

Research Article

Performance of Commonly-Used Modified Exercise Tests in Patients with COVID-19 Infection

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Abstract

Introduction: Although hypoxaemia is an important prognostic factor in COVID-19, its absence is not always reassuring, as some patients with initially mild symptoms can rapidly progress into severe or critical diseases. The aim was to compare the performance of modified exercise tests against a 6-minute walk test and investigate if modified exercise tests can be used as an early severity prediction tool.

Methods: This prospective cross-sectional study included all patients aged 12 and above admitted to the University Medical Unit of Teaching Hospital Anuradhapura with COVID-19 infection and normal resting oxygen saturation (94–100%). Patients with acute and chronic cardiorespiratory diseases were excluded. Each participant was randomly allocated to perform one of the three selected modified exercise tests, a 1-minute sit-to-stand test, a 30-second sit-to-stand test, and a 40-step walk test. All underwent a 6-minute walk test after 15 minutes of rest, as the latter is validated in some respiratory diseases. Saturation before and after each test and patient outcomes were recorded. Desaturation by 3% or more was considered a positive test.

Results: Males were the majority (56.5%, n=62), and the mean age was 45.8(SD+16.3) years. Proportions for positive tests were 5/22(22.7%) for 1-minute sit-to-stand test, 4/23(17.3%) for 30-second sit-to-stand test, 5/17(29.4%) for 40-step walk test and 9/62(14.5%) for 6-minute walk test. None developed severe disease in this sample. Only two patients (3%) developed moderate disease needing oxygen; one had both negative 30-second sit-to-stand test and 6-minute walk test, while the other was positive for the 40-step walk test and the 6-minute walk test. Eleven (17.7%) had a negative 6-minute walk test despite a positive modified exercise test.

Conclusions: Modified exercise tests and the 6-minute walk test are not comparable. We recommend adequately powered large-scale studies to test the validity of these tests in clinical practice.

Keywords: COVID-19, modified exercise tests, six-minute walk test

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Introduction

COVID-19 infection is an acute respiratory illness caused by SARS-CoV-2, a new variant of coronavirus first recognised in Wuhan, China, in December 2019 [1]. This pandemic has caused enormous challenges to the healthcare systems of both developed and developing countries [2]. The clinical spectrum of COVID-19 can range from no symptoms to life-threatening illness [3]. Patients with other comorbid medical conditions and who are aged more than 65 years are more likely to develop severe disease [3]. The percentage of individuals who remain asymptomatic throughout infection is variable and incompletely defined. Currently, it is unclear what percentage of individuals who present with asymptomatic infection progress to clinical disease [3]. Respiratory involvement may range from mild upper respiratory infection to acute respiratory distress syndrome [4].

Hypoxaemia and the need for supplemental oxygen are independent predictors of severe outcomes in hospitalised patients with COVID-19 [5,6]. The National Institute for Health and Care Excellence (NICE) guidelines in the UK recommend the use of oximetry in the assessment of COVID-19 patients, as there is a poor correlation between subjective dyspnoea and hypoxia [7]. A retrospective cohort study showed the presence of dyspnoea had a positive predictive value of only 42% for hypoxia, and the absence of dyspnoea had a negative predictive value of 86% for excluding it [8]. The presence of profound hypoxemia at rest in the absence of proportional clinical features of respiratory distress is termed 'silent' or 'happy' hypoxia. It has now been recognised as a feature of COVID-19 [9,10]. Development of severe hypoxaemia usually takes about 7 to 12 days from symptom onset [07,11]. Although hypoxaemia is a critical prognostic factor in COVID-19, the absence is not always reassuring, as some patients with initially mild symptoms can rapidly progress into severe or critical disease [12]. It is widely reported that a proportion of patients with COVID-19 have normal pulse oximetry at rest, but they are desaturated after exertion (unpublished data). UK guidelines recommend exercise desaturation tests to identify early deterioration [13]. Desaturation by 3% or more is a reason for serious concern in COVID-19, irrespective of the amount of exercise needed to produce it [14].

Currently, exercise tests are primarily used to monitor chronic lung disease. The six-minute walk test is widely used for monitoring and assessing exercise capacity in individuals with chronic lung disease. Variables measured during the 6-minute walk test, such as six-minute walk distance and desaturation, strongly predict

mortality in patients with idiopathic pulmonary fibrosis [15]. Measurement of post-exertion oxygen saturation has been proposed as a method to predict and assess the severity of COVID-19. However, there is no consensus on what tests should be used.

In this study, we aimed to compare modified exercise tests with the widely used 6-minute walk test and to investigate the performance of these tests in predicting severe outcomes in COVID-19.

Methods

Eligibility criteria

This cross-sectional analytical study was conducted at the University Medical Unit of the Teaching Hospital in Anuradhapura from February 16, 2022, to June 18, 2022. All patients admitted with COVID-19 infection were assessed for eligibility. All male and female patients aged 12 years and above with a confirmed COVID-19 infection and a pulse oximetry (SpO₂) reading between 94% and 100% were included in the study. Patients who had a contraindication for exercise tests, such as acute coronary syndromes, acute heart failure, suspected myocarditis, or severe anaemia, were excluded. Those with chronic lung diseases with exercise-induced desaturation and persons with suspected or confirmed pulmonary embolism or pulmonary hypertension were also excluded.

Modified exercise tests

For this study, we selected three widely used modified exercise tests: the 1-minute sit-to-stand test, its 30-second variant, and the 40-step walk test. These modified exercise tests were compared with the 6-minute walk test.

1. One-minute sit-to-stand test

Participants were asked to sit and stand on a chair as quickly as possible for 60 seconds.

2. 30 seconds sit-to-stand test

Participants were asked to sit and stand on a chair as quickly as possible for 30 seconds.

3. 40-step walk test

Participants took a 40-step walk as fast as they could.

Six-Minute Walk Test

Participants were asked to walk at their fastest pace for 6 minutes.

Randomisation

Permuted block randomisation was used to assign participants to three groups using an online computer application [16]. Varying block sizes were used, and block sizes were blinded to investigators to avoid predictability. Group A performed the 1-minute sit-to-stand test, group B performed the 30-second sit-to-stand test, and group C performed the 40-step walk test. After a 15-minute rest, all participants performed the 6-minute walk test. SpO₂ was measured before and immediately after each exercise test. We used a Philips G30E patient monitor to take SpO₂ measurements using the middle finger. The number of sit-stand cycles was also counted for the two sit-stand tests. The walking distance for the 6-minute walk test was measured. A 3% or more desaturation was considered a positive test [14]. All participants were managed according to the unit protocol, and those who fulfilled discharge criteria were discharged. However, they were reassessed for outcomes at one week and 4 weeks through telephone conversations.

Outcome measures

Outcome measures were the need for supplemental oxygen, noninvasive or invasive ventilation, development of severe or critical disease, need for organ support, and death.

Definitions

Case definition

A person with a positive nucleic acid amplification test (NAAT) for COVID-19 or a positive COVID-19 rapid antigen test with clinical features suggestive of COVID-19 infection (fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of smell, and shortness of breath).

Definition of severity [3]

Mild illness

Patients with mild illness may exhibit various signs and symptoms (e.g. fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhoea, loss of taste and smell). They do not have shortness of breath, dyspnea on exertion, or abnormal chest imaging.

Moderate illness

Moderate illness is defined as evidence of lower respiratory disease during clinical assessment or imaging, with a SpO₂ $\geq$ 94% on room air at sea level.

Severe illness

Patients with COVID-19 are considered to have severe illness if they have SpO₂ <94% on room air at sea level, a respiratory rate >30 breaths/min, PaO₂/FiO₂ <300 mm Hg, or lung infiltrates >50%.

Critical illness

Critically ill patients may have acute respiratory distress syndrome, septic shock that may represent virus-induced distributive shock, cardiac dysfunction, an exaggerated inflammatory response, and/or exacerbation of underlying comorbidities. In addition to pulmonary disease, patients with critical illness may also experience cardiac, hepatic, renal, central nervous system, or thrombotic disease.

Results

Sixty-two participants were recruited for this study, with males comprising the majority (56.5%), and the mean age was 45.8 (SD 16.3) years (Figure 1).

The most common symptom was fever (79%, n = 62), followed by shortness of breath (37.1%) and cough (27.4%). The least common respiratory symptom was anosmia (6.5%). The median day of admission was day two, and the median duration of hospital stay was one day. No participants were readmitted with worsening symptoms after being discharged home or to intermediate care centres. All participants completed the exercise tests.

Nine participants (14.5%) had a positive 6-minute walk test. Out of those nine participants, the proportions of positive modified exercise tests were 1/4 for the one-minute sit-to-stand test, 1/3 for the 30-second sit-to-stand test, and 1/2 for the 40-step walk test (Table 1). There were 53 participants (85.5%) with a negative 6-minute walk test. In this group, the proportions for negative modified exercise tests were 14/18 in the one-minute sit-to-stand test, 17/20 in the 30-second sit-to-stand test, and 11/15 in the 40-step walk test (Table 1). Proportions for positive modified exercise tests were 5/22 (22.7%) for the one-minute sit-to-stand test, 4/23 (17.3%) for the 30-second sit-to-stand test, and 5/17 (29.4%) for the 40-step walk test.

However, when positive modified exercise test results were compared with the 6-minute walk test, only 1 in 5 of the participants in the one-minute sit-to-stand test, 1 in 4 in the 30-second sit-to-stand test, and 1 in 5 in the 40-step walk test had a positive 6-minute walk test result (Table 1).

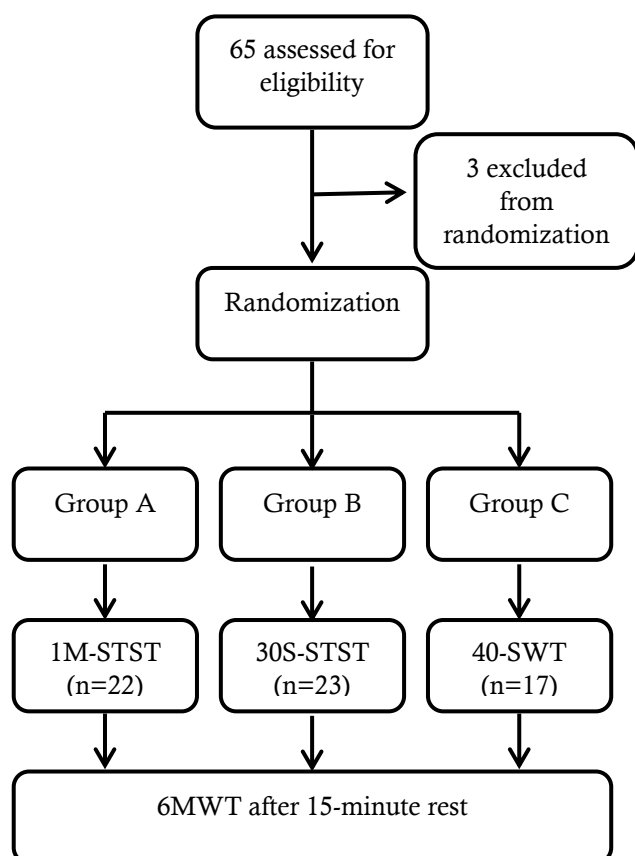


Figure 1: Flow chart of participants' recruitment to different exercise tests (1M-STST; one-minute sit-to-stand test, 30S-STST; 30-second sit-to-stand test, 40-SWT; 40-step walk 6MWT; 6-minute walk test).

Only two patients (3%) developed moderate disease requiring oxygen. One had a negative 30-second sit-to-stand test and a 6-minute walk test, while the other was positive for both the 40-step walk test and the 6-minute walk test. None developed severe or critical disease or organ failures in this cohort.

Discussion

The 6-minute walk test was positive in 9 out of 62 participants (14.5%). Percentages for positive modified exercise tests were 22.7% for the one-minute sit-to-stand test, 17.3% for the 30-second sit-to-stand test, and 29.4% for the 40-step walk test. When the 6-minute walk test is compared with modified exercise tests, we found that out of 14 participants with a positive modified exercise test, only three had a positive 6-minute walk test, and out of 9 participants with a positive 6-minute walk test, only 03 had a positive modified exercise test. Eleven (17.7%, $n = 62$) had a negative 6-minute walk test despite a positive modified exercise test (Table 1). Therefore, based on these results, it appeared that the 6-minute walk test was not comparable to modified exercise tests.

Furthermore, in our study, 14 participants were significantly desaturated (by 3% or more) during modified exercise tests, and nine participants exhibited a similar degree of desaturation during the 6-minute walk test. However, none of them developed severe disease outcomes. Therefore, further studies are required in patients with COVID-19 before recommending these exercise tests in clinical practice.

Table 1: The results of Modified Exercise Tests and 6-minute walk test.

		6MWT		Median number of sit-standing cycles
		Positive	Negative	
1M-STST	Positive	1	4	15 (IQR 14-24)
	Negative	3	14	18 (IQR 14-23)
30S-STST	Positive	1	3	18 (IQR 12.5-14.5)
	Negative	2	17	14 (IQR 13-14.75)
40SWT	Positive	1	4	N/A
	Negative	1	11	N/A
Mean distance in 6MWT		366.9 m	365.4 m	

(1M-STST; one-minute sit-to-stand test, 30S-STST; 30-second sit-to-stand test, 40SWT; 40-step walk test, 6MWT; 6-minute walk test)

Measurement of exercise-induced oxygen desaturation has been proposed as a predictor of the severity of COVID-19, and numerous exercise tests have been described in the literature. A review by Lee et al. summarises different walking tests, stair-climbing tests, and sit-to-stand tests that have been studied [17]. However, all the tests described by this review have been designed to monitor the severity of chronic lung diseases, and some have been shown to correlate with survival [17]. Another recent systematic review examined the validity of a one-minute sit-to-stand test in measuring exercise capacity in individuals with chronic lung disease [18]. It was found that the test correlated with the severity of lung disease, and the test score (measured by the number of sit-to-stand cycles) correlated with the 6-minute walk test. They concluded, "The one-minute sit-to-stand test appears to be a practical, reliable, valid, and responsive alternative for measuring exercise capacity, particularly where space and time are limited." However, these authors did not examine the one-minute sit-to-stand test in their assessment of exertional desaturation [18]. We also found a smaller study involving 107 patients with chronic interstitial lung disease, which compared the nadir SpO₂ measured by oximetry during the 6-minute walk test and the one-minute sit-to-stand test [19]. They reported a high correlation between these two values ($r = 0.9$; $p < 0.0001$).

Although some exercise tests have been validated for chronic lung diseases, we found no published literature on validation studies of exertional desaturation tests in COVID-19 patients. However, the PRIEST observational cohort study done in the UK aimed to determine if post-exertion oxygen saturation can be used as a prognostic factor for adverse outcomes in suspected COVID-19 [20]. They concluded that post-exertion desaturation tests provided modest prognostic value in assessing patients suspected of having COVID-19. However, this study collected data regarding post-exertion desaturation retrospectively. Therefore, exercise tests have not been standardised in the PRIEST study.

Only 8 out of 23 participants who complained of shortness of breath on admission were positive for one of the three modified exercise tests, and 6 out of 39 participants who were not short of breath were positive for one of the three modified exercise tests. The maximum drop of SpO₂ following a modified exercise test was 14%. However, this participant recovered uneventfully without developing severe disease. Interestingly, an improvement in post-test SpO₂ up to 3% was observed in 17 (27.4%) participants who underwent modified exercise tests.

Poor correlation between shortness of breath and hypoxia has been described earlier [7]. A retrospective cohort study showed the presence of dyspnoea had a positive predictive value of only 42% for hypoxia [8]. However, we found no published literature on the sensitivity of shortness of breath in predicting an abnormal exercise test result. In our study, we observed an improvement in post-test arterial saturation up to 3% in 17 (27.4%) participants who underwent a modified exercise test. Previous studies regarding the changes in oxygen saturation after acute exercise have reported contrasting results. Simanjuntak et al. reported that SpO₂ rose [21], while Daglioglu et al. reported that SpO₂ decreased [22] after acute exercise in healthy subjects. Rompas et al. observed no change in SpO₂ after exercise [23]. However, none of these tests have been conducted in patients with acute respiratory infections; all were healthy subjects.

Conclusions

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None of the participants with exercise-induced desaturation (22.6%) developed severe or critical disease in this study. Modified exercise tests and the 6-minute walk test do not seem to be comparable. None of the participants in our study group developed severe or critical disease. Therefore, we were not able to conclude whether one or more of the modified exercise tests or the 6-minute walk test can be used as a severity prediction tool for COVID-19 infection. We recommend adequately powered large-scale studies to test the validity of these tests before recommending them for clinical practice.

Limitations

A small sample size is the major limitation. The absence of severe outcomes in this cohort precludes calculating the sensitivity of these tests in predicting severe outcomes.

Conflicts of interest

Authors have no conflicts of interests

Ethical statement

Ethical approval was obtained from the Ethics Review Committee of the Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka.

Written informed consent was obtained from the participants before they were recruited for the study. In the case of a minor (<18 years), consent was obtained from the guardian with the patient's assent. Those willing to participate in the study were assessed using the aforementioned clinical tests; however, we did not alter the management protocol of the unit under any circumstances.

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