## Forty-steps desaturation test does not have prognostic value in COVID-19 due to omicron variant

Dear Editor,

Field walking tests are frequently employed to evaluate exercise capacity, assess prognosis, and evaluate treatment response in chronic respiratory diseases. [1] The prototype of these tests is the 6-minute walk test, which has been well-validated as a reliable prognostic tool in a variety of diseases like COPD, ILD, and pulmonary hypertension. A shorter 6MWD was associated with increased mortality in 13 (93%) out of the 14 COPD studies. [2]

Exercise desaturation is a reliable prognostic marker in infective conditions like pneumocystis pneumonia. [3] Hypoxia is a hallmark of severity in COVID-19 patients. However, in the early stages, patients may not have hypoxia, and it is not easy to predict who will develop severe disease. It is of utmost importance to identify early signs of deterioration, and exercise tests may be helpful in that aspect. Early in the pandemic, the Centre for Evidence Based Medicine, Oxford had suggested that two tests have potential: the 1-minute sit-to-stand test (in which the

patient goes from sit to stand as many times as they can in one minute) and the 40-steps test (in which the patient takes 40 steps on a flat surface). The former correlated well with the validated 6-minute exercise test. The latter is less demanding (hence safer) and in more widespread use but has to be validated.<sup>[4]</sup>

NHS England introduced the use of a "40-steps desaturation test" in discharge planning from the Emergency department. A systematic review of rapid exercise tests for exercise desaturation in COVID-19 concluded that these tests have not yet been validated in patients with COVID-19. They suggested that although stronger evidence base exists for the diagnostic accuracy of the 1 MSTST in chronic long-term pulmonary disease; the relative intensity of this test may raise safety concerns in remote consultations or unstable patients and that the less strenuous 40-steps walk test should be evaluated.

Patients diagnosed with RT-PCR confirmed COVID-19 illness were consented for recruitment into this prospective observational study. The study was approved by Institutional Review Board (IRB Min. No. 14032 IOBSERVE) dated 30.06.2021). Patients with mild COVID-19 disease, confirmed by RT-PCR, were recruited if they had room air oxygen saturation >/=96% and were able to walk unaided. Assuming an 80% sensitivity of the 40-steps desaturation test to pick up those who require admission with a precision of 15%, we needed 29 patients to get admitted. Assuming a 7% rate of admission among those who undergo a 40-steps desaturation test, we needed 414 patients to achieve the target of 29 patients getting admitted.

The study commenced with the start of the third wave (Omicron), and we recruited eligible patients from January 2022 till March 2022. However, due to the rapid decline in COVID-19 cases, we could not achieve the sample size.

Demographic and clinical features were recorded. The 40-steps test was performed according to standard protocol

by a respiratory therapist, and the baseline and end-of-test oxygen saturation values and pulse rates were documented. The patients were sent home and were followed up as per clinical care protocol by the home care team. In addition, regular phone calls were made until 28 days from the onset of symptoms. If they required hospitalisation at any time during the follow-up, the following information was captured: the reason for hospitalization the severity of the illness at admission, need for low flow oxygen, need for NIV/HFNC, need for IMV, and death. Such patients were followed up till discharge and till the 28 days post the onset of symptoms.

We recruited 137 patients (83 males). There was a reduction in mean oxygen saturation from baseline of 98.5 ( $\pm$ 1.1) to 97.8 ( $\pm$ 1.7) after the test. This was statistically significant (P < 0.001) but not clinically relevant. Eight patients had significant desaturation  $\geq$ 3% during the baseline 40-steps test, but none required hospitalization. Four patients were admitted to the hospital due to the worsening of their COVID-19 illness; however, they did not have significant desaturation during the 40-steps test. There was no mortality in this cohort. There was no relationship between desaturation ( $\geq$ 3%) and other demographic parameters, symptoms, comorbidities, or vaccination status [Table 1].

Rhys GH et al. [8] published the first prospective study of this test in COVID-19 patients, where they recruited 64 patients. They showed that changes in saturation, respiratory rate, heart rate and breathlessness were not predictive of death or readmission to hospital within 30 days. Of 13 patients who had a desaturation of 3% or more during exercise, none were readmitted to the hospital within 30 days. Due to the small sample size, they concluded that further studies are required to validate the 40-steps study. Our study with a large sample size yielded results similar to the study by Rhy GH et al. with the 40-steps test not predicting the need for future hospitalization. There was no mortality in this cohort,

Table 1: Association of desaturation during the 40-steps test to demographic, comorbidities, symptomatology and vaccination status

Variable	Category	SpO2 fall ≥=3 <i>n</i> =8 (%)	SpO2 fall <3 <i>n</i> =129 (%)	OR (95% CI)	P
Sex	Female	3 (37.5)	51 (39.5)	0.91 (0.21,4.01)	1.000
Age	<50 years	3 (37.5)	71 (55)	0.49 (0.11,2.13)	0.470
Diabetes mellitus	Yes	2 (25)	39 (30.2)	1.3 (0.25,6.72)	1.000
Cardiovascular disease	Yes	3 (37.5)	17 (13.2)	0.25 (0.55,1.15)	0.093
Hypertension	Yes	2 (25)	38 (29.5)	1.25 (0.24,6.48)	1.000
Malignancy	Yes	1 (12.5)	9 (7)	0.52 (0.05, 4.74)	0.464
Immunosuppressive condition	Yes	0	3 (2.3)		
Chronic liver disease	Yes	0	3 (2.3)		
Chronic kidney disease	Yes	0	4 (3.1)		
Asthma	Yes	2 (25)	7 (5.4)	0.17 (0.02,1.01)	0.088
COPD	Yes	0	2 (1.6)		
Asymptomatic	Yes	1 (14.3)	9 (8)	0.52 (0.05,4.79)	0.465
Fever	Yes	3 (37.5)	83 (64.3)	3.01 (0.68,13.15)	0.148
Dry cough	Yes	4 (50)	84 (65.1)	1.87 (0.44,7.81)	0.456
Dyspnoea	Yes	0	11 (8.5)		
COVID Vaccination	Yes	7 (87.5)	89 (69)	3.14 (0.37, 26.42)	0.435

which may be due to the milder severity of the COVID-19 illness during the third wave, predominately caused by the Omicron variant. Whether the test would have helped predict patients with the delta variant with more propensity to respiratory failure is not known. As such, we were unable to prove the validity of the test as a predictor of future deterioration, hospitalization or mortality.

In conclusion, the 40-steps test does not have prognostic value in patients with COVID-19 illness due to the Omicron variant.

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## **Conflicts of interest**

There are no conflicts of interest.

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