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The Glittre-ADL test in non-hospitalized patients with post-COVID-19 syndrome and its relationship with muscle strength and lung function

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A R T I C L E I N F O

Keywords:
COVID-19
Exercise
Muscle
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A B S T R A C T

Background: Patients with post-acute COVID-19 syndrome tend to have limitations in performing activities of daily living, which may negatively impact performance during the Glittre-ADL test. This study aimed to verify if the Glittre-ADL test is associated with measures of pulmonary function, muscle function, and health-related quality of life in the assessment of non-hospitalized patients with sequelae of COVID-19, and also to identify the predictor variables related to the Glittre-ADL test in order to create a predictive model.
Methods: Cross-sectional study with 37 women with post-acute COVID-19 syndrome who underwent Glittre-ADL test. They performed pulmonary function tests and measurements of handgrip strength and quadriceps strength. Additionally, they completed the Post-COVID-19 Functional Status scale and the Short Form-36 questionnaire.
Findings: The mean value of Glittre-ADL test time was 4.8 ± 1.1 min, which was 163.7 ± 39.7% of the predicted. The Glittre-ADL test time showed correlation with diffusing capacity for carbon monoxide ($r = -0.671$, $P < 0.0001$), forced vital capacity ($r = -0.588$, $P = 0.0001$), maximum inspiratory pressure ($r = -0.391$, $P = 0.015$), handgrip strength ($r = -0.453$, $P = 0.005$), quadriceps strength ($r = -0.591$, $P = 0.0001$), and various dimensions of the Short Form-36 questionnaire. In the regression analysis, diffusing capacity for carbon monoxide, quadriceps strength, and forced vital capacity explained 64% of the Glittre-ADL test time variability.
Interpretation: In patients with post-acute COVID-19 syndrome, lung function and quadriceps strength strongly affect the time to perform Glittre-ADL test multiple tasks.

1. Introduction

Millions of people around the world have developed or are at risk of developing post-acute COVID-19 syndrome (PCS). It is characterized by persistent and debilitating symptoms that are still present at least 12 weeks after the initial infection (Ayoubkhani et al., 2021). Clinical manifestations usually occur in the absence of severe acute infection, clinically explainable physical symptoms, or pre-existing comorbidities (Bliddal et al., 2021). It is believed that persistent symptoms after acute infection by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) would result from an immune-mediated disruption of the autonomic nervous system, and thus COVID-19 infection would act as an immune trigger (Dani et al., 2021; Tabacof et al., 2022). The treatment and evolution of these cases, after the acute infection, are still under investigation, given the little knowledge that there is about the natural history of the disease in the long term.

Abbreviations: 6MWT, 6-min walk test; ADLs, Activities of daily living; DLCO, Diffusing capacity for carbon monoxide; FEV_1, Forced expiratory volume in one second; FVC, Forced vital capacity; HGS, Handgrip strength; HRQoL, Health-related quality of life; IPAQ, International Physical Activityquestionnaire; MEP, Maximum expiratory pressure; MIP, Maximum inspiratory pressure; PCS, Post-acute COVID-19 syndrome; PCFS, Post-COVID-19 Functional Status; PFTs, Pulmonary function tests; QS, Quadriceps strength; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; SF-36, Short Form-36; TGlittre, Glittre-ADL test; VIF, Variance inflation factor.

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COVID-19 is known to cause lung damage that can range from asymptomatic cases to acute respiratory failure with severe hypoxemia and the need for ventilatory support (Yang et al., 2020). As a consequence, pulmonary function tests (PFTs) may show either a restrictive pattern, an obstructive pattern or small airways dysfunction after acute infection (Lopes et al., 2021a, 2021b), which can negatively impact long-term functional capacity (Johnsen et al., 2021). Although the lungs are often the first target organ of SARS-CoV-2 infection, the virus can spread to many different organs (Johnsen et al., 2021). In muscles, COVID-19 can act as a catabolic stimulus, with weight loss and risk of acute sarcopenia (Damanti et al., 2022). The state of hyperinflammation caused by SARS-CoV-2 exacerbates the immunosenescence process, increases endothelial damage, and induces myofibrillar breakdown and muscle degradation due to mitochondrial dysfunction and autophagy (Damanti et al., 2022; Piotrowicz et al., 2021). Muscle symptoms in PCS can be persistent even in mild cases, and the consequences arising from muscle dysfunction may significantly reduce functional capacity during exercise (Li, 2020).

The assessment of functional capacity is a crucial component in physical reconditioning programmes in patients with PCS (Souza et al., 2020). Among the methods used for its evaluation are field tests, capable of simulating objectively the activities of daily living (ADLs). Despite being widely used in clinical practice, the 6-min walk test (6MWT) measures only walking activity, making it impossible to assess limitations in other problematic activities for patients with multiple functional sequelae. More recently, the Glittre-ADL test (TGlittre) was developed to address the need for a broader objective assessment of physical function, using ADL-like activities such as sitting on and rising from a chair, walking, going up and down stairs, and moving objects from one shelf to another (Monteiro et al., 2017; Skumlien et al., 2006).

The TGlittre has already proved itself valid, reliable, and capable of reflecting the perception of functional limitation in patients with different clinical conditions (Gulart et al., 2018). Furthermore, it has the potential for clinical use in PCS as it simulates ADLs and detects potential defects in cardiopulmonary and skeletal muscle functioning. Thus, TGlittre – as it involves large muscle groups of the lower and upper limbs and is a functional test that provides information about the daily capabilities of patients – seems to fulfil requirements for the common practice. We hypothesized that the TGlittre is an important tool in the assessment of patients with PCS and that it presents a relationship with measures provided by PFTs, muscle function, and health-related quality of life (HRQoL). This study aimed to verify whether the TGlittre is associated with measures of pulmonary function, muscle function, and HRQoL in previously non-hospitalized patients with sequelae resulting from SARS-CoV-2 infection, and also to identify the predictor variables related to the TGlittre in order to create a predictive model.

2. Methods

2.1. Subjects

Between September 2021 and March 2022, we conducted a cross-sectional study with 37 (out of 41 who were eligible) women aged ≥18 years with PCS who were regularly followed up at the Pedro Ernesto University Hospital of the State University of Rio de Janeiro, Rio de Janeiro, Brazil. Patients who were diagnosed with COVID-19 by a positive reverse transcription-polymerase chain reaction test and who did not require hospital admission were included. The following exclusion criteria were used: hypoxemia at rest (peripheral oxygen saturation < 88%); unstable cardiovascular disease; and musculoskeletal, neurological, or rheumatic disorders that could limit the ability to participate in physical tests.

The protocol was approved by the Research Ethics Committee of the State University of Rio de Janeiro under CAAE-30135320.0.0000.5259 and was conducted in accordance with the principles of the Declaration of Helsinki. All patients signed the consent form.

2.2. Measurements

The level of physical activity in daily life was assessed using the short form of the International Physical Activity (IPAQ) questionnaire (Craig et al., 2003), which evaluates total energy expenditure and time spent in ADLs. The ADLs were divided into different intensities (light, moderate and vigorous) for the following domains: work-related activities; transport-related activities; housework; recreation, sport, physical exercise, and leisure activities; and time spent in passive activities performed in the sitting position. Individuals were instructed to answer the questions based on the seven days before the application of the IPAQ questionnaire.

The Post-COVID-19 Functional Status (PCFS) scale [available at https://osf.io/qgpdv/ (CC-BY 4.0)] was applied following the instructions provided in the primary source. Briefly, participants were asked about their average situation in the previous week regarding symptoms (e.g., dyspnoea, pain, fatigue, muscle weakness, memory loss, depression, and anxiety). The meaning of each of the PCFS scale grades are as follows: grade 0 (no functional limitations); grade 1 (negligible functional limitations); grade 2 (slight functional limitations); grade 3 (moderate functional limitations); and grade 4 (severe functional limitations) (Klok et al., 2020).

We used the Short Form-36 (SF-36) questionnaire in its short version to assess HRQoL. This multidimensional, patient-reported tool comprises 36 items grouped into 8 dimensions: physical functioning, physical role limitations, bodily pain, general health perceptions, vitality, social functioning, emotional role limitations, and mental health (Brazier et al., 1992). The results are provided in scores ranging from 0 to 100, and the higher the score, the better the HRQoL.

PFTs consisted of spirometry, measurement of diffusing capacity for carbon monoxide (DLCO), and measurement of respiratory muscle strength (maximum inspiratory pressure [MIP] and maximum expiratory pressure [MEP]). All these tests were performed on an HDpft 3000 device (nSpire Health, Inc., Longmont, CO, USA), and followed the standardization developed by the American Thoracic Society (Miller et al., 2005). We adopted national equations to calculate the predicted values of each participant (Neder et al., 1999a; Neder et al., 1999b; Pereira et al., 2007). The obstructive pattern was defined by a forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) ratio < 70%, while the restrictive pattern was inferred by an FVC < 80% of the predicted value in the absence of reduced expiratory flows (Kang et al., 2019).

Handgrip strength (HGS) was expressed in kilograms and measured using a handheld digital dynamometer (SH5001, Saehan Corporation, Korea). HGS was assessed with participants seated in an armless chair, elbows flexed at 90°, forearms in a neutral position, and wrist extension between 0° and 30° (Nonato et al., 2020). Maximum strength was assessed after a 3-s sustained contraction with the dominant hand; the highest value of three attempts (with a 1-min interval between them) was considered for analysis. Additionally, we evaluated quadriceps strength (QS) using a traction dynamometer with a sensor capacity of 200 kg (*E*-lastic 5.0, E-sporte SE, Brazil). Participants were asked to position themselves in a flexo-extending chair and assume a seated posture with an erect trunk, hips flexed at 90°, legs hanging without support, and crossed upper limbs in front of the trunk. The range of motion in the test was determined starting at 90° with the knee flexed. Maximum strength was assessed after a 5-s sustained contraction (dominant leg), with the knee extended at 90°. The highest value of three attempts with 1-min intervals was considered for analysis (Assis and Lopes, 2022).

The TGlittre (Fig. 1) was performed as previously proposed by Skumlien et al. (2006). This test showed excellent validity and reliability in different populations with the most varied clinical conditions (Corrêa et al., 2011; José and Dal Corso, 2015; Montemezzo et al., 2019; Reis et al., 2018; Skumlien et al., 2006). It consists of carrying a backpack weighing 2.5 kg for women on their backs and running a circuit with a

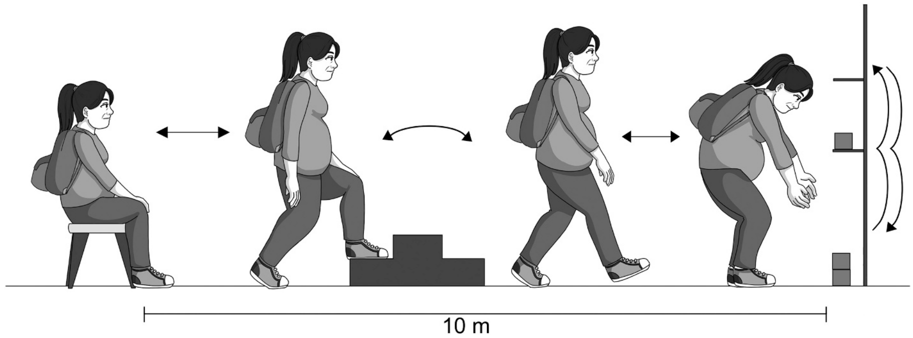

Fig. 1. Tasks involved in Glittre ADL-test.

length of 10 m. In it, the individual, from the sitting position, walks on a flat path interposed in its half by a box with two steps to go up and two to go down (17 cm high X 27 cm long). After covering the rest of the route, the individual comes across a shelf containing three objects of 1 kg each, positioned on the highest shelf, and must then move them, one by one, to the lowest shelf and, later, until the floor. Objects must be replaced on the lowest shelf and later on the highest shelf. Then, the individual returns, taking the route in reverse; immediately after, he starts another lap, covering the same circuit. The participant must complete five laps in the shortest possible time to perform the test. The protocol was performed twice with a 30-min interval or until signs and symptoms returned to baseline. The TGlittre of shorter duration was used for analysis because of the learning effect associated with this test (de Alegria et al., 2021; Reis et al., 2018). Thus, the interpretation of TGlittre time was based on comparisons of data measured in an individual patient with reference (predicted) values based on healthy subjects (Reis et al., 2018).

2.3. Statistical analysis

We used parametric methods, as the variables had a Gaussian distribution according to the rejection of the normality hypothesis by the Shapiro-Wilk test. The association between TGlittre time and clinical variables, PFT results, respiratory and peripheral muscle strength, and HRQoL assessed by the SF-36 questionnaire was analysed by Pearson's correlation coefficient for numerical variables and by Student's *t*-test for independent samples for categorical variables (type-I error $\alpha = 0.05$).

We used multiple linear regression with the process of selecting variables through stepwise forward regression analysis to identify the independent variables that would explain the TGlittre time. The following variables were included in the regression model: age; weight; height; body mass index; FVC; FEV_1/FVC; DLCO; MIP; MEP; HGS; and QS. Multicollinearity was assessed using the variance inflation factor (VIF); a VIF value >5 indicates that the associated regression coefficients are poorly estimated (Marquardt, 1970). Results were expressed as mean values ± SD or as frequencies (percentages), and statistical significance was considered if a $P < 0.05$. Data analysis was performed by statistical software SPSS version 26.0 for Windows.

To provide context for interpreting the null findings, a post hoc power analysis was performed using GPower 3.1.1 software (Faul et al., 2007) based on the actual sample size ($n = 37$) and the observed correlations between the main outcome (TGlittre time) and PFT results, respiratory and peripheral muscle strength, and SF-36 dimensions. Based on a priori type-I error $\alpha = 0.05$ (two-tailed), a complete-case analysis showed that the observed significant effects were detected with a power ranging from 97% to 61%. For the regression model for TGlittre time, the significant effect was observed with a power of 95%, showing the adequacy of the studied sample size to obtain significant results (Fleiss et al., 2003).

3. Results

Among the 41 women who were evaluated for inclusion in the study, 4 were excluded for the following reasons: 1 patient had difficulty walking due to lower limb paralysis, 1 patient was unable to go up and down stairs due to knee arthroplasty, 1 patient was unable to move objects on the shelf due to joint stiffness in the shoulders, and 1 patient interrupted the test due to dyspnoea and muscle fatigue. The mean age was 52.9 ± 12.8 years, while the mean time after diagnosis of COVID-19 was 8.1 ± 3.2 months. Spirometry showed a normal pattern, restrictive pattern, and obstructive pattern in 24 (64.9%), 11 (29.7%), and 2 (5.4%) participants, respectively, while 18 (48.6%) participants had reduced DLCO. Regarding the SF-36 questionnaire, there was a negative impact on all dimensions, with the worst evaluations being on the dimensions referring to physical role limitations and emotional role limitations. Demographic data, clinical variables, lung function, and HRQoL are

Table 1
Anthropometry data, comorbidities, pulmonary function, and health-related quality of life in the studied sample ($n = 37$).

Variable	Values
Anthropometry	
Age (years)	52.9 ± 12.8
Weight (kg)	81.2 ± 19.1
Height (m)	1.62 ± 0.07
BMI (kg/m^2)	31.1 ± 7.4
Comorbidities, *n* (%)	
Hypertension	17 (45.9)
Diabetes	10 (27)
Chronic lung disease	5 (13.5)
Chronic heart disease	1 (2.7)
Pulmonary function	
FVC (% predicted)*	83.8 ± 20.3
FEV_1 (% predicted)*	81.9 ± 21.4
FEV_1/FVC (%)	79.8 ± 8.3
DLCO (% predicted)*	64.1 ± 15.9
Short Form-36	
Physical functioning (score)	50 ± 25.1
Physical role limitations (score)	30.8 ± 15.5
Bodily pain (score)	40.1 ± 17.2
General health perceptions (score)	45.9 ± 17.5
Vitality (score)	42.3 ± 18.6
Social functioning (score)	53 ± 23.1
Emotional role limitations (score)	38.2 ± 24.3
Mental health (score)	56 ± 17.4

The values shown are mean ± SD or number (%). BMI = body mass index; FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second; DLCO = diffusing capacity for carbon monoxide.

* The value is based on comparisons of data measured in an individual patient with reference (predicted) values based on healthy subjects.

shown in Table 1.

Regarding the IPAQ questionnaire, 1 (2.7%), 9 (24.3%), 22 (59.5%) and 5 (13.5%) participants were considered very active, active, irregularly active, and sedentary, respectively. As to the evaluation of functionality on the PCFS scale, most were categorized with moderate functional limitations ($n = 14$, 37.9%) or slight functional limitations ($n = 12$, 32.4%).

In relation to TGlittre, the mean value of the total time ('best test') was 4.8 ± 1.1 min, with 30 (81.1%) participants performing better on the second TGlittre. Using Brazilian predicted values for healthy women with the same anthropometric characteristics (Reis et al., 2018), the TGlittre time was approximately 64% longer than the expected time to complete it. Most participants reported that the greatest difficulty presented at the end of the TGlittre was squatting to perform shelving tasks, which was reported by 17 (45.9%) participants. Functionality, muscle function and physical capacity data are shown in Table 2.

The associations between total time to perform TGlittre multiple tasks and lung function, HRQoL, and muscle function measurements are shown in Table 3 and Fig. 2. TGlittre time showed negative correlation with respiratory muscle strength (MIP, $r = -0.391$, $P = 0.015$) and peripheral muscle strength (QS, $r = -0.591$, $P = 0.0001$; HGS, $r = -0.453$, $P = 0.005$). There was a negative correlation between TGlittre time and FVC ($r = -0.588$, $P = 0.0001$) and DLCO ($r = -0.671$, $P < 0.0001$). Additionally, we also observed significant correlations between the TGlittre time and various dimensions of the SF-36. Participants who were considered very active/active by the IPAQ questionnaire had a shorter TGlittre time than those considered irregularly active/sedentary [142.5 ± 44.9 vs. 171.5 ± 35.4% predicted, $P = 0.046$]. Participants with negligible/slight functional limitations on the PCSF scale had a shorter TGlittre time than those with moderate/severe functional limitations [145.3 ± 15 vs. 190.6 ± 11.4% predicted, $P = 0.0002$].

In the stepwise forward regression analysis, DLCO, QS, and FVC were the independently predictive variables for the TGlittre time, explaining 64% of its variability (Table 4). Multicollinearity was not identified in this explanatory model as determined by a low VIF value (VIF = 1.32). The scatter plot for the TGlittre time according to the regression model is shown in Fig. 3.

Table 2
Functionality, muscle function, and functional capacity in the studied sample ($n = 37$).

Variable	Values
Post-COVID-19 Functional Status scale, *n* (%)	
1 (negligible)	10 (27)
2 (slight)	12 (32.4)
3 (moderate)	14 (37.9)
4 (severe)	1 (2.7)
Muscle function	
MIP (% predicted)*	73.8 ± 24.3
MEP (% predicted)*	57.6 ± 19.9
HGS (kgf)	31 ± 13.8
QS (kgf)	24.9 ± 9
Glittre-ADL test	
Total time (min)	4.8 ± 1.1
Total time (% predicted)*	163.7 ± 39.7
Highest-difficulty task, *n* (%)	
Squatting to perform shelving tasks	17 (45.9)
Stair tasks	11 (29.7)
No difficulty	5 (13.5)
Manual tasks	3 (8.1)
Chair tasks	1 (2.7)

The values shown are mean ± SD or number (%). MIP = maximum inspiratory pressure; MEP = maximum expiratory pressure; HGS = handgrip strength; QS = quadriceps strength.

* The value is based on comparisons of data measured in an individual patient with reference (predicted) values based on healthy subjects.

Table 3
Pearson's correlation coefficients for Glittre ADL-test, anthropometry data, pulmonary function, health-related quality of life, and muscle function among women with post-acute COVID-19 syndrome.

	Total time (% predicted)	
	r_s	*p*-value
Age	−0.154	0.36
Weight	0.274	0.10
Height	0.053	0.75
BMI	0.260	0.12
FVC	−0.588	**0.0001**
FEV_1	−0.491	**0.002**
FEV_1/FVC	0.278	0.095
DLCO	−0.671	**<0.0001**
Physical functioning	−0.563	**0.0003**
Physical role limitations	−0.520	**0.0009**
Bodily pain	−0.346	**0.035**
General health perceptions	−0.382	**0.019**
Vitality	−0.340	**0.039**
Social functioning	−0.164	0.33
Emotional role limitations	−0.496	**0.002**
Mental health	−0.150	0.38
MIP	−0.397	**0.015**
MEP	−0.312	0.060
HGS	−0.453	**0.005**
QS	−0.591	**0.0001**

FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second; DLCO = diffusing capacity for carbon monoxide; MIP = maximum inspiratory pressure; MEP = maximum expiratory pressure; HGS = handgrip strength; QS = quadriceps strength.

4. Discussion

Our main findings were that patients with PCS who were not hospitalized during the acute phase of COVID-19 spend a long time performing TGlittre tasks. Patients with worse functional limitations and with low levels of physical activity had greater difficulties in completing TGlittre multiple tasks. In these patients, there was a correlation between the time required to perform TGlittre multiple tasks and measures of respiratory and peripheral muscle strength, pulmonary function parameters, and HRQoL measurements. Lung function (DLCO and FVC) and muscle function (QS) explained >60% of the variance in the time to complete the TGlittre test. To our knowledge, this is the first study that has created a regression model to explain functional exercise capacity in patients with PCS.

Despite evaluating the same construct of functional status, the TGlittre differs from the 6MWT in that it involves activities other than walking, which, in turn, can induce limiting symptoms at different levels. In our study, patients spent 64% more time completing the TGlittre compared to the time spent by healthy subjects, and the mean time to complete TGlittre multiple tasks was nearly 5 min. Assessing patients with chronic lung disease, Gulart et al. (2018) demonstrated that the 3.5-min cut-off point in the TGlittre is accurate to distinguish patients with abnormal functional capacity from those with normal functional capacity. Since the reduction of functional capacity is a matter addressed in rehabilitation programmes, we believe that the TGlittre can be recommended as an instrument for evaluating the limitation of effort and prescribing physical exercises to patients with PCS.

Squatting is a difficult task for many people, as it involves multiple muscular and biomechanical aspects (de Alegria et al., 2021). In fact, almost half of our sample pointed out that squatting to perform shelving tasks was their biggest difficulty to fulfil the TGlittre tasks. Interestingly, we also observed that completion of the TGlittre was more difficult for patients who reported low levels of physical activity. A recent study showed that when compared to their levels of activity pre-COVID-19 infection, patients were performing 150 min per week of physical activity less frequently in their post-COVID-19 infection period when asked separately about moderate and vigorous intensities (Tabacof

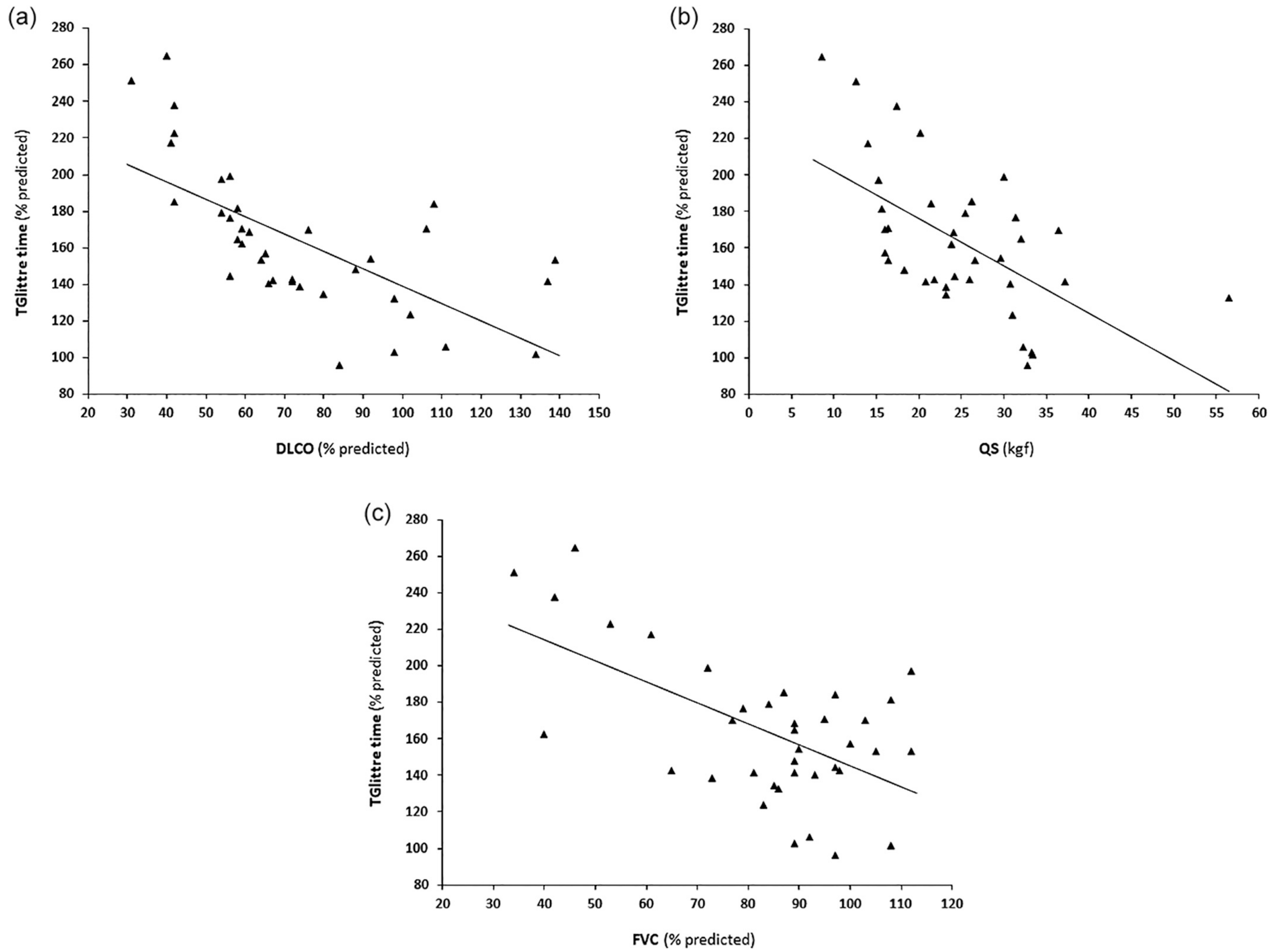

Fig. 2. Relationships of Glittre-ADL test (TGlittre) time with the diffusing capacity for carbon monoxide ($r = -0.671$, $P < 0.0001$) **(A)**, the quadriceps strength-QS ($r = -0.591$, $P = 0.0001$) **(B)**, and the forced vital capacity-FVC ($r = -0.588$, $P = 0.0001$) **(C)**.

Table 4
Independent linear model for the Glittre ADL-test time using demographic parameters, pulmonary function, health-related quality of life, and muscle function.

Variables	B	SEB	*P* value	Cumulative R^2
DLCO	−0.523	0.182	0.007	0.64
QS	−1.559	0.507	0.004	
FVC	−0.605	0.237	0.015	

B = regression coefficient; SEB = sandard error of the regression coefficient; R^2 = determination coefficient; DLCO = diffusing capacity for carbon monoxide; QS = quadriceps strength; FVC = forced vital capacity.

et al., 2022). In addition to deconditioning, persistent low-grade inflammation following acute SARS-CoV-2 infection may also contribute to systemic health problems (Townsend et al., 2021).

The main focus of the present study was to create a regression model that could explain the time taken to perform the TGlittre multitasking. Considering the sample size, we paid attention to the plausibility and multicollinearity for the choice of explanatory variables in the model (Marquardt, 1970; Smith, 2018). In addition to demographic and anthropometric variables, we focused on pulmonary and muscle function variables that are frequently compromised in patients with PCS (Nopp et al., 2022). Pulmonary function monitoring is desired in patients with PCS, as the lungs are the most affected organs in the acute phase of the disease and, moreover, this involvement can greatly impact functional capacity (Lopes et al., 2021a, 2021b). In addition, COVID-19 causes deep changes in the structure and function of skeletal muscles that can potentially impair performance during exertion (Damanti et al., 2022). In our regression model, interestingly, the explanation of the variables related to lung and muscle function for the TGittre time was much higher than that observed in healthy Brazilian women evaluated by Reis et al. (2018) (64% versus 32%). Since many variables included in our model were evaluated as percentages of predicted values rather than absolute values, this may have had a positive impact on our modelling (Pellegrino et al., 2005).

In the present study, abnormality in DLCO was the most common finding, followed by a restrictive pattern. These results are in conformity with a systematic review on the pulmonary function in patients with PCS that showed a prevalence of 39% and 15% for DLCO abnormality and restrictive pattern, respectively (Torres-Castro et al., 2021). It is worth noting that in our multiple regression model, the drop in DLCO (a marker of pulmonary vascular damage) and, to a lesser extent, the drop in FVC (a marker of impaired lung mechanics) resulted in a longer TGlittre time (Kersten et al., 2022; Lopes, 2019). Using 6MWT in PCS, a recent study showed that patients with lower DLCO had a worse performance during the test, including a higher frequency of desaturation during exercise (van den Borst et al., 2021). Another study showed a correlation of well-being to functional values of DLCO and the 6MWT in patients with PCS (Kersten et al., 2022). Using linear regression for the

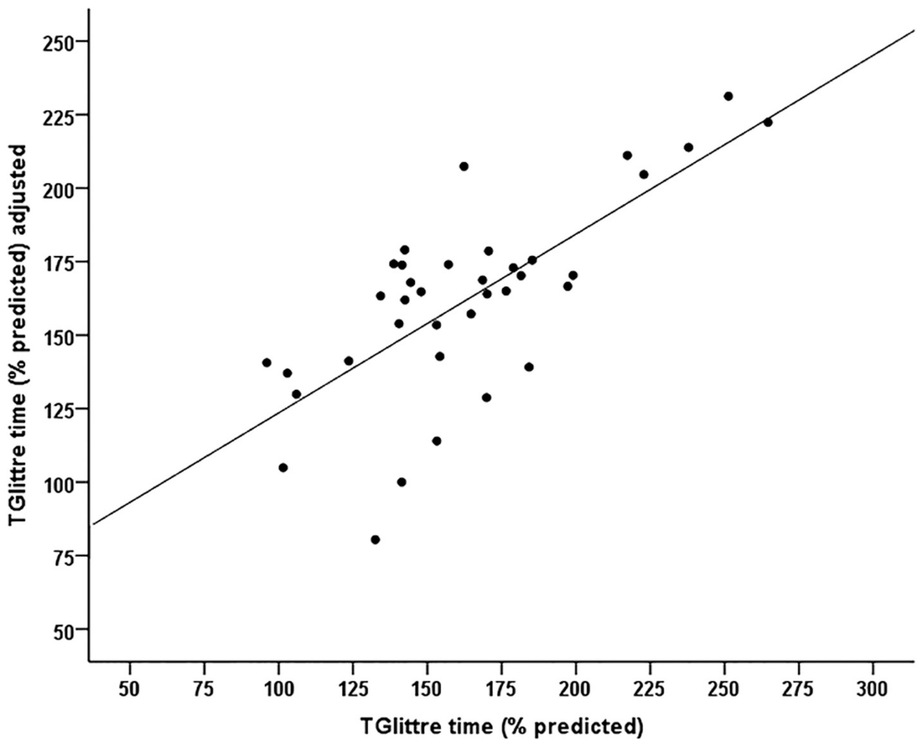

Fig. 3. Scatter plot for the AVD-Glittre test time (TGlittre time, % predicted) showing recorded values (*x*-axis) versus adjusted values (*y*-axis) according to the regression model.

6MWT distance as a dependent variable, Townsend et al. (2021) observed that the reduced covered distance was associated with the length of hospital stay in patients with PCS, but no other features; however, these authors did not assess the impact of lung function on functional exercise capacity.

In our study, we observed that the lower the respiratory/peripheral muscle strength, the longer the time spent performing the TGlittre tasks. However, the decline in muscle mass is not homogeneous across different anatomical regions of the body, as sarcopenia occurs earlier in the lower limbs (Damanti et al., 2022). In fact, in our multiple regression model, the only measure of muscle strength that can explain the TGlittre time was the QS. In line with our findings, Paneroni et al. (2021) noticed a reduced QS in 86% of patients who recovered from post-COVID-19 pneumonia, with significant correlations between QS and physical performance indices. Using linear regression model for the 6MWT distance in adolescents post-SARS-CoV-2 infection, Palacios et al. (2022) demonstrated that obesity, anxiety, cough, and dyspnoea at presentation were associated with reduced functional exercise capacity; however, these authors did not analyse the impact of muscle strength measurements on functional exercise capacity. In COVID-19, skeletal muscle abundantly expresses the angiotensin-converting enzyme-2 which, together with the furin-dependent pathway for the viral spread, creates the basis for prolonged skeletal muscle damage throughout the body (Piotrowicz et al., 2021).

Patients recovering from COVID-19 have a higher incidence of negative health indicators, including worse functional status, and may need additional clinical support such as physical and mental health rehabilitation services (Al-Aly et al., 2021). We observed that PCS impacted all dimensions of the SF-36 questionnaire, with the worst evaluations being in the dimensions referring to physical role limitations and emotional role limitations. In line with our findings, van den Borst et al. (2021) observed that all domains of the SF-36 questionnaire were lowered in PCS, especially in the physical role limitations dimension. This last dimension is related to difficulties in performing work or other ADLs. It is also worth noting that our sample consisted basically of patients with slight/moderate functional limitations on the PCSF scale. Analysing 1939 subjects with PCS (95% of which were not hospitalized during the acute infection) approximately 3 months after the onset of symptoms, Machado et al. (2021) also observed that most subjects reported slight/moderate functional limitations on the PCFS scale.

The strength of this study is that it evaluated the viability of TGlittre in a sample of non-hospitalized subjects during the acute phase of COVID-19, which is the majority of patients who had the disease. In the acute post-COVID phase, lung damage together with muscle damage strongly contribute to the reduction in functional exercise capacity assessed by TGlittre. However, we should point out some of the limitations of the study. First, this was a cross-sectional observational study, which impairs a cause-and-effect analysis. Patients' conditions before COVID-19 were often unknown, so it is possible that the abnormalities we found were unrelated to the patients' COVID-19 and could exist previously. Second, we are aware that our patient cohort is small; however, the patients in this study were very well characterized for their post-COVID-19 clinical picture and complications using a wide variety of objective tests. Third, stepwise regression is less effective the greater the number of potential explanatory variables. However, in our study the number of potential explanatory variables is relatively small because the values of almost all of them were evaluated in relation to the predicted values; this previous step allowed the control of variables for demographic and anthropometric confounders. Fourth, the reference equations for the TGlittre by Reis et al. (2018) used in our study explain only 32% of the variance in the TGlittre time. This suggests that the equations do not include all variables that contribute to the explanation of TGlittre time variation, even in healthy subjects. Considering that the TGlittre is a standardized test with activities representative of several ADLs capable of evaluating the functional capacity of patients with PCS, we think that future studies with larger numbers of patients should be oriented to evaluate longitudinally the changes in TGlittre, including those occurring after rehabilitation programmes.

5. Conclusion

PCS patients who have not been hospitalized during the acute phase of COVID-19 spend a long time performing TGlittre multiple tasks. In these patients, there is a relationship between TGlittre time and respiratory and peripheral muscle strength, pulmonary function, and HRQoL. DLCO, QS, and FVC greatly explained the variance in the TGlittre time. Furthermore, patients with worse functional limitations and with low levels of physical activity have greater difficulties in completing the TGlittre tasks. Since the TGlittre is easy to perform and incorporates upper and lower limb activities, it can become an interesting tool in the follow-up of this patient population.

Ethical approval

The protocol was approved by the Research Ethics Committee of the State University under number CAAE-30135320.0.0000.5259, and written informed consent was obtained from all participants.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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