J Bras Pneumol. 2023;49(3):e20230027
https://dx.doi.org/10.36416/1806-3756/e20230027

ORIGINAL ARTICLE

Role of the one-minute sit-to-stand test in the diagnosis of post COVID-19 condition: a prospective cohort study

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Submitted: 26 January 2023.
Accepted: 23 March 2023.

Study carried out in the Serviço de Pneumologia, Centro Hospitalar Universitário do Porto, Porto, Portugal.

ABSTRACT

Objective: To analyze the relationship between one-minute sit-to-stand test (1MSTST) parameters and a diagnosis of post COVID-19 condition in a cohort of patients who previously had COVID-19. **Methods:** This was a prospective cohort study of patients with post COVID-19 condition referred for body plethysmography at a tertiary university hospital. Post COVID-19 condition was defined in accordance with the current WHO criteria. **Results:** Fifty-three patients were analyzed. Of those, 25 (47.2%) met the clinical criteria for post COVID-19 condition. HR was lower in the patients with post COVID-19 condition than in those without it at 30 s after initiation of the 1MSTST (86.2 ± 14.3 bpm vs. 101.2 ± 14.7 bpm; $p < 0.001$) and at the end of the test (94.4 ± 18.2 bpm vs. 117.3 ± 15.3 bpm; $p < 0.001$). The ratio between HR at the end of the 1MSTST and age-predicted maximal HR (HR_{end}/HR_{max}) was lower in the group of patients with post COVID-19 condition ($p < 0.001$). An HR_{end}/HR_{max} of < 62.65% showed a sensitivity of 78.6% and a specificity of 82.0% for post COVID-19 condition. Mean SpO_2 at the end of the 1MSTST was lower in the patients with post COVID-19 condition than in those without it (94.9 ± 3.6% vs. 96.8 ± 2.4%; $p = 0.030$). The former group of patients did fewer repetitions on the 1MSTST than did the latter ($p = 0.020$). **Conclusions:** Lower SpO_2 and HR at the end of the 1MSTST, as well as lower HR at 30 s after initiation of the test, were associated with post COVID-19 condition. In the appropriate clinical setting, an HR_{end}/HR_{max} of < 62.65% should raise awareness for the possibility of post COVID-19 condition.

Keywords: COVID-19; Post-acute COVID-19 syndrome; Heart rate; Respiratory function tests.

INTRODUCTION

After confirmation of the potential for sequelae of COVID-19, statements were formulated recommending clinical, pulmonary function, physical capacity, and imaging evaluation of these patients.[1,2] The term "long COVID" was initially coined to describe COVID-19 patients experiencing lingering symptoms, being subsequently defined as post COVID-19 condition in the WHO ICD-11 (code RA02). The WHO also provided recommendations for the definition of post COVID-19 condition in adults: individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis; these symptoms include fatigue, shortness of breath, and cognitive dysfunction, and have an impact on activities of daily living in most cases.[3] Therefore, post COVID-19 condition is a diagnosis of exclusion, based on clinical findings. Post COVID-19 condition is a prevalent disorder; it has been estimated to affect 13.9% of individuals with a history of COVID-19, having affected 1.7% of all adults in the U.S. in 2022.[4] However, the prevalence of post COVID-19 condition decreases over time, being = 4.5% and 2.3% at 8 and 12 months after SARS-CoV-2 infection, respectively.[5]

The sit-to-stand test has been recommended as a useful and safe tool to assess physical capacity in post COVID-19 patients, provided that the test is performed under supervision (but not via telemonitoring).[2] In addition, it has been reported that the one-minute sit-to-stand test (1MSTST) can be used for evaluating exertional desaturation in COVID-19 patients because it has been validated for use in patients with chronic interstitial lung disease and in those with obstructive airway disease; however, the 1MSTST should be used only under clinical supervision because it can produce a high cardiorespiratory stress.[6] On the basis of this recommendation, the 1MSTST has been integrated into a clinical trial protocol as an assessor of improvement in exertional dyspnea/SpO_2.[7]

The current literature on the role of the 1MSTST in the assessment of COVID-19 focuses on the ability of the test to evaluate hospitalization or home discharge, or to assess the clinical status of patients after hospitalization or pulmonary rehabilitation[8]; it does not focus on the role of the 1MSTST in the diagnosis of post COVID-19 condition. In the evaluation of pulmonary rehabilitation, the thirty-second sit-to-stand test has been shown to improve leg strength, endurance, and SpO_2 in patients with post COVID-19 condition after hospital discharge.[9,10]

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Financial support: None.

Similar results have been reported for the roles of the 1MSTST and the three-minute sit-to-stand test in pulmonary rehabilitation.[11,12]

There are knowledge gaps in the diagnosis of post COVID-19 condition. The European Respiratory Society statement on long COVID follow-up suggests that longitudinal cohort studies are needed to determine effective interventions for assessing and monitoring disability in patients with post COVID-19 condition.[1] After a diagnosis of COVID-19, the understanding of what distinguishes those with from those without post COVID-19 condition allows the design of studies of lung capacity/pulmonary rehabilitation based on the expected baseline for these patients. It also allows the use of appropriate tools for an accurate diagnosis of post COVID-19 condition.

The objective of the present study was to establish a relationship between 1MSTST parameters and post COVID-19 condition as defined by the current WHO criteria.[3]

METHODS

Study setting

We prospectively enrolled adults referred for outpatient pulmonary function testing between April of 2021 and June of 2022 in the Pathophysiology Laboratory of the *Centro Hospitalar Universitário do Porto*, located in the city of Porto, Portugal. Inclusion criteria were being ≥ 18 years of age, being an outpatient followed at the *Centro Hospitalar Universitário do Porto*, and having at least one positive RT-PCR nasal/pharyngeal swab result for SARS-CoV-2 in the last 18 months. Patients performed the 1MSTST under the supervision of a cardiopulmonary technician who was blinded to whether or not they had symptoms of post COVID-19 condition.

Exclusion criteria were having a second episode of possible/confirmed SARS-CoV-2 infection before the 1MSTST, declining to participate in the study, and having any contraindication to the 1MSTST (inability to perform the test because of limited mobility or limited joint mobility/joint pain, for example; systolic blood pressure > 180 mmHg; and diastolic blood pressure > 100 mmHg). For a power of 80% and a two-sided type I error of 5%, a minimum sample size of 34 was calculated to be required to detect an effect size of at least 0.5 for HR, SpO_2, and number of repetitions over the course of the 1MSTST.

The present study was approved by the local research ethics committee, and all participating patients gave written informed consent. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Procedures and data collection

We collected data on the following: baseline demographic and anthropometric characteristics; patient medical history (including hospitalization records); tobacco exposure history; and underlying comorbidities. All patients underwent chest CT scans in the post COVID-19 period (8.9 ± 3.9 months after the diagnosis of COVID-19, at a minimum of 4 months but at no more than 14 months after diagnosis).

To determine whether patients with post COVID-19 condition had pulmonary function test results that were different from those in other post COVID-19 patients, all of the patients included in the present study underwent body plethysmography (MasterScreen™ Body/Diff v-707340; CareFusion, Hoechberg, Germany; and MasterScreen™ Body/Diff; Jaeger, Hoechberg, Germany), with the equipment being calibrated in accordance with the manufacturer recommendations. Percent predicted DL_{CO} and spirometric values were based on the Global Lung Function Initiative equations for patients ≤ 85 years of age and on the European Community for Steel and Coal equations for those > 86 years of age.[13,14] For static lung volumes, the European Community for Steel and Coal equations for adults were used.[13]

The 1MSTST was performed on a standard-height (46-cm) fixed-leg chair with no armrests and the backrest against a wall. Participants were not allowed to use their hands or arms to push against the chair seat or their body. Participants were instructed to complete as many sit-to-stand actions as possible in 1 min at a self-paced speed. Cardiorespiratory parameters, as well as systolic and diastolic blood pressure, together with shortness of breath and leg fatigue (as assessed by the modified Borg scale) were recorded before and immediately after the 1MSTST. Oxygen saturation and HR were recorded at the beginning of the test, at 30 s after initiation of the test, at the end of the test, and at 1 min after completion of the test. The evaluator had previous experience in applying the 1MSTST. In order to assess blood pressure, HR, and SpO_2, a vital signs monitor (CARESCAPE V100; GE HealthCare Technologies Inc., Chicago, IL, USA) was used.

Post COVID-19 condition was defined in accordance with the WHO criteria, i.e., adult individuals with RT-PCR–confirmed SARS-CoV-2 infection presenting with new-onset symptoms up to 3 months from the diagnosis of COVID-19 that last for at least 2 months and cannot be explained by an alternative diagnosis.

Statistical analysis

All patient data were anonymized before statistical analysis, which was performed with the IBM SPSS Statistics software package, version 26.0 (IBM Corporation, Armonk, NY, USA). The demographic and clinical characteristics of the patients were described with descriptive statistics. Data are presented as number (proportion) for categorical variables; mean ± standard deviation for continuous variables with normal distribution; and median (interquartile range) for continuous variables with non-normal distribution. The age-predicted maximal heart rate (HR_{max}) was calculated by the following equation: $HR_{max} = 220 - age$.[15,16]

Univariate analysis was performed with the chi-square test or Fisher's exact test, whereas continuous variables were compared by means of the Student's t-test or the Mann-Whitney test for nonparametric data. The multivariate model included age, sex, and variables showing p < 0.2 in the univariate analysis. Taking into consideration that the prevalence of post COVID-19 condition decreases over time,[(5)] we also adjusted our findings for the time elapsed between the diagnosis of COVID-19 and the performance of the 1MSTST. A two-tailed value of p < 0.05 was considered statistically significant.

RESULTS

A total of 53 patients (43.4% of whom were male, with a mean age of 49.8 ± 17.0 years) were analyzed. Of those 53 patients, 25 (47.2%) had post COVID-19 condition (Table 1). In the 25 patients with post COVID-19 condition, the most common symptoms were fatigue/insomnia (n = 12; 48%), dyspnea (n = 9; 36%), cough (n = 2; 8%), upper airway symptoms (n = 1; 4%), and headache (n = 1; 4%).

The BMI was higher in the patients with post COVID-19 condition than in those without it (28.9 ± 5.4 kg/m^2 vs. 26.7 ± 3.8 kg/m^2), although the difference was not significant (p = 0.082). Healthcare workers were mostly previously healthy patients, with 31.6% with prior lung disease. The remaining population had prior lung disease in 64.7% of the cases (p=0.021).

New-onset chest CT findings (i.e., findings that were nonexistent before COVID-19) were more common in the patients with post COVID-19 condition than in those without it (p = 0.045). In addition, the latter group of patients did not present with reticular/fibrotic opacities. The chest CT scans were performed in a similar time frame for both groups (p = 0.223), i.e., 10 ± 4.7 months after the diagnosis of COVID-19 in those with post COVID-19 condition and 7.4 ± 1.6 months in those without it.

Pulmonary function test results were overall similar between the two groups of patients (Table 2). There were no significant differences between the patients with post COVID-19 condition and new-onset respiratory symptoms (n = 12) and those with other symptoms regarding demographic characteristics, clinical characteristics, 1MSTST results, and imaging findings. However, those with new-onset respiratory symptoms had a significantly lower percent predicted carbon monoxide transfer coefficient (86.7 ± 14.2% vs. 101.6 ± 15.7%; p = 0.021).

Figure 1 shows HR at the beginning of the 1MSTST, at 30 s after initiation of the test, at the end of the test, and at 1 min after completion of the test. The groups of patients with and without post COVID-19 condition showed similar HR at rest (76.0 ± 12.8 bpm vs. 78.5 ± 12.1 bpm; p = 0.476). HR was lower in those with post COVID-19 condition at 30 s after initiation of the test (86.2 ± 14.3 bpm vs. 101.2 ± 14.7 bpm; p < 0.001) and at the end of the test (94.4 ± 18.2 bpm vs. 117.3 ± 15.3 bpm; p < 0.001), as well as at 1 min after completion of the test (81.2 ± 14.4 bpm vs. 90.5 ± 12.9 bpm; p = 0.016). Regarding mean SpO_2, there were significant differences between the groups of patients with and without post COVID-19 condition, although only at the end of the 1MSTST (94.9 ± 3.6% vs. 96.8 ± 2.4%; Figure 2).

As can be seen in Table 3, the patients with post COVID-19 condition performed fewer repetitions on the 1MSTST than did those without it (p = 0.020). The

Table 1. Characteristics of the study population.[a]

Characteristic	Total sample (N = 53)	Group		p
		Post COVID-19 condition (n = 25; 47.2%)	No post COVID-19 condition (n = 28; 52.8%)	
Age, years	49.8 ± 17.0	52.9 ± 14.8	47.0 ± 18.7	0.216
Male sex	23 (43.4)	10 (40.0)	13 (46.4)	0.637
Current/former smoker	20 (37.7)	9 (36.0)	11 (39.3)	0.805
Smoking history, pack-years[b]	31.1 ± 16.3	30.6 ± 15.5	31.5 ± 17.7	0.703
BMI, kg/m^2	27.7 ± 4.7	28.9 ± 5.4	26.7 ± 3.8	0.082
Hospitalization for COVID-19	11 (20.8)	6 (24.0)	5 (17.9)	0.582
Time elapsed between the diagnosis of COVID-19 and the 1MSTST	7.0 [5.0-9.5]	7.0 [5.0-10.5]	7.0 [5.0-9.0]	0.535
New-onset chest CT findings	25 (47.2)	16 (64.0)	8 (28.6)	0.045
Ground-glass opacities	17 (32.1)	8 (32.0)	8 (28.6)	
Reticular/fibrotic opacities	8 (15.1)	8 (32.0)	0	
Preexisting lung disease	29 (54.7)	14 (56.0)	15 (53.6)	0.662
Asthma	18 (34.0)	8 (32.0)	10 (35.7)	
COPD	5 (9.4)	1 (4.0)	4 (14.3)	
Interstitial lung disease	2 (3.8)	2 (8.0)	0 (0.0)	
OSA	4 (7.5)	3 (12.0)	1 (3.6)	

1MSTST: one-minute sit-to-stand test; and OSA: obstructive sleep apnea. [a]Values expressed as n (%), mean ± SD, or median [IQR]. [b]For current/former smokers only.

Table 2. Pulmonary function test results.[a]

Parameter	Total sample	Group		p
		Post COVID-19 condition	No post COVID-19 condition	
	(N = 53)	(n = 25; 47.2%)	(n = 28; 52.8%)	
FVC, L	3.45 ± 0.94	3.24 ± 0.63	3.38 ± 0.98	0.460
FVC, % predicted	94.1 ± 15.7	93.6 ± 13.3	94.0 ± 17.1	0.856
FEV_1, L	2.73 ± 0.79	2.61 ± 0.60	2.64 ± 0.78	0.561
FEV_1, % predicted	92.2 ± 18.8	92.7 ± 17.3	92.1 ± 20.7	0.975
FEV_1/FVC ratio	78.5 ± 9.0	78.8 ± 9.1	77.9 ± 8.8	0.830
Airway resistance	0.30 ± 0.18	0.31 ± 0.22	0.29 ± 0.14	0.747
Airway resistance, % predicted	101.4 ± 61.9	104.7 ± 75.3	97.8 ± 45.5	0.725
RV	2.03 ± 0.80	2.05 ± 0.97	2.02 ± 0.59	0.895
RV, % predicted	108.2 ± 31.0	108.4 ± 36.3	107.9 ± 25.3	0.963
TLC	5.45 ± 1.18	5.42 ± 1.10	5.48 ± 1.28	0.871
TLC, % predicted	102.9 ± 16.4	103.2 ± 16.3	102.6 ± 17.0	0.911
Single-breath DL_{CO}	6.68 ± 1.61	6.97 ± 1.47	6.37 ± 1.74	0.643
Single-breath DL_{CO}, % predicted	82.7 ± 17.2	86.2 ± 17.9	79.1 ± 16.1	0.496
K_{CO}	1.50 ± 0.56	1.63 ± 0.73	1.37 ± 0.25	0.599
K_{CO}, % predicted	93.2 ± 16.6	96.9 ± 17.0	89.3 ± 15.7	0.117

K_{CO}: carbon monoxide transfer coefficient. [a]Values expressed as mean ± SD.

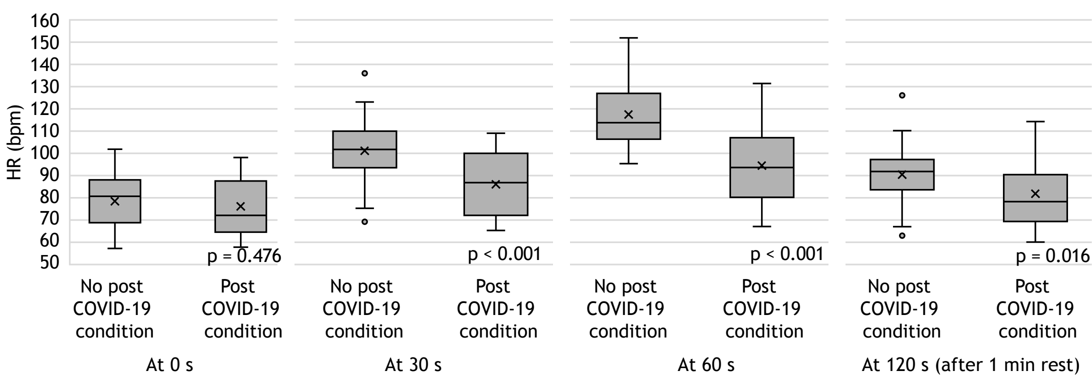

Figure 1. HR over the course of the one-minute sit-to-stand test in the groups of patients with and without post COVID-19 condition.

ratio between HR at the end of the 1MSTST and HR_{max} (HR_{end}/HR_{max}) was lower in the group of patients with post COVID-19 condition ($p < 0.001$). The HR_{end}/HR_{max} cutoff that maximized both sensitivity and specificity was 62.65% (sensitivity, 78.6%; specificity, 82.0%). In our cohort, all of the patients without post COVID-19 condition had an HR_{end}/HR_{max} above 51.48% (sensitivity, 100%; specificity, 48.0%).

Systolic blood pressure and diastolic blood pressure were similar between the two groups at the beginning of the 1MSTST ($p = 0.464$ and $p = 0.864$, respectively) and at the end of the test ($p = 0.784$ and $p = 0.475$, respectively), as well as at 1 min after completion of the test ($p = 0.261$ and $p = 0.768$, respectively).

DISCUSSION

In this study, new-onset chest CT findings were more common in the patients with post COVID-19 condition than in those without it. Although there have been reports of an increased number of CT abnormalities after the diagnosis of COVID-19 (particularly severe COVID-19), there are currently no studies comparing COVID-19 patients with and without post COVID-19 condition.[17] Regarding pulmonary function tests, the results were similar between the groups of patients with and without post COVID-19 condition in the present study. Those with post COVID-19 condition and new-onset respiratory symptoms had a significantly lower percent predicted carbon monoxide transfer coefficient (86.7 ± 14.2% vs. 101.6 ± 15.7%; $p = 0.021$). However, the results of this subgroup analysis should be interpreted with caution because of the small sample size (n = 12). The most commonly described abnormalities in COVID-19 patients are changes in DL_{CO}, a restrictive ventilatory pattern, and an obstructive ventilatory pattern.[18] However, there have been no studies comparing patients with and without post COVID-19 condition.

Regarding the 1MSTST, the patients with post COVID-19 condition in the present study had lower HR at 30 s after initiation of the test, at the end of

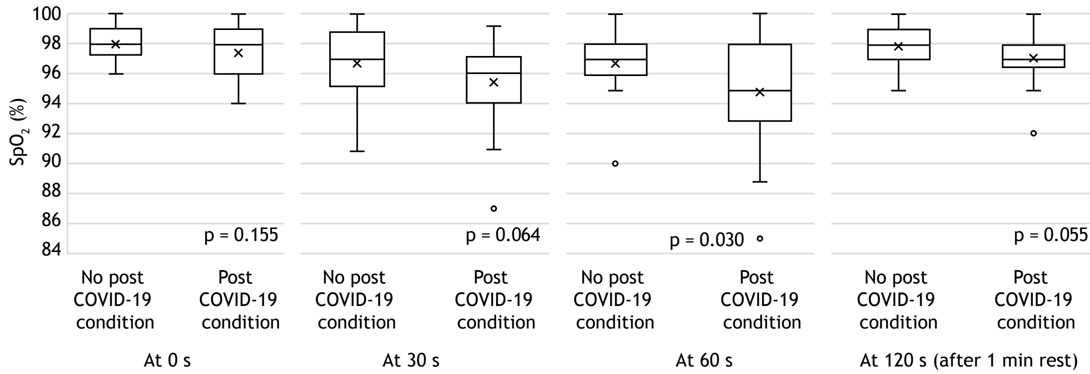

Figure 2. SpO_2 over the course of the one-minute sit-to-stand test in the groups of patients with and without post COVID-19 condition.

Table 3. HR, SpO_2, blood pressure, and number of repetitions over the course of the one-minute sit-to-stand test.[a]

	Total sample	Group		p (univariate)	p* (multivariate)
		Post COVID-19 condition	No post COVID-19 condition		
	(N = 53)	(n = 25; 47.2%)	(n = 28; 52.8%)		
HR, bpm					
At the beginning of the 1MSTST	77.3 ± 12.4	76.0 ± 12.8	78.5 ± 12.1	0.476	
At 30 s after initiation of the 1MSTST	94.1 ± 16.2	86.2 ± 14.3	101.2 ± 14.7	< 0.001	0.005
At the end of the 1MSTST	106.5 ± 20.2	94.4 ± 18.2	117.3 ± 15.3	< 0.001	< 0.001
At 1 min after completion of the 1MSTST	86.1 ± 14.3	81.2 ± 14.4	90.5 ± 12.9	0.016	0.073
HR_{end}/HR_{max}, %	62.9 ± 12.4	56.8 ± 11.7	68.4 ± 10.4	< 0.001	< 0.001
SpO_2, %					
At the beginning of the 1MSTST	97.7 ± 1.5	97.4 ± 1.8	98.0 ± 1.0	0.155	0.368
At 30 s after initiation of the 1MSTST	96.1 ± 2.6	95.3 ± 2.8	96.7 ± 2.3	0.064	0.117
At the end of the 1MSTST	95.9 ± 3.1	94.9 ± 3.6	96.8 ± 2.4	0.030	0.037
At 1 min after completion of the 1MSTST	97.6 ± 1.5	97.2 ± 1.7	97.9 ± 1.2	0.055	0.183
No. of repetitions on the 1MSTST	35.5 ± 8.6	32.6 ± 7.0	38.0 ± 9.1	0.020	0.060
Systolic BP, mmHg					
At the beginning of the 1MSTST	128.2 ± 16.0	129.7 ± 15.5	126.7 ± 16.5	0.464	
At the end of the 1MSTST	147.2 ± 22.6	146.3 ± 18.6	148.1 ± 26.2	0.784	
Diastolic BP, mmHg					
At the beginning of the 1MSTST	74.8 ± 9.6	74.5 ± 8.5	75.2 ± 10.6	0.864	
At the end of the 1MSTST	79.1 ± 10.3	80.2 ± 9.4	78.1 ± 11.1	0.475	

1MSTST: one-minute sit-to-stand test; HR_{end}/HR_{max}: ratio between HR at the end of the 1MSTST and age-predicted maximal HR; and BP: blood pressure. [a]Values expressed as mean ± SD. *The multivariate model included age, sex, time elapsed between the diagnosis of COVID-19 and the performance of the 1MSTST, and variables showing p < 0.2 in the univariate analysis of patient demographic data (i.e., BMI).

the test, and at 1 min after completion of the test, as well as lower SpO_2 at the end of the test and lower HR_{end}/HR_{max}. After adjusting for age, sex, time elapsed between the diagnosis of COVID-19 and the performance of the 1MSTST, and variables showing $p < 0.2$ in the univariate analysis, we found that all of the variables remained statistically significant, the exception being HR at 1 min after completion of the test. In an attempt to find an HR_{end} cutoff adjusted for the expected HR_{max} to support the diagnosis of post COVID-19 condition, we found that all of the patients without post COVID-19 condition in our cohort had an HR_{end}/HR_{max} above 51.48%, and the optimal threshold value (Youden index) for a diagnosis of post COVID-19 condition was 62.65% (sensitivity, 78.6%; specificity, 82.0%).

An inappropriate sinus tachycardia at rest appears to affect 20% of all patients with post COVID-19 condition; this is probably due to autonomic nervous system disorder (postinfectious dysautonomia).[19] It is not known whether patients with post COVID-19 condition are more affected by inappropriate sinus tachycardia at rest than are other COVID-19 patients. Sinus bradycardia is known to occur during sleep in patients with COVID-19.[20] Orthostatic hypotension and postural orthostatic tachycardia syndrome have also been reported to be common after SARS-CoV-2 infection,[19,21] with both conditions being interpreted as complications of dysautonomia.[21] The higher prevalence of exertional bradycardia in patients with post COVID-19 condition occurs in opposition to the high prevalence of inappropriate sinus tachycardia at rest in these patients. A major role of the autonomic nervous system in the pathophysiology of HR dysregulation is consistent with inadequate HR responses to rest and exercise in patients with post COVID-19 condition.[19,21,22]

Although we did not perform continuous HR monitoring throughout the 1MSTST, we recognize that it would be valuable to perform a cardiac stress test to understand whether post COVID-19 condition is associated with sinus bradycardia or bradyarrhythmia during exercise tests. Furthermore, the 1MSTST requires a reasonable degree of lower limb joint integrity, and this explains the limited sample size for the study period and the relatively low mean age of the study population (49.8 years). In order to validate the exercise capacity results obtained with the 1MSTST, it would have been of interest to perform the six-minute walk test. However, this study was initiated at a time when the six-minute walk test was performed only in selected patients, after having been suspended worldwide because of the COVID-19 outbreak.

In the appropriate clinical setting, an HR_{end}/HR_{max} below 62.65% (in particular, an HR_{end}/HR_{max} below 51.48%) appears to be suggestive of a diagnosis of post COVID-19 condition.

AUTHOR CONTRIBUTIONS

NF: conceptualization, data curation, formal analysis, investigation, methodology, project administration, software, visualization, drafting of the manuscript, and reviewing and editing of the manuscript. TO: conceptualization, formal analysis, methodology, validation, and reviewing and editing of the manuscript. PP and VA: conceptualization, data curation, formal analysis, methodology, project administration, software, validation, and reviewing and editing of the manuscript. RC and MJF: data curation and investigation. MS: formal analysis, project administration, and reviewing and editing of the manuscript. JG: conceptualization, formal analysis, investigation, methodology, project administration, software, supervision, validation, drafting of the manuscript, and reviewing and editing of the manuscript. All of the authors read and approved the final manuscript.

CONFLICTS OF INTEREST

None declared.

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