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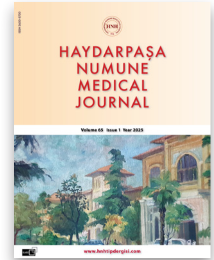

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ORIGINAL ARTICLE

Comparison of Exercise Tolerance and Detectability of Silent Hypoxia in Patients with Moderate and Severe COVID-19 Preparing for Discharge Using Different Field Tests

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Abstract

Introduction: The prevalence of silent hypoxia in patients with COVID-19 has been reported as 20–50%. There is a need for specific field tests to detect silent hypoxia. This comparative study aimed to investigate whether the 2-minute walk test (2MWT), 40-step walk test (40SWT), and 1-minute sit-to-stand test (1MSTST) can be used as alternatives to the 6-minute walk test (6MWT) in the evaluation of silent hypoxia and functional capacity in COVID-19 patients.

Methods: Of 135 patients in the COVID-19 ward, 30 participants with moderate-to-severe COVID-19 who met the inclusion criteria were included in the study. Participants performed the 6MWT, 2MWT, 40SWT, and 1MSTST in that order. In addition to performance results, the participants' heart rate, respiratory rate, saturation levels, and perceived dyspnea and fatigue levels were recorded before and immediately after each test.

Results: Saturation values measured during the 6MWT were positively correlated with those in the 2MWT (r=0.793, p<0.001), 40SWT (r=0.554, p=0.001), and 1MSTST (r=0.806, p<0.001). In terms of performance, there was a moderate positive correlation between 6MWT and 2MWT distances (r=0.542, p=0.002) and a moderate negative correlation between 6MWT distance and 40SWT time (r=-0.605, p<0.001).

Discussion and Conclusion: The 2MWT, 40SWT, and 1MSTST could be used in the clinic as alternatives to the 6MWT in the assessment of silent hypoxia, while the 2MWT and 40SWT could also be used as alternatives for determining functional capacity in patients with acute COVID-19.

Keywords: 6-minute walk test; COVID-19; exercise tests; exercise tolerance; hypoxia.

Coronavirus disease 2019 (COVID-19) is a major infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In December 2019, the virus was identified as the cause of a cluster of pneumonia cases in Wuhan, China [1]. In March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic [2]. Globally, more than 757 million cases have been reported, with nearly 7 million deaths attributed to the disease [3].

Patients with COVID-19 may be asymptomatic or present with a wide spectrum of clinical manifestations, ranging from mild upper respiratory tract symptoms to severe acute respiratory distress syndrome (ARDS) [4]. Even individuals with mild initial symptoms can rapidly progress to severe or critical illness. Because hypoxemia and increased

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oxygen demand are important indicators for identifying such patients, resting oxygen saturation levels are routinely monitored [5]. However, resting oxygen saturation alone may not be sufficient. Some patients with COVID-19 may develop hypoxia during mild exertion despite showing no desaturation at rest [6], a condition referred to as *silent hypoxia* [7]. Early recognition of hypoxia, risk stratification, and appropriate treatment planning are therefore essential in this population. The prevalence of silent hypoxia in patients with COVID-19 has been reported to be 20–50% [8,9].

Interest in clinical field tests has increased in recent years because they more closely reflect activities of daily living than cardiopulmonary exercise testing, are safe and easy to administer, and can be used to assess exercise capacity, predict morbidity and mortality risk, and detect oxygen desaturation [10]. However, relatively few studies have evaluated these tests in patients with COVID-19. The 6-minute walk test (6MWT) [11], commonly used in individuals with moderate cardiac or pulmonary disease, can detect silent hypoxia in patients with COVID-19 and is frequently used for this purpose [12]. Nevertheless, the 6MWT has important practical limitations in pandemic wards, including overcrowding, staff shortages, the time and space required to perform the test, and the potential risk of disease transmission in the testing area.

Consequently, guidelines have emphasized the need for studies identifying more practical alternative field tests to detect silent hypoxia and assess exercise tolerance before discharge [10,13]. Shorter field tests, such as the 2-minute walk test (2MWT) [14], the 40-step walk test (40SWT) [13], and the 1-minute sit-to-stand test (1MSTST) [15], have been proposed as potential alternatives. Therefore, this comparative study aimed to investigate the utility of the 2MWT, 40SWT, and 1MSTST as alternatives to the 6MWT for evaluating silent hypoxia and functional capacity in patients with COVID-19.

Materials and Methods

Study Design

A descriptive, cross-sectional study was conducted between December 2021 and May 2022 at Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital. Ethical approval was obtained from the Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee (approval number: 2021/03-07; approval date: March 17, 2021), and the study was retrospectively registered at ClinicalTrials.gov (NCT: 05709262). The study was conducted in accordance with the Declaration of Helsinki.

Participants

The inclusion criteria were as follows: (i) age 18–80 years; (ii) COVID-19 diagnosis confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) with positive chest computed tomography (CT) findings; (iii) peripheral oxygen saturation (SpO_2) ≥93% on room air; (iv) ability to stand from a seated position and walk independently; (v) prior receipt of intravenous steroid therapy (daily dexamethasone 6 mg or methylprednisolone 40 mg) for a minimum of 5 and a maximum of 10 days during hospitalization, but not receiving this therapy at the time of evaluation; (vi) moderate or severe COVID-19 involvement according to evaluation by an experienced radiologist; and (vii) willingness to participate in the study.

The exclusion criteria were: (i) central nervous system disorders (e.g., stroke, epilepsy, Parkinson's disease, or multiple sclerosis); (ii) gait or balance disorders; (iii) moderate-to-advanced heart failure or chronic obstructive pulmonary disease (COPD); (iv) requirement for active oxygen support; (v) tachycardia, tachypnea, or dyspnea at rest on room air; (vi) pregnancy; (vii) inability to cooperate; (viii) ongoing physiotherapy or rehabilitation; and (ix) receipt of antibiotic or steroid therapy at the time of the study.

A total of 135 individuals with moderate or severe COVID-19 who were hospitalized and preparing for discharge from the COVID-19 wards (seven wards in total) at Kütahya Health Sciences University Evliya Çelebi Training and Research Hospital were invited to participate and assessed for eligibility. Among the 105 excluded individuals, 68 declined participation, 24 required oxygen support, 11 had gait or balance disorders, and 2 were excluded because of lack of cooperation. Patients who agreed to participate provided written informed consent.

Procedures

All participants were evaluated by the same investigator using a standardized procedure under identical room conditions (temperature approximately 23°C). First, demographic and clinical information was recorded. Participants then performed the 6MWT, 2MWT, 40SWT, and 1MSTST in that order. The field tests were administered at 2-hour intervals to allow complete recovery between tests.

Heart rate, SpO_2 level, respiratory rate, and perceived dyspnea and fatigue levels were recorded by the same researcher immediately before and after each field test.

Descriptive Characteristics

For each participant, demographic data including age, sex, height, weight, and body mass index (BMI) were recorded. In addition, C-reactive protein (CRP; mg/dL), D-dimer (ng/

mL), and fibrinogen (mg/dL) values from the most recent laboratory tests, as well as resting SpO_2 values, were documented.

Field Tests

6-Minute Walk Test (6MWT): The 6MWT was conducted according to the criteria recommended by the American Thoracic Society (ATS) in 2002 [11]. Participants walked at a self-selected pace along a straight, 30-meter hospital corridor marked at 1-meter intervals. They were instructed to walk as far as possible within 6 minutes and received standardized verbal encouragement during the test. The total distance walked was calculated and recorded in meters.

2-Minute Walk Test (2MWT): Similar to the 6MWT, participants walked at their own pace along the same 30-meter corridor for 2 minutes. The test was demonstrated by the assessor beforehand, and verbal encouragement was provided during the test. The total distance walked was calculated and recorded in meters [16].

40-Step Walk Test (40SWT): The 40SWT is a rapid field test used as a discharge criterion for patients with COVID-19, particularly in the United Kingdom. The assessor demonstrated the procedure before testing. Participants were instructed to walk 40 steps along the corridor, as in the 6MWT and 2MWT. The completion time was recorded in seconds [13].

1-Minute Sit-to-Stand Test (1MSTST): Participants were seated in a chair without armrests and with a seat height of 46 cm. They were instructed to cross their arms over their chest to prevent support from the upper limbs and to stand up and sit down as many times as possible within 1 minute at a self-selected pace. The number of completed stands without support was recorded. The procedure was demonstrated beforehand [17].

Pre- and Post-Test Measurements

For all participants, heart rate (beats/minute), respiratory rate (breaths/minute), and SpO_2 levels were recorded immediately before and after each field test by the same researcher (B.A.) using a portable pulse oximeter (Soulfix, Türkiye). Participants also rated their perceived dyspnea and leg fatigue using the Modified Borg Scale (0–10). Differences between pre- and post-test measurements were calculated and recorded as delta (Δ) values for all tests.

Statistical Analysis

Data were analyzed using SPSS Statistics version 17 (SPSS Inc., Chicago, IL, USA). Normality of data distribution was evaluated using skewness and kurtosis coefficients. Because the data were normally distributed, parametric tests were applied. Categorical variables were presented as number and percentage, and continuous variables were presented as mean ± standard deviation (SD).

Pearson correlation coefficients were used to examine relationships between the 6MWT and the other tests. Correlation coefficients were interpreted as follows: ≥0.90 very strong, 0.70–0.89 strong, 0.40–0.69 moderate, 0.10–0.39 weak, and ≤0.10 very weak [18].

Power Analysis

A post hoc power analysis was conducted to evaluate the statistical power of the study with a sample size of 30 participants. Based on the correlation between pre- and post-test changes in oxygen saturation measured during the 6MWT and 2MWT, the study achieved 99% power at a 95% confidence level, with a 5% margin of error and a large effect size (d=0.89).

Results

Of the 135 individuals invited to participate, 105 were excluded because they did not meet the inclusion criteria or were unable to complete the assessments. The study was therefore conducted with 30 participants. No complications occurred during the tests. The descriptive characteristics of the participants are presented in Table 1.

Data obtained from the 6MWT, 2MWT, 40SWT, and 1MSTST are summarized in Table 2.

The relationships between 6MWT distance and 2MWT distance, 40SWT time, and 1MSTST score are shown in Table

Table 1. Descriptive data of the participants

Variable	Mean±SD
Age (years)	63.17±10.33
Weight (kg)	75.43±10.01
Height (cm)	162.60±8.17
BMI (kg/cm^2)	28.10±3.93
CRP (mg/dL)	11.29±12.33
D-dimer (ng/mL)	918.43±751.51
Fibrinogen (mg/dL)	392.96±108.42
Resting SpO_2 at enrollment (%)	93.97±2.31
	n (%)
Gender	
Female	16 (53.3)
Male	14 (46.7

%: Percentage, mg: Milligram; ng: Nanogram; dL: Deciliter; cm: Centimeter; s: Second; SpO_2: Peripheral oxygen saturation; SD: Standard Deviation; BMI: Body mass index; CRP: C-reactive protein

Table 2. Test data of the participants

Variable	Pre-test Mean±SD	Post-test Mean±SD	Δ Mean±SD
6MWT			
Heart Rate (beats/min)	80.20±11.41	121.30±14.44	41.10±10.65
SpO_2 (%)	93.97±2.17	87.40±5.85	-6.57±4.41
Respiratory Rate (breaths/min)	19.20±3.99	32.00±4.73	12.80±3.74
Perceived Dyspnea	0.77±0.82	4.87±1.36	4.10±1.12
Perceived Fatigue	0.43±0.90	2.23±1.55	1.80±1.10
Test score (m)		355.91±65.24	
2MWT			
Heart Rate (beats/min)	81.10±11.31	105.37±16.17	24.27±11.24
SpO_2 (%)	94.83±1.74	91.07±3.35	-3.23±2.29
Respiratory Rate (breaths/min)	18.17±2.23	26.37±4.99	8.20±4.54
Perceived Dyspnea	0.77±0.82	2.80±1.10	2.03±0.89
Perceived Fatigue	0.43±0.90	1.03±1.40	0.60±0.77
Test score (m)		135.71±34.85	
40SWT			
Heart Rate (beats/min)	80.30±11.50	89.83±15.61	9.53±10.66
SpO_2 (%)	94.00±2.20	92.60±5.06	-1.40±4.41
Respiratory Rate (breaths/min)	19.27±4.02	21.00±4.69	1.73±2.61
Perceived Dyspnea	0.77±0.82	1.67±1.21	0.90±0.99
Perceived Fatigue	0.43±0.90	0.60±1.33	0.17±0.75
Test score (s)		25.53±5.66	
1MSTST			
Heart Rate (beats/min)	80.43±10.39	110.53±12.77	30.10±10.80
SpO_2 (%)	94.83±1.91	89.00±5.05	-5.83±3.95
Respiratory Rate (breaths/min)	18.47±2.06	28.87±3.66	10.40±3.27
Perceived Dyspnea	0.77±0.82	3.80±1.24	3.03±0.89
Perceived Fatigue	0.43±0.90	3.00±1.76	2.57±1.33
Test score		24.80±5.10	

SpO_2: Peripheral oxygen saturation; 6MWT: 6-minute walk test; 2MWT: 2-minute walk test; 40SWT: 40-step walk test; 1MSTST: 1-minute sit-to-stand test; Δ: Difference between post-test and pre-test values; %: Percentage; min: Minute; m: Meter; s: Second; SD: Standard deviation.

3. The 6MWT distance demonstrated a moderate positive correlation with 2MWT distance (r=0.542, p=0.002) and a moderate negative correlation with 40SWT time (r=-0.605, p<0.001).

Table 3. Relationships between data obtained with 6MWT and other field tests

Variable			2MWT	40SWT	1MSTST
6MWT	Performance	r	**0.542**	**-0.605**	0.227
		p	**0.002**	**<0.001**	0.228
	Δ SpO_2	r	**0.793**	**0.554**	**0.806**
		p	**<0.001**	**0.001**	**<0.001**
	Δ Heart Rate	r	**0.600**	0.188	0.360
		p	**<0.001**	0.320	0.051
	Maximum Heart Rate	r	**0.788**	**0.580**	**0.600**
		p	**<0.001**	**0.001**	**<0.001**
	Δ Respiration Rate	r	**0.648**	0.079	**0.555**
		p	**<0.001**	0.678	**0.001**
	Δ Perceived Dyspnea	r	**0.823**	**0.595**	**0.582**
		p	**<0.001**	**0.001**	**0.001**
	Δ Perceived Fatigue	r	**0.719**	**0.464**	**0.530**
		p	**<0.001**	**0.010**	**0.003**

SpO_2: Peripheral oxygen saturation; 6MWT: 6-minute walk test; 2MWT: 2-minute walk test; 40SWT: 40-step walk test; 1MSTST: 1-minute sit-to-stand test; Δ: Difference between pre-test and post-test

The change in heart rate during the 6MWT was correlated only with the change in heart rate during the 2MWT. Analysis of peak heart rate achieved during the tests revealed strong positive correlations between the 6MWT and 2MWT and moderate correlations with the 40SWT and 1MSTST. All tests showed correlations with the 6MWT in terms of change in SpO_2. There was a strong positive correlation between the 6MWT and both the 2MWT and 1MSTST, and a moderate positive correlation between the 6MWT and the 40SWT. Changes in respiratory rate showed moderate positive correlations between the 6MWT and both the 2MWT and 1MSTST. For perceived dyspnea and fatigue, strong correlations were observed between the 6MWT and 2MWT and moderate correlations with the 40SWT and 1MSTST.

Discussion

In this study, we found that the 2MWT and 1MSTST could be used as alternatives to the 6MWT for detecting silent hypoxia in patients with acute moderate-to-severe COVID-19, and that the 2MWT and 40SWT could serve as alternatives to the 6MWT for evaluating functional capacity. Although the 1MSTST strongly correlated with the 6MWT in detecting changes in oxygen saturation, performance and heart rate responses were not correlated. In addition, the 40SWT did not correlate with the 6MWT in detecting changes in respiratory rate or heart rate. Therefore, when the 40SWT or 1MSTST is used instead of the 6MWT, the results should be interpreted cautiously.

Maintaining adequate oxygen levels is essential for mitochondrial activity and cellular function. COVID-19 can lead to a significant reduction in oxygen saturation, resulting in alveolar collapse and a substantial decrease in pulmonary diffusion capacity [19,20]. Pulse oximetry, arterial blood gas analysis, and the 6MWT are commonly used to detect desaturation and silent hypoxia in patients with COVID-19 [12]. However, the duration of the test and the required corridor length limit the practicality of the 6MWT in clinical settings.

Previous studies have reported associations between the 6MWT and 2MWT in detecting exercise-induced desaturation in patients with severe COPD [21] and between the 6MWT and 1MSTST in patients with interstitial lung disease [22]. However, no studies have evaluated the use of the 40SWT for detecting exercise-induced desaturation. Because the 40SWT imposes a lower workload and requires less time and space than the 6MWT and 2MWT, the need to investigate this test has been emphasized [10].

In our study, the largest changes in SpO_2 and respiratory rate occurred during the 6MWT, followed by the 1MSTST and 2MWT. Correlation analysis demonstrated that changes in SpO_2 during the 6MWT were correlated with those of all other tests. However, changes in respiratory rate correlated only between the 6MWT and the 2MWT and 1MSTST, not with the 40SWT. The presence of correlations in both oxygen saturation and respiratory rate suggests that the 2MWT and 1MSTST can substitute for the 6MWT in detecting silent hypoxia in patients with COVID-19.

The 40SWT, however, can be performed more quickly and in a smaller space rather than a long corridor, reducing transmission risk and improving practicality [13]. Therefore, the 40SWT may represent an important alternative to the 6MWT for detecting silent hypoxia in individuals with COVID-19. Nevertheless, the absence of correlation with the 6MWT for respiratory and heart rate responses requires cautious clinical interpretation.

A substantial proportion of patients with COVID-19 experience persistent multisystem symptoms after discharge, making functional capacity assessment important during follow-up. Although 6MWT distance is commonly used to evaluate functional capacity, it is influenced by corridor length [23], and mobility, balance, and cognitive impairments common in COVID-19 patients may limit its applicability [24]. These limitations have led to the increased use of the 2MWT, 40SWT, and 1MSTST in clinical and research settings [10].

Our findings demonstrated correlations in functional capacity parameters between the 6MWT and both the 2MWT and 40SWT, but not the 1MSTST. No previous studies have evaluated the relationship among these tests specifically in patients with COVID-19. Studies in COPD populations similarly reported correlations between 6MWT and 2MWT distances [21,25]. Our results further indicate that the 40SWT is another test associated with 6MWT performance. However, clinicians should recognize that this test may be limited in detecting changes in heart and respiratory rates.

The 1MSTST is also used to assess functional capacity, but in our study its score did not correlate with 6MWT distance. Previous studies have shown a moderate correlation between 6MWT distance and 1MSTST score in post-COVID-19 patients [26]. The discrepancy in findings may be due to our evaluation of patients during the acute phase of COVID-19, whereas prior studies examined patients in the chronic phase. Similarly, moderate correlations between these two tests have been reported in patients with interstitial lung disease [22], suggesting disease-specific pathophysiological mechanisms may influence the relationship.

We observed moderate positive correlations between 6MWT distance and 2MWT distance and a moderate negative correlation with 40SWT time. Although these were not strong correlations, their magnitude remains clinically meaningful. The findings indicate that the 2MWT and 40SWT can provide a reasonable approximation of functional capacity as measured by the 6MWT. Furthermore, changes in SpO_2 during the 6MWT correlated with those of all other tests, suggesting that the 2MWT, 40SWT, and 1MSTST may detect exercise-induced desaturation—a key indicator of silent hypoxia in COVID-19. Considering the time and space limitations of the 6MWT, these shorter and more practical tests may streamline patient assessment and help clinicians identify individuals requiring closer monitoring or oxygen support.

This study has several limitations. The primary limitation is the small sample size, partly due to strict exclusion criteria related to comorbidities. Additionally, because the study included only patients with moderate-to-severe COVID-19, the utility of these tests in mild disease could not be evaluated. Finally, the fixed order of test administration may have introduced fatigue or learning effects. Future studies should consider randomizing test order to minimize this bias.

Conclusion

This study suggests that the 2MWT, 1MSTST, and 40SWT can serve as alternatives to the 6MWT for detecting silent hypoxia in patients with COVID-19, and that the 2MWT and 40SWT may also be used to assess functional capacity before discharge. However, the 40SWT and 1MSTST may be less sensitive for detecting changes in heart and respiratory rates; therefore, their results should be interpreted cautiously in clinical practice.

The broader use of these tests in COVID-19 clinics may help overcome practical barriers associated with the 6MWT by providing clinicians with feasible alternatives when the standard test cannot be performed. Future studies should further investigate the clinical utility of different field tests, particularly the 40SWT, in larger samples and across various pulmonary disorders.

Ethics Committee Approval: Ethics committee approval was obtained from Ethics Committee of the Kütahya Health Sciences University Non-Interventional Clinical Research Ethics Committee (Approval Number: 2021/04-15, Date: 10.03.2021). The study was retrospectively registered at ClinicalTrials.gov (NCT: 05709262).

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