction in the last 30 days, confirmed heart failure, any cardiological diseases, neuromuscular disorders and contraindications for performing the 6MWT were excluded.

Ethics

An ethical committee of the Mashhad University of Medical Sciences approved this study, and its national register code is IR.MUMS.REC.1400.034 , with considering the 1964 Helsinki Declaration. We obtained written informed consent from all cases prior to participation in the study. The privacy and private information of the participants have been preserved. All cases had the option to withdraw from the study at any stage if they were dissatisfied with the procedure.

Procedures

6MWT

According to ATS guidelines, participants were required to complete 6MWT(12). The 6MWT should be performed along a flat, straight indoor course of at six minutes with a hard surface and little pedestrian traffic. To minimize time variations, the test was conducted at a specific ,fixed and definite time of the day. A chair was provided near the test area for the patients to sit on for 10 minutes before the test started, during which time questions about the test contraindications were addressed. Participants wore comfortable clothes and shoes . The first step involved measuring the patient's heart rate and blood pressure, followed by checking their oxygen saturation using one pulse oximetry (12). After the

6MWT , heart rate (HR), SpO2%, blood pressure, perceived exertion, and dyspnea scale (based on the Modified Medical Research Council, mMRC) were noted (12,13). The Borg Rating of Perceived Exertion (RPE) scale, developed by Swedish researcher Gunnar Borg is used for measuring an individual's effort and exertion, breathlessness and fatigue during physical work and so is highly relevant for occupational health and safety practice . The Borg questionnaire is then used to assess the patient's level of shortness of breath and fatigue after the test (14).

Statistical analysis

Frequency tests were used to describe qualitative variables, while mean and standard deviation were used for quantitative variables. Data analysis utilized t-tests, chi-square tests, and Pearson correlation. ANOVA analysis was employed to compare the mean of a quantitative traits across more than two populations. The results' significance threshold (p-value) was set at less than 0.05. And all analyses were performed using SPSS26 software.

Results

Study population

The present investigation enrolled a comprising 60 patients who satisfactorily completed the requisite assessments. Among these participants, there were 32 male individuals (53%) and 28 female individuals (46.7%), with a mean age of 44.2 ± 10.3 years, alongside a mean body mass index (BMI) of 27.4 ± 2.0 kg/m2. Notably, 16 individuals (26.7%) reported active smoking habits, while the majority, consisting of 44 individuals (73.3%), were categorized as non-smokers. The prevailing co-morbidities observed within this population included hypertension (18.3%), cardiovascular disease (15%), and diabetes mellitus (8.3%). Significantly there existed no concurrent occurrence of underlying illnesses among the patients under examination, with none presenting underlying conditions such as asthma, chronic obstructive pulmonary disease (COPD), or another chronic lung illness. Subsequent to the implementation of the 6MWT among the 60 participants, a majority comprising 43 individuals (71.7%) reported an absence of dyspnea, as denoted by a Modified Medical Research Council (mMRC) score of 0. Conversely 11 individuals (18.3%) were classified under mMRC grade 1, while 5 individuals (8.3%) in grade 2, and 1 individual (1.7%) was assigned to grade 3 (Table 1). Furthermore, the assessment of physical activity intensity was conducted utilizing the Borg scale, revealing a mean value of 6.15 ± 0.4 prior to the commencement of the 6MWT, which notably escalated to 10.25 ± 2.03 following the completion of the test (Table2). The average distance traversed during the 6-minute duration of the test was quantified at 454.97 ± 95.32 meters.

Pulmonary involvement and 6MWT:

Pulmonary involvement in patients was assessed lung CT scans, and the extent was calculated based on the radiologist's report, with a scoring range of 3 to 13 out of 24 points(11). The overall pulmonary involvement in the study patients was 6.58 ± 2.60. Based on the division, pulmonary involvement is classified into three groups; mild (score <8), moderate (score 8-15), and severe (score≥16). In our study, 26 patients were mild (43.3%), and 34 patients were moderate (56.7%), and no severe involvement was reported. Based on correlation statistical analysis, no significant positive correlation (p-value= 0.80, Pearson= -0.03) was reported between patients' pulmonary involvement in CT-scans at the time of infection, and 6MWT. Also no significant association observed between age, BMI, heart rate, SPO2 (before and after 6MWT), and patients' pulmonary involvement (p-value>0.05).(Table 3).

Pulmonary assessment factors and 6MWT:

A paired-sample t-test was employed to examine the alterations in systolic and diastolic blood pressure, heart rate, SpO2, and Borg scale ratings pre and post the 6MWT.

Table1. Demographic and characteristic parameters

Variables	N=60	%
Age (Mean)	44.2 ± 10.3	
Sex		
Female	28	46.7
Male	32	53.3
Height range (Mean + SD)	170.8 ± 8.2	
Weight range (Mean+SD)	80.5±10.7	
BMI	27.4±2 kg/m 2	
Smoking history		
Smoker	16	26.7
Non-smoker	44	73.3
Co-morbidity		
COPD	0	0
Asthma	0	0
Cardiovascular disease	9	15
Diabetes mellitus	5	8.3
Hypertension	11	18.3
Malignancy	0	0
mMRC scale (After 6MWT)		
0	43	71.7
1	11	18.3
2	5	8.3
3	1	1.7
4	0	0

Table 2 . Pulmonary assessment factors (paired and independent t-test)

Variable	Before 6MWT	After 6MWT	P-value
SPO2	97.93±1.24	95.85±2.00	0.00
Heart rate	72.58±3.93	109.05±7.73	0.00
Systolic blood pressure	120.00±9.56	125.50±8.32	0.00
Diastolic blood pressure	80.33±1.81	78.17±4.31	0.02
Borg scale	6.15±0.40	10.25±2.03	0.00

Table 3 . Comparing variables and smoking with 6MWT (paired and independent t-test)

Variable	Smokers	Non-smokers	P-value
6MWT	421.38±118.63	467.18±83.58	0.10
HR before 6MWT	73.75±3.96	72.16±3.88	0.17
HR after 6MWT	111.13±8.90	108.30±7.23	0.21
SpO2 before 6MWT	97.56±1.63	98.07±1.07	0.26
SpO2 after 6MWT	95.13±2.92	96.11±1.51	0.21
Systolic blood pressure before 6MWT	123.13±6.02	118.6±10.39	0.13
Systolic blood pressure after 6MWT	126.88±7.04	125.0±8.76	0.45
Diastolic blood pressure before 6MWT	77.95±4.62	78.75±3.42	0.53
Diastolic blood pressure after 6MWT	80.23±1.51	80.63±2.50	0.46
Patients' pulmonary involvement in CT-scans	6.88±2.66	6.48±2.60	0.61

The analysis revealed statistically significant changes in systolic blood pressure ($p < 0.05$), manifesting as an average increase of 5.5 units from pre (120.00 ± 9.56) to post (125.50 ± 8.32) 6MWT. Similarly, diastolic blood pressure displayed a statistically significant elevation ($p = 0.02$), with an increase of 2.16 units observed from pre (78.17 ± 4.31) to post (80.33 ± 1.81) 6MWT. Moreover, a notable decline in SpO2 ($p < 0.05$, pre: 97.93 ± 1.24, post: 95.85 ± 2.00), along with an increase in heart rate ($p < 0.05$, pre: 72.58 ± 3.93, post: 109.05 ± 7.73), and Borg scale scores ($p < 0.05$, pre: 6.15 ± 0.40, post: 10.25 ± 2.03), were evident before and after the execution of the 6MWT (Table 2). The statistical analyses further indicated a significant inverse correlation between 6MWT and SpO2 ($p < 0.05$). Additionally, a negative Pearson correlation was observed between 6MWT and age ($p < 0.00$). Conversely, no significant associations were found between height, weight, BMI, and the 6MWT ($p > 0.05$) (Table 3).

Smoking and 6MWT:

We conducted an independent samples t-test to assess potential disparities between smokers and non-smokers in the context of the 6MWT. The results revealed no statistically significant difference ($p = 0.10$) between the two groups, with smokers exhibiting a distance of 421.38 ± 118.63 meters and non-smokers displaying a distance of 467.18 ± 83.58 meters. Moreover, our analysis did not indicate any significant correlation between heart rate among smokers (pre-6MWT: 73.75 ± 3.96; post-6MWT: 111.13 ± 8.90) and non-smokers (pre-6MWT: 72.16 ± 3.88; post-6MWT: 108.30 ± 7.23) before ($p = 0.17$) or after ($p = 0.21$) completing the 6MWT. Subsequently, we assessed the SpO2 levels before (smokers: 97.56 ± 1.63; non-smokers: 98.07 ± 1.07) and after (smokers: 95.13 ± 2.92; non-smokers: 96.11 ± 1.51) the 6MWT using independent samples t-tests. The findings revealed no significant differences between smokers and non-smokers in SpO2 levels both before ($p = 0.26$) and after ($p = 0.21$) the 6MWT. Furthermore, we compared the pulmonary involvement of patients in the smokers (6.88 ± 2.66) and non-smokers (6.48 ± 2.60) groups using an independent samples t-test, which revealed no significant association. Employing paired samples t-tests, we examined systolic blood pressure before (smokers: 123.13 ± 6.02; non-smokers: 118.6 ± 10.39) and after (smokers: 126.88 ± 7.04; non-smokers: 125.0 ± 8.76) the 6MWT, yielding non-significant differences ($p = 0.13$ and $p = 0.45$, respectively). Similarly, diastolic blood pressure in smokers (78.75 ± 3.42 before, 80.63 ± 2.50 after) and non-smokers (77.95 ± 4.62 before, 80.23 ± 1.51 after) before and after the 6MWT did not exhibit significant statistically differences ($p = 0.53$ and $p = 0.46$, respectively) (Table 3).

Gender and 6MWT:

According to our statistical analysis using the independent t-test, no statistically significant difference of walking distance was found between the measurements for men (470.63 ± 103.47) and women (437.07 ± 83.30)(p value 0.17) . In terms of heart rate (HR) prior to the 6MWT, the independent t-test revealed a significant difference between genders (males: 74.38 ± 3.39, females: 70.54 ± 3.59). Similarly after completing the 6MWT, there was a disparity in HR between men (110.69 ± 6.95) and women (107.18 ± 8.27), although this difference was not statistically significant ($p = 0.08$). As illustrated in Table 4, there was no significant association ($p = 0.56$ before 6MWT, $p = 0.98$ after 6MWT) found between gender and the levels of SPO2 before and after performing the 6MWT. Furthermore, no significant relationship ($p = 0.97$) was detected between the extent of pulmonary involvement for men (6.59 ± 2.35) and women (6.57 ± 2.90). Also no significant differences (based on paired t-test) were noted in systolic and diastolic blood pressure before and after the 6MWT with respect to gender. Specifically for the systolic group, the p-values were 1.0 and 0.86 before and after 6MWT, respectively, while for the diastolic group, the p-values were 0.20 and 0.93 before and after 6MWT, respectively (Table 4).

mMRC dyspnea level and 6MWT:

As Table 5 shows there is a clear trend that the amount of 6MWT is inversely related to the mMRC level (p value=0.00), and also there is a significant association (p value=0.05) between age and mMRC level.

The results, as shown in Table 5 indicate that there is no significant correlation between weight and mMRC level (P value=0.21), height and mMRC level (P value=0.54), BMI and mMRC level (P value=0.21).

Discussion

In our study, we performed the 6MWT in post-recovery COVID-19 patient after 3 months. We observed a significant difference in SpO2 % before and after the 6MWT . As stated, Covid 19 virus can cause persistent symptoms and physical weakness leads to activities limitation of daily living.Post-COVID-19 syndrome patients have declined maximal and submaximal physical performance as well as limitations in quality of life, especially in prominent physical components (14,15). The 6MWT is a simple tool, benefit index of functional and therapeutic response in chronic lung disease patients (16). The American Thoracic Society created guidelines for the 6MWT in clinical settings. In healthy subjects, the 6-min walk distance (6MWD) ranges from 400 to 700 m, the main predictor variables being gender, age and height (12). Strumiliene E and et al presented 51 post-COVID-19 patients and conducted two months after their admission. The patients had fatigue, lowered corporeal activeness, and shortness of breath as the most prevalent remaining complications, respectively. Ninety-six percent of patients had pathologic CT scan findings two months after admission, with the severity of disease being associated with the level of CT scan abnormality both at hospitalization and follow-up (17). Another study on 65 patients recovering from sever COVID-19 six months after admission described weakness-malaise, fever, and muscle pain as the most prevalent complications (18). Several parameters in SF-36 showed the quality of life in great percentages of study population to be notably decreased. Sixty-five percent of patients' CT scans demonstrated abnormal findings. 6MWT results and showed remarkable associations with SF-36 parameters, however, CT scan reports and SF-36 parameters did not have statistical concordance. Also, spirometry findings and CT scan reports showed significant association with each other (18). Another study evaluated the well-being of 124 post-COVID-19 patients three months after convalescence and reported the average 6MWT distance of patients to be normal despite 22% of the cases recording less than 80% of the expected distance. The mMRC scores were observed to be worse in patients with mild disease. Abnormal CT scan findings were associated with lower DLCO. DLCO reports were also lower in patients with higher disease severity, while CT scan findings did not correlate with mMRC or Borg dyspnea scores. (9). Another study investigating post-COVID-19 patients found a clear connection between dyspnea and lower exertional capability, using the Borg dyspnea scale and 6MWT (19). Rao C.M and et al showed the 6MWT plays a significant role in assessing the progress of recovery in post-Covid patients, especially in resolving shortness of breath. This finding which could indicate a decrease in the functional capacity of lungs after COVID-19 infection and showed SpO2% decrease in the end of 6MWT of Covid19 patients (20). Another study including 53 COVID-19 patients reported 45 patients experiencing a drop in SpO2 while 6MWT (21). Cecchetto A et al observed Spo2 reduction in several participants five months after the Covid 19 involvement , with a clear relationship between the SpO2 decline and shortness of breathing(22). Another study on post-COVID-19 patients, found the SpO2% after 6MWT in infected population to be lower than the healthy papulation, but the difference was not remarkable (23). Our study presented pulmonary involvement CT scan level imaging did not statistical concordance with mMRC scores for dyspnea. This finding supports a former study, which states no significant diversity in MMRC grades between patients with normal and abnormal lung CT scan , also the severity level in pathologic CT scan findings is reported to have no apparent impact on patients' mMRC grades (24).Another study on patients recuperating from COVID-19 found no connection between lung CT scan scores and dyspnea using both mMRC and Borg dyspnea scale (9). The distance walked in 6MWT and the CT scan scores did not show statistical association, suggesting the recovery of lung function to be independent of radiologic results(9).

Table 4 . Comparing variables and gender with 6MWT (paired and independent t-test)

Variable	Male (32)	Female (28)	P-value
6MWT	470.63±103.47	437.07±83.30	0.17
HR before 6MWT	74.38±3.39	70.54±3.59	0.01
HR after 6MWT	110.69±6.95	107.18±8.27	0.08
SpO2 before 6MWT	97.84±1.44	98.04±1.10	0.56
SpO2 after 6MWT	95.84±2.14	95.86±1.88	0.98
Systolic blood pressure before 6MWT	120.0±6.72	120.0±12.17	1.00
Systolic blood pressure after 6MWT	125.31±6.21	125.71±10.34	0.86
Diastolic blood pressure before 6MWT	77.50±4.40	78.93±4.16	0.20
Diastolic blood pressure after 6MWT	80.31±1.77	80.36±1.89	0.93
Patients' pulmonary involvement in CT-scans	6.59±2.35	6.57±2.90	0.97

Table 5. Comparing mMRC and demographics data (ANOVA test)

Variable	mMRC				P-value
	0	1	2	3	
6MWT	485.84±76.51	422.09±86.06	309.00±16.17	219.00±00	0.00
Age	42.16±10.41	48.45±8.78	49.80±6.34	61.0±0.0	0.05
Height	170.60±7.92	170.0±9.71	175.4±8.02	165.0±0.0	0.54
Weight	79.42±10.46	80.91±11.95	89.40±9.58	89.40±9.58	0.28
BMI	27.17±2.05	27.90±1.94	29.02±1.83	29.02±1.83	0.21

Contrary to, Prestes, G D S et al study showed higher pathologic lung CT scan scores correlated with lower the average 6MWT results (25). Unlike another study that stated a compelling relationship between higher HRCT severity score and lower 6MWT findings (8). Rincon-Alvarez E et al investigated the radiologic anomalies in post-COVID-19 patients, no disparity was noted between patients with abnormal and normal CT scan reports three months and six months after discharge, and both groups showing 6MWT improvement over time (26). Eksombatchai D et al was noted abnormal spirometry in 17.2% of COVID-19 survivors with both restrictive and obstructive defects. Severe COVID-19 pneumonia patients had higher prevalence rates of abnormal spirometry and residual fibrosis on the chest radiographs when compared to patients in the mild symptom and non-severe pneumonia group(27). Mohamed Hussein AA et al study used post COVID 19 functional status (PCFS) scale to evaluate the impact of certain factors including age , gender ,smoking , duration since symptoms onset, need for oxygen or ICU admittance, and finally the presence of coexisting comorbidity on physical restrictions experienced by post-COVID-19 patients and found a clear association between smoking history and downgraded exertional capacity (28). Emecen AN et al study also recognized smoking as a risk factor for the continuance of symptoms in post-COVID-19 patients(29) . Although post-COVID-19 female patients are reported to cover a shorter distance in 6MWT than male patients expression of post-COVID-19 complications, including physical insufficiency (30) ,our study did not detect any statistical significance in 6 MWT results between male and female participants.

A previous study of post-COVID-19 patients showed an association between systolic and diastolic blood pressure and the physical limitations experienced, as assessed by the post-COVID-19 functional status score. (31). Lanidhi K B study showed 6MWT for Covid and post-Covid patients can be useful for oxygen requirements in the hospital and at home(32). So 6MWT predicts physical performance and lung function in post recovery of covid 19 . Beyer S et al presented post-COVID-19 syndrome patients have declined maximal and submaximal physical performance as well as limitations in quality of life, especially in prominent physical components (33).

Limitation

This study has several limitations, a relatively small number of participants might

affect the identification of relationships between certain variables. Additionally, exertional dyspnea was assessed using the mMRC score, limited range of options presented by this score could cause difficulties for participants in expressing their subjective sense of breathlessness. The incomplete medical history of included patients might affect the interpretation of results. Also, the study was done on patients admitted to a single health care center. Future studies with large populations across multiple centers could be instrumental in closing the knowledge gap on this matter.

Conclusion

COVID-19 patients recovery have a higher probability of experiencing altered exertional capacity with dyspnea showing a direct relationship with the level of exhaustion. Lower SpO2 percentages after physical challenges are noted in this group, which may indicate lung damages. Our study showed the 6MWT was concomitant with reduction SPO2 and exertional dyspnea in COVID19 pateints after three months recovery.

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Conflicts of interest

The authors declare that they no conflict of interest.

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