Journal of Exercise Science & Fitness 22 (2024) 271–277

Contents lists available at ScienceDirect

Journal of Exercise Science & Fitness

journal homepage: www.elsevier.com/locate/jesf

Evaluating performance on the Glittre-ADL test in men with long COVID 3 years after a SARS-CoV-2 infection

Mayra Gomes Soares Silva [a], Thiago Lemos Carvalho [a], João Eduardo de Azevedo Vieira [b], Lohana Resende da Costa [c], Davi Luiz Olimpio da Silva [c], Alexsandra Lima Barcellos Costa [c], Hendyl Pereira Soares dos Anjos [c], Agnaldo José Lopes [a,d,*]

[a] Rehabilitation Sciences Post-Graduation Program, Augusto Motta University Center (UNISUAM), Rio de Janeiro, Brazil
[b] Faculty of Physiotherapy, Positive University (UP), Curitiba, Paraná, Brazil
[c] Faculty of Physiotherapy, Augusto Motta University Center (UNISUAM), Rio de Janeiro, Brazil
[d] Medical Sciences Post-Graduation Program, State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil

ARTICLE INFO

Keywords:
Long COVID
Exercise
Muscle
Respiratory function tests
Quality of life

ABSTRACT

Background/objective: Many COVID-19 survivors, especially those who have been hospitalized, have been suffering numerous complications that limit their activities of daily living, although changes that persist 3 years after infection are still not known. We aimed to investigate the impact of long COVID on the Glittre-ADL test (TGlittre) 3 years after acute infection in men who needed hospitalization and explore whether the performance on the TGlittre is associated with impairments in lung function, muscle strength, physical function and quality of life (QoL).
Methods: Cross-sectional study with 42 men with long COVID who took the TGlittre. They underwent pulmonary function tests and measurements of handgrip strength and quadriceps strength (QS). Additionally, they also completed the Saint George Respiratory Questionnaire (SGRQ) and Functional Independence Measure (FIM).
Results: The mean age was 52 ± 10.6 years, while the mean time after diagnosis of COVID-19 was 37 ± 3.5 months. The mean TGlittre time was 3.3 (3.1–4.1) min, which was 10% greater than the time expected for normal individuals to complete it. The TGlittre time was correlated significantly with the QS ($r_s = -0.397$, $p = 0.009$), pulmonary diffusion ($r_s = -0.364$, p = 0.017), FIM ($r_s = -0.364$, p = 0.017) and the "activity" domain score of the SGRQ ($r_s = 0.327$, p = 0.034).
Conclusion: Functional capacity on exertion as measured by the TGlittre time is normal in most men with long COVID 3 years after hospitalization. However, this improvement in functional capacity does not seem to be reflected in muscle strength or QoL, requiring continued monitoring even after 3 years.

1. Introduction

After acute infection by the SARS-CoV-2 virus, a considerable number of people remain symptomatic with pathological changes in various organs.[1] Particularly, those with more severe lung involvement by COVID-19 have worse long-term lung damage, with the patient-reported symptom burden remaining high and quality of life (QoL) remaining poor even 1 year after COVID-19 infection.[2] Despite the large number of patients who have recovered from COVID-19, long COVID is a condition that is not yet fully understood, although potential mechanisms have included the persistence of the virus or its components, autoimmune processes, metabolic and endocrine dysregulation, psychosocial factors, and microvascular and mitochondrial damage.[1] The constellation of symptoms of long COVID includes exercise intolerance and functional impairment, but among these symptoms, fatigue can be particularly debilitating.[3]

The respiratory system is a central component in the oxygen supply chain for working muscles, and as the lungs are often involved in acute COVID-19 infection, they are a potential contributor to poor exercise performance.[4] However, in long-term COVID, the contribution of respiratory function to low exercise tolerance appears to be small, except for the diffusing capacity of the lungs for carbon monoxide (DLCO).[4] In

* Corresponding author. Rehabilitation Sciences, Augusto Motta University Centre (UNISUAM), Rua Dona Isabel, 94, Bonsucesso, 21032-060, Rio de Janeiro, Brazil.
E-mail address: agnaldolopes.uerj@gmail.com (A.J. Lopes).

https://doi.org/10.1016/j.jesf.2024.03.010
Received 10 October 2023; Received in revised form 8 March 2024; Accepted 25 March 2024
Available online 29 March 2024

fact, the prevalence of restrictive lung damage seems to decrease with recovery from long COVID.[5] Importantly, those who were more severely ill during hospitalization seem to have more severe impairment of lung function, especially in terms of the DLCO, despite being the main target population for long-term recovery interventions.[6] However, whether there is a complete normalization of pulmonary function tests needs to be investigated in long-term follow-up studies.

Peripheral factors such as reduced muscle mass and strength may contribute to the low exercise tolerance in long COVID, although current studies do not support deconditioning as the main mechanism of this intolerance.[4] In long COVID, the potential pathogenesis of muscle fatigue and weakness may include virus-induced myositis, long periods of bed rest during convalescence, and the use of systemic corticosteroids.[7] In fact, these patients may have lower peripheral oxygen extraction during exercise, and such peripheral changes may contribute to poor exercise performance even 1 year after discharge.[8] After almost 2 years of infection, most COVID-19 convalescents have an overall improvement in health status, while symptoms of sequelae, residual abnormalities in lung function and exercise impairment can still be observed in a small proportion of people.[7] A particularly useful tool for evaluating this population is the Glittre-ADL test (TGlittre), which, although it is a submaximal test, uses activities similar to the activities of daily living and has been shown to be sensitive in detecting changes even after 8 months of follow-up post- SARS-CoV-2 infection.[9] However, whether these changes in functional capacity upon exertion correspond to a transient functional disability or whether they are related to defined organ damage remains unknown.

In patients with long COVID, exercise intolerance likely has multiple causes and is not explained by deconditioning.[4] Persistent symptoms, impaired lung function and impairment of functional capacity for exercise in the short-term follow-up after COVID-19 infection are common, but the long-term consequences have not yet been sufficiently studied. In fact, it is not yet known whether these findings persist after 3 years of infection, as the pandemic began in mid-2020. Since the TGlittre involves multiple tasks that require both the action of the upper and lower limbs,[10] we hypothesized that it is capable of capturing possible changes that persist in the long term. As men have greater muscular strength compared to women, implying a better performance in functional capacity tests[11] and, also, because the time to perform the TGlittre is significantly shorter for men,[12] we thought about evaluating only men due to limitations for comparison between the sexes. Thus, this study aimed to investigate the impact of COVID-19 on the TGlittre 3 years after acute infection in men who needed hospitalization and to explore whether performance on the TGlittre is associated with impairments in lung function, muscle strength, physical function and QoL.

2. Methods

2.1. Study design and participants

A cross-sectional study was conducted between March and July 2023 with 42 (out of 50 eligible) men ≥18 years of age with long COVID who were regularly followed up at the Pedro Ernesto University Hospital of the State University of Rio de Janeiro, Rio de Janeiro, Brazil. We included patients who were diagnosed with COVID-19 by a positive reverse transcription-polymerase chain reaction and who needed hospitalization without the need for admission to an intensive care unit. The exclusion criteria included a previous diagnosis of chronic obstructive pulmonary disease, asthma or pulmonary fibrosis; a history of previous heart disease; mobility impairment due to concomitant osteoarthropathy; and immobility before or after hospital discharge due to diseases such as stroke or pulmonary embolism. These patients were admitted during the acute phase of COVID-19 at our institution and followed up via telemonitoring or outpatient consultations. Three years after the acute infection, they were contacted again by telephone about their clinical manifestations for face-to-face evaluation if they still had persistent symptoms and dysfunctions that could not be attributed to alternative diagnoses, characterizing long COVID.[13]

All patients provided informed consent prior to any study procedure. The protocol was approved by the Research Ethics Committee of the Augusto Motta University Center (UNISUAM) under number CAAE-50700921.5.0000.5235.

2.2. Saint George Respiratory Questionnaire (SGRQ)

To measure QoL, a version of the SGRQ previously validated and adapted for the Brazilian population was applied.[14] This instrument covers aspects in three domains: symptoms, with questions about complaints of respiratory problems; activities, with questions related to activities that have usually caused dyspnea in recent days; and impact, where the patient describes the respiratory disease and whether it interferes with their activities of daily living. In the SGRQ, values > 10% reflected altered QoL.[14]

2.3. Functional Independence Measure (FIM)

The FIM is a functional assessment with 18 items in the areas of personal care, sphincter control, mobility, communication and social cognition. It was designed to measure the patient's level of independence through the assessment of activities such as self-care, transference, locomotion, toilet training, communication and social cognition, which includes memory, social interaction and problem solving. Each of these activities is evaluated and receives a score ranging from 1 (total dependence) to 7 (complete independence). In intermediate values, there is modified independence (score 6), moderate dependence with the need for supervision or preparation (score 5) or direct assistance (scores 1 to 4). The total score ranges from 18 (the lowest) to 126 (the highest level of function).[15] The MIF measures the personal care and basic activities of daily living that the individual performs exactly at the time of the assessment; therefore, the more dependent the person is on performing self-care and usual tasks, the lower the total score.[16]

2.4. Pulmonary function tests

The pulmonary function tests consisted of spirometry, whole-body plethysmography, measurement of DLCO and measurement of respiratory muscle strength (maximum inspiratory pressure and maximum expiratory pressure). All these exams were performed with an HDpft 3000 (nSpire Health, Inc., Longmont, CO, USA) and followed previously established recommendations.[17,18] The Brazilian predicted equations were adopted for comparison with the absolute values of the participants.[19–22] Obstructive damage, restrictive damage and pulmonary diffusion disorder were defined as forced expiratory volume in 1 s/forced vital capacity, total lung capacity and DLCO below the respective lower limits of normal.[23]

2.5. Muscle strength

Handgrip strength was measured using a digital dynamometer (SH5001, Saehan Corporation, Korea). Handgrip strength was assessed with the participants seated in an armless chair, elbow flexion of 90°, forearms in neutral position and wrist extension from 0 to 30°.[24] Maximum strength was assessed after a 3-s sustained contraction of the dominant hand, and the highest value from three attempts at 1-min intervals was considered for analysis. The cutoff point adopted for the diagnosis of sarcopenia was the one previously proposed for males (27 kgf).[25] We also measured quadriceps strength (QS) using a traction dynamometer (E-lastic 5.0, E-sporte SE, Brazil). The range of motion during the test was 90°, starting at 90° with the knee in flexion. Maximum strength was assessed after a 5-s sustained contraction of the dominant leg, and the highest value of three attempts at 1-min intervals was considered for analysis.[26] The cutoff point adopted for the diagnosis of sarcopenia was the one previously proposed for males (25.3 kgf).[27]

2.6. Glittre-ADL test

The TGlittre was executed as previously proposed.[10] It consists of carrying a backpack weighing 5 kg (for men) and walking a 10-m circuit. From the sitting position, the participant walks in a flat route interposed in its half by a box with two steps to go up and two to go down. After walking the rest of the way, 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, to the bottom shelf and the floor. Then, the objects must be replaced on the lowest shelf and later on the highest shelf. Afterwards, the individual returns to his chair, making the course in reverse and, immediately after, starts another round. When performing the TGlittre, the individual must attempt to complete five laps in the shortest time possible.[28] In TGlittre, the variable used to evaluate performance during the test is the total time to complete the tasks; therefore, the shorter the time, the better the patient's performance. The TGlittre time was compared to Brazilian predicted values[29]; therefore, the higher the TGlittre time value in relation to the predicted value, the worse the patient's performance will be.

2.7. Statistical analysis

The normality of the data distribution was assessed using the Shapiro–Wilk test and graphical analysis of the histograms. The observed data are expressed as measures of central tendency and dispersion for numerical data and as frequencies and percentages for categorical data. TGlittre time, lung function parameters and respiratory muscle strength measurements were expressed as percentage values in relation to predicted values for the healthy population, which consider sex, age, height, weight and body mass index.[19–22] The relationship between the TGlittre time and the numerical variables was analyzed using the Spearman correlation coefficient, after adjustment for sociodemographic confounding variables. Using the Mann–Whitney U test, we compared the subgroup of people without obesity vs. the subgroup of people with obesity (the latter was defined by the presence of a body mass index $\geq$30 kg/m^2).[30] Using the Mann–Whitney U test, we also compared the subgroup of people with normal lung function vs. the subgroup of people with impaired lung function (the latter was defined by the presence of any lung function parameter <80% predicted).[31] The significance level adopted was 5%. Statistical analysis was performed using SPSS statistical software version 26.

3. Results

Among the 50 men who were evaluated for inclusion in the study, 8 were excluded for the following reasons: history of heart failure ($n = 3$); diagnosis of chronic obstructive pulmonary disease ($n = 3$); diagnosis of asthma ($n = 2$); and mobility impairment preventing undertaking the TGlittre ($n = 2$). The mean age was 52 ± 10.6 years, while the mean time after diagnosis of COVID-19 was 37 ± 3.5 months. In the spirometric test, normal breathing, restrictive damage and obstructive damage were diagnosed in 30 (71.4%), 10 (23.8%) and 2 (4.8%) participants, respectively, while 14 (33.3%) participants had reduced DLCO. The median total score of the SGRQ was 26.3 (10–44). The patient demographic data, clinical variables, pulmonary function and QoL are shown in Table 1.

Table 1
Anthropometry data, comorbidities, pulmonary function and quality of life in the studied sample ($n = 42$).

Variable	Values
Anthropometry	
Age (years)	52 ± 10.6
Weight (kg)	93.1 ± 18.8
Height (cm)	176 ± 6.2
Body mass index (kg/m^2)	30.1 ± 5.3
Comorbidities, *n* (%)	
Obesity	19 (45.2)
Hypertension	16 (38.1)
Diabetes	10 (23.8)
Pulmonary function	
Forced vital capacity (% predicted)	87.2 ± 11.6
Forced expiratory volume in 1 s (% predicted)	88.5 ± 14.7
Forced expiratory volume in 1 s/forced vital capacity (% predicted)	101 ± 10.5
Total lung capacity (% predicted)	89 ± 11.3
Residual volume (% predicted)	78.2 ± 19
Residual volume/total lung capacity (% predicted)	84.8 ± 16.7
DLCO (% predicted)	86 ± 35
SGRQ	
Symptoms scores	19.7 (6.6–47)
Activity scores	36.3 (14–70)
Impacts scores	18.6 (4.2–31)
Total scores	26.3 (10–44)

Abbreviation: DLCO, diffusing capacity for carbon monoxide; SGRQ, Saint George Respiratory Questionnaire.
The values shown are mean ± SD, median (interquartile range) or number (%).

In the FIM, only 6 (14.3%) participants did not score the maximum value, which indicated that the sample had good functional status. However, maximum inspiratory pressures and maximum expiratory pressures <70% of the predicted values were observed in 15 (35.7%) and 22 (52.4%) participants, respectively, indicating respiratory muscle weakness in most of the participants. Twenty-five (59.5%) participants had a handgrip strength <27 kgf, while 12 (28.6%) participants had a QS < 27 kgf. Regarding the TGlittre, the average total time was 3.3 (3.1–4.1) minutes. Using the Brazilian predicted values for healthy men with the same anthropometric characteristics as a reference,[29] the TGlittre time was approximately 10% longer than the expected time to complete it [3.3 (3.1–4.1) vs. 3 (2.7–3.5) min, $p = 0.09$], with only 12 (28.6%) participants showing a time >120% of the predicted time. The data on functional status, muscle function and functional capacity during exercise are shown in Table 2.

The associations between the total time spent performing the multiple tasks of the TGlittre and the measures of lung function, functional status, muscle strength and QoL are shown in Table 3 and Fig. 1. Regarding lung function, the TGlittre time correlated significantly only with DLCO ($r_s = -0.364$, $p = 0.017$). There was a significant correlation between TGlittre time and FIM ($r_s = -0.364$, $p = 0.017$). Among the muscle strength measures, the only one that significantly correlated with the TGlittre time was the QS ($r_s = -0.397$, $p = 0.009$). Regarding the SGRQ, the activity domain score correlated significantly with the TGlittre time ($r_s = 0.327$, $p = 0.034$). Participants with obesity did not

Table 2
Functional status, muscle strength and functional capacity to exertion in the studied sample (n = 42).

Variable	Values
Functional status	
FIM (points)	126 (124–126)
Muscle strength	
Maximum inspiratory pressure (% predicted)	75.5 ± 20.6
Maximum expiratory pressure (% predicted)	63.9 ± 20.7
Handgrip strength (kgf)	25.3 ± 4.1
QS (kgf)	34.1 ± 15
Glittre-ADL test	
Total time observed (min)	3.3 (3.1–4.1)
Total time predicted (min)	3 (2.7–3.4)
Total time (% predicted)	110 (87–134)

Abbreviation: FIM, Functional Independence Measure; QS, quadriceps strength.
The values shown are mean ± SD or number (%).

Table 3
Spearman's correlation coefficients for Glittre ADL-test, pulmonary function, functional status, muscle strength and quality of life in man with long COVID ($n = 42$).

	Total time (% predicted)	
	r_s	*p*-value
Pulmonary function		
Forced vital capacity (% predicted)	−0.035	0.83
Forced expiratory volume in 1 s (% predicted)	−0.056	0.72
Forced expiratory volume in 1 s/forced vital capacity (% predicted)	0.006	0.97
Total lung capacity (% predicted)	0.088	0.58
Residual volume (% predicted)	0.049	0.76
Residual volume/total lung capacity (% predicted)	0.123	0.44
DLCO (% predicted)	**−0.364**	**0.017**
Functional status		
FIM (points)	**−0.364**	**0.017**
Muscle strength		
Maximum inspiratory pressure (% predicted)	−0.126	0.43
Maximum expiratory pressure (% predicted)	−0.106	0.50
Handgrip strength (kgf)	−0.230	0.14
QS (kgf)	**−0.397**	**0.009**
SGRQ		
Symptoms scores	0.121	0.44
Activity scores	**0.327**	**0.034**
Impacts scores	0.212	0.17
Total scores	0.266	0.088

Abbreviation: DLCO, diffusing capacity for carbon monoxide; FIM, Functional Independence Measure; QS, quadriceps strength; SGRQ, Saint George Respiratory Questionnaire.
Bold type indicates significant correlations.

have a significantly different TGlittre time than participants without obesity [113 (84–141) vs. 107 (88–119) % predicted, $p = 0.44$]. Participants with lung function impairment did not have a significantly different TGlittre time from those without [107 (88–132) vs. 109 (102–134) % predicted, $p = 0.51$].

To provide context for interpreting the null findings, a *post hoc* power analysis was performed using G*Power 3.1.1 software based on the actual sample size ($n = 42$) and the observed correlations between the main outcome (TGlittre time) and the other studied variables. 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 99 to 63%, showing the adequacy of the studied sample size to obtain significant results.[32]

4. Discussion

Although long COVID appears with similar frequency between men and women,[1] the proportion is higher among men with greater severity of the initial infection[6,33] and, therefore, we focused on evaluating this patient population. In addition, there is an urgent and ongoing need to investigate the exercise functional capacity of these patients 3 years after infection to improve our understanding and management of long COVID. In this regard, the main findings of the present study were that in men with long COVID 3 years after hospitalization, there is an important recovery of functional capacity, with less than one-third of them showing an abnormal TGlittre. At this point in the evolution of long COVID, only one-third of patients have mechanical and/or diffusion pulmonary changes. However, most of them maintain some damage in muscle strength, and QoL remains deteriorated. Furthermore, there is a relationship between TGlittre time and QS, pulmonary diffusion, functional status and QoL. To the best of our knowledge, this is the first study to assess functional capacity during exercise 3 years after acute SARS-CoV-2 infection.

Cardiorespiratory fitness is markedly low soon after hospital discharge and remains low in the medium and long term, which may be due to the effects related to inactivity during hospitalization, the side effects of drugs and the direct sequelae related to COVID-19.[4] Our study, however, showed a functional capacity to exercise, as assessed by TGlittre, close to normal in most patients 3 years after acute infection. In line with our findings, Guo et al. (2023) evaluated a prospective cohort of patients with long COVID 18.5 months after acute infection and observed continuous improvement in symptoms of sequelae and the 6-min walking distance, although symptoms of sequelae (at least one) and abnormal patterns on chest computed tomography persisted in 45.2% and 30% of participants, respectively. This emphasizes the need to implement rehabilitative strategies for these patients, especially in the first months after acute SARS-CoV-2 infection.

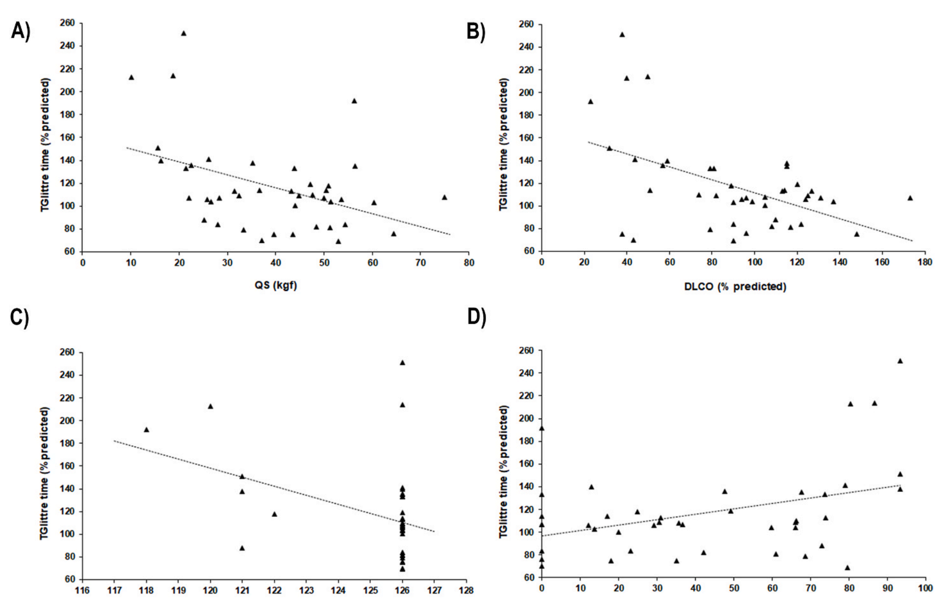

Fig. 1. Relationships of Glittre-ADL test (TGlittre) time with (A) the quadriceps strength (QS, $r_s = -0.397$, $p = 0.009$), (B) the diffusing capacity of the lungs for carbon monoxide (DLCO, $r_s = -0.364$, $p = 0.017$), (C) the Functional Independence Measure (FIM, $r_s = -0.364$, $p = 0.017$), and (D) the activity scores measured by Saint George Respiratory Questionnaire ($r_s = 0.327$, $p = 0.034$).

In our study, unlike studies conducted before 3 years, pulmonary function was within the normal range in most patients.[34,35] However, it is worth noting that one-third of our patients still had reduced DLCO, which is in agreement with the study by Sperling et al. (2023) in a cohort study at 12 months after hospitalization, where 39.4% of the patients had DLCO <80% of the predicted value. The measurement of DLCO is of interest as a marker of diffuse limitations, as it may provide additional information about pulmonary vascular limitations in long COVID.[1,4] DLCO can be altered by both pulmonary and parenchymal vascular diseases, and COVID-19 may have a course characterized by overlap between interstitial pneumonia and altered pulmonary perfusion with microthrombosis and/or macrothrombosis; therefore, DLCO appears to be the most sensitive parameter among those available for monitoring patients with COVID-19 during follow-up.[34] Importantly, we found an association between low DLCO and performance on the TGlittre, which reinforces the importance of vascular damage as a contributor to low exercise performance in these patients.[36]

Muscle tissue undergoes changes induced by SARS-CoV-2, including systemic microvascular dysfunction and the development of a myopathic process.[4,8] In our study, we showed that changes in muscle strength, both central and peripheral, persisted less than 3 years after discharge following hospitalization due to COVID-19. Of note, we also observed a significant association between QS and TGlittre time. In line with our findings, Clavario et al.[37] evaluated muscle strength using the dominant leg extension exercise in patients with long COVID. Based on the finding that muscle strength was independently associated with performance during the exercise, the authors concluded that muscle impairment may be responsible for most of the functional decrease. The relationship between reduced muscle strength and poor exercise performance was also noted by Nascimento et al.[38], in which a probable diagnosis of sarcopenia was associated with worse functional capacity on exertion according to the 6-min walking distance. These authors also noted that hospitalization was associated with worse muscle strength and reduced DLCO. It is worth noting that, unlike our study, the studies by Clavario et al.[37] and Nascimento et al.[38] were performed at a very early stage of long COVID, which reinforces the importance of continuing to monitor muscle function in the long term.

The return of patients to their active lives has spurred interest in quantifying changes in capacities related to human functions through scales that measure functional independence. In the present study, we used the FIM because it is a low-cost, noninvasive scale that can be replicated over time and can be successfully applied to evaluate different populations, such as elderly and postoperative patients.[39,40] Although our patients obtained high FIM scores, possibly due to the ceiling effect, it is evident that the motor and cognitive conditions were satisfactorily recovered for the performance of the activities of daily living, as shown by the correlation between the FIM score and the TGlittre time. Since a higher functional status as assessed by the FIM is independently associated with lower mortality in hospitalized patients,[40] this opens perspectives on the potential value of FIM in establishing a more accurate prognosis in patients with long COVID who needed hospitalization.

Using the SGRQ to assess QoL, we observed high scores in all of its domains, which shows the ability of this questionnaire to capture QoL in this population. In line with our results, Marando et al.[41] observed that 50% of patients reported a pathological QoL according to the SGRQ 1 year after COVID-19, while Liao et al.[42] observed high SGRQ scores (especially in the activity score) among health care workers who survived COVID-19 1 year after discharge in Wuhan. Of note, we observed an association between the SGRQ activity domain score and the TGlittre time. In fact, previous hospitalization in the intensive care unit, an SGRQ score >25 points and reduction in DLCO have been identified as potential risk factors for poor exercise performance in patients 1 year after COVID-19.[2] Since the extent of the harmful effects of SARS-CoV-2 infection on the QoL of survivors continues for more than 3 years after acute infection, it is essential to mitigate the factors that may impact the QoL of these patients.

Some of the clinical and practical implications of our results should be highlighted. Most patients maintain some damage in muscle strength 3 years after the SARS-CoV-2 infection, especially in handgrip strength. Since handgrip strength is a simple, reliable and low-cost measure, it can be used as a proxy indicator of functional impairment in this population.[43] In parallel, the deteriorated QoL after 3 years of the acute illness can make it difficult for these people to return to work. In this sense, occupational physicians and health professionals must better assume their crucial role in returning these patients to work, including raising awareness among employers about the specific difficulties related to long COVID.[44,45] Taken together, our findings show the importance of early initiation of rehabilitation and pharmacological-based therapeutic strategies following acute COVID-19 infection.[46] Although functional capacity is close to that observed in healthy people, it is related to both lung function and QS. Therefore, along with pulmonary rehabilitation, it is important to employ physiotherapeutic techniques aimed at restoring peripheral muscle strength in patients with long COVID.

4.1. Limitations

This study extends the existing knowledge about long-term sequelae after hospitalization with COVID-19, describing changes in functional capacity on exertion 3 years after discharge. However, some limitations should be noted. First, this study has a cross-sectional design and does not establish causality. Second, we used an observational research design with no preinfection data; this makes it difficult to separate the contributions of preexisting chronic conditions before COVID-19 infection and lifestyle factors to poor performance on the TGlittre. Third, our study evaluated only men, which prevents the generalization of our results. Fourth, our cohort consists of individuals who were not vaccinated at the time of acute infection, as this is the population that has only now reached 3 years of follow-up. In this regard, there is still no population for assessing the impact of vaccination on the effects of long COVID after 3 years, although it is already known that post-COVID-19 sequelae may be less frequent in individuals who received at least two doses of a two-dose vaccine schedule for COVID-19.[47] Despite these limitations, our findings illustrate the need for continued monitoring of this population even 3 years after infection. Therefore, even longer follow-up studies are needed to understand the full spectrum of health consequences for this population.

5. Conclusions

This research revealed that 3 years after acute SARS-CoV-2 infection, functional capacity as measured by the TGlittre time was normal in most men with long COVID, with less than a third of them still showing exercise intolerance and functional dependence when performing activities of daily living. Approximately one-third of the patients still showed reduced pulmonary diffusion, but most persisted with respiratory and/or peripheral muscle dysfunction and impaired QoL. Furthermore, there was a relationship between performance on the TGlittre and QS, pulmonary diffusion, functional status and QoL. Our results indicated that patients who were hospitalized for COVID-19 require post discharge care even after 3 years. In this regard, the implementation of rehabilitative strategies and proper management for mitigating the effects of long COVID must be guaranteed.

Funding

The authors wish to thank the Conselho Nacional de Desenvolvimento Científico e Tecnólogico (CNPq; Grant numbers #301967/2022-9 and #401633/2023-3), Brazil, the Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ; Grant number #E−26/200.929/2022), Brazil, and the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, FinanceCode 001, 88881.708719/2022-01, and 88887.708718/2022-00), Brazil.

Data availability statement

The data presented in this study are available on request from the corresponding author.

Declaration of competing interest

The authors have no conflicts of interest to report.

Acknowledgements

The authors appreciate all patients participated in this study.

Abbreviations

DLCO	diffusing capacity for carbon monoxide
FIM	Functional Independence Measure
QoL	quality of life
SGRQ	Saint George Respiratory Questionnaire
TGlittre	Glittre-ADL test

References

1. Kersten J, Wolf A, Hoyo L, et al. Symptom burden correlates to impairment of diffusion capacity and exercise intolerance in long COVID patients. *Sci Rep*. 2022;12 (1):8801. https://doi.org/10.1038/s41598-022-12839-5.
2. Steinbeis F, Knape P, Mittermaier M, et al. Functional limitations 12 months after SARS-CoV-2 infection correlate with initial disease severity: an observational study of cardiopulmonary exercise capacity testing in COVID-19 convalescents. *Respir Med*. 2022;202, 106968. https://doi.org/10.1016/j.rmed.2022.106968.
3. Huynh Q, Wexler N, Smith J, et al. Associations between symptoms and functional capacity in patients after COVID-19 infection and community controls. *Intern Med J*. 2023;53(9):1540–1547. https://doi.org/10.1111/imj.16185.
4. Schwendinger F, Knaier R, Radtke T, et al. Low cardiorespiratory fitness post-COVID-19: a narrative review. *Sports Med*. 2023;53(1):51–74. https://doi.org/10.1007/s40279-022-01751-7.
5. Johnsen S, Sattler SM, Miskowiak KW, et al. Descriptive analysis of long COVID sequelae identified in a multidisciplinary clinic serving hospitalised and non-hospitalised patients. *ERJ Open Res*. 2021;7(3):205–2021. https://doi.org/10.1183/23120541.00205-2021.
6. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet*. 2023;401(10393):e21–e33. https://doi.org/10.1016/S0140-6736(20)32656-8.
7. Guo Y, Wang H, Xiao M, et al. Long-term outcomes of COVID-19 convalescents: an 18.5-month longitudinal study in Wuhan. *Int J Infect Dis*. 2023;127:85–92. https://doi.org/10.1016/j.ijid.2022.12.008.
8. Singh I, Joseph P, Heerdt PM, et al. Persistent exertional intolerance after COVID-19: insights from invasive cardiopulmonary exercise testing. *Chest*. 2021;161(1):54–63. https://doi.org/10.1016/j.chest.2021.08.010.
9. de Oliveira TCP, Gardel DG, Ghetti ATA, et al. The Glittre-ADL test in non-hospitalized patients with post-COVID-19 syndrome and its relationship with muscle strength and lung function. *Clin Biomech*. 2022;100, 105797. https://doi.org/10.1016/j.clinbiomech.2022.105797.
10. Skumlien S, Hagelund T, Bjørtuft O, et al. A field test of functional status as performance of activities of daily living in COPD patients. *Respir Med*. 2006;100(2): 316–323. https://doi.org/10.1016/j.rmed.2005.04.022.
11. Hora AL, Guimarães FS, Menezes SLS, et al. The relationship between muscle function, lung function and quality of life in patients with chronic obstructive pulmonary disease (COPD). *Isokinet Exerc Sci*. 2018;26(1):17–27. https://doi.org/10.3233/IES-171179.
12. Mendes LPS, Parreira VF, Spencer LM, et al. Validity and responsiveness of the Glittre-ADL test without a backpack in people with chronic obstructive pulmonary disease. *COPD*. 2020;17(4):392–400. https://doi.org/10.1080/15412555.2020.1756236.
13. Soriano JB, Murthy S, Marshall JC, et al. A clinical case definition of post-COVID-19 condition by a Delphi consensus. *Lancet Infect Dis*. 2022;22(4):e102–e107. https://doi.org/10.1016/S1473-3099(21)00703-9.
14. De Sousa TC, Jardim JR, Jones P. Validation of the Saint George's Respiratory Questionnaire in patients with chronic obstructive pulmonary disease in Brazil. *J Bras Pneumol*. 2000;26(3):119–128. https://doi.org/10.1590/S0102-35862000000300004.
15. Riberto M, Miyazaki MH, Jucá SSH, et al. Validation of the Brazilian version of functional independence measure. *Acta Fisiatr*. 2004;11(2):72–76. https://doi.org/10.5935/0104-7795.20040003.
16. da Silva GA, Schoeller SD, Gelbcke FL. Functional assessment of people with spinal cord injury: use of the functional independence measure – FIM. *Text & Context Nursing*. 2012;21(4):929–936. https://doi.org/10.1590/1980-265X-TCE-2023-E001pt.
17. Graham BL, Steenbruggen I, Miller MR, et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. *Am J Respir Crit Care Med*. 2019;200(8):e70–e88. https://doi.org/10.1164/rccm.201908-1590ST.
18. Graham BL, Brusasco V, Burgos F, et al. Executive summary: 2017 ERS/ATS standards for single-breath carbon monoxide uptake in the lung. *Eur Respir J*. 2017; 49(1), 1600016. https://doi.org/10.1183/13993003.E0016-2016.
19. Pereira CAC, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. *J Bras Pneumol*. 2007;33(4):397–406. https://doi.org/10.1590/s1806-37132007000400008.
20. Neder JA, Andreoni S, Peres C, et al. Reference values for lung function tests. III. Carbon monoxide diffusing capacity (transfer factor). *Braz J Med Biol Res*. 1999;32 (6):729–737. https://doi.org/10.1590/s0100-879x1999000600008.
21. Neder JA, Andreoni S, Castelo-Filho A, et al. Reference values for lung function tests. I. Static volumes. *Braz J Med Biol Res*. 1999;32(6):703–717. https://doi.org/10.1590/s0100-879x1999000600006.
22. Neder JA, Andreoni S, Lerario MC, et al. Reference values for lung function tests. II. Maximal respiratory pressures and voluntary ventilation. *Braz J Med Biol Res*. 1999; 32(6):719–727. https://doi.org/10.1590/s0100-879x1999000600007.
23. Stanojevic S, Kaminsky DA, Miller MR, et al. ERS/ATS technical standard on interpretive strategies for routine lung function tests. *Eur Respir J*. 2022;60(1), 2101499. https://doi.org/10.1183/13993003.01499-2021.
24. Nonato CP, Azevedo BLPA, Oliveira JGM, et al. The Glittre Activities of Daily Living Test in women with scleroderma and its relation to hand function and physical capacity. *Clin Biomech*. 2020;73:71–77. https://doi.org/10.1016/j.clinbiomech.2020.01.008.
25. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):16–31. https://doi.org/10.1093/ageing/afy169.
26. Assis ACB, Lopes AJ. Functional exercise capacity in rheumatoid arthritis unrelated to lung injury: a comparison of women with and without rheumatoid disease. *J Back Musculoskelet Rehabil*. 2022;35(2):449–458. https://doi.org/10.3233/BMR-210056.
27. Canavan JL, Maddocks M, Nolan CM, et al. Functionally relevant cut point for isometric quadriceps muscle strength in chronic respiratory disease. *Am J Respir Crit Care Med*. 2015;192(3):395–397. https://doi.org/10.1164/rccm.201501-0082LE.
28. de Alegria SG, Kasuki L, Gadelha M, et al. The Glittre Activities of Daily Living Test in patients with acromegaly: associations with hand function and health-related quality of life. *J Back Musculoskelet Rehabil*. 2021;34(3):441–451. https://doi.org/10.3233/BMR-200089.
29. Reis CMD, Karloh M, Fonseca FR, et al. Functional capacity measurement: reference equations for the Glittre Activities of Daily Living test. *J Bras Pneumol*. 2018;44(5): 370–377. https://doi.org/10.1590/S1806-37562017000000118.
30. World Health Organization. Obesity and overweight. Available at: WHO Web site www.who.int/mediacentre/factsheets/fs311/en/; 2024. Accessed March 2, 2024.
31. Lopes AJ. Advances in spirometry testing for lung function analysis. *Expet Rev Respir Med*. 2019;13(6):559–569. https://doi.org/10.1080/17476348.2019.1607301.
32. Fleiss JL, Levin B, Paik MC. *Statistical Methods for Rates and Proportions*. third ed. Hoboken: John Wiley & Sons. Inc.; 2003.
33. Kattainen S, Lindahl A, Vasankari T, et al. Lung function and exercise capacity 6 months after hospital discharge for critical COVID-19. *BMC Pulm Med*. 2022;22(1): 243. https://doi.org/10.1186/s12890-022-02023-w.
34. Faverio P, Luppi F, Rebora P, et al. Six-month pulmonary impairment after severe COVID-19: a prospective, multicentre follow-up study. *Respiration*. 2021;00(11): 1078–1087. https://doi.org/10.1159/000518141.
35. Sperling S, Leth S, Fløe A, et al. Twelve-month follow-up after hospitalization for SARS-COV-2: physiology improves, symptoms remain. *Infect Dis News*. 2023;53(6), 104686. https://doi.org/10.1016/j.idnow.2023.104686.
36. Guo T, Jiang F, Liu Y, et al. Respiratory outcomes in patients following COVID-19-related hospitalization: a meta-analysis. *Front Mol Biosci*. 2021;8, 750558. https://doi.org/10.3389/fmolb.2021.750558.
37. Clavario P, De Marzo V, Lotti R, et al. Cardiopulmonary exercise testing in COVID-19 patients at 3 months follow-up. *Int J Cardiol*. 2021;340:113–118. https://doi.org/10.1016/j.ijcard.2021.07.033.
38. Nascimento WLCD, Moura DM, Almeida KO, et al. Lung and physical function in post COVID-19 and clinical and functional associations: a cross-sectional study in Brazil. *Rev Assoc Med Bras*. 2023;69(4), e20221436. https://doi.org/10.1590/1806-9282.20221436.
39. Morais DB, Lopes ACR, de Sá VM, et al. Evaluation of functional performance in patients undergoing cardiac surgery. *Rev Bras Cardiol*. 2010;23(5):263–269.
40. D'Andrea A, Le Peillet D, Fassier T, et al. Functional Independence Measure score is associated with mortality in critically ill elderly patients admitted to an intermediate care unit. *BMC Geriatr*. 2020;20(1):334. https://doi.org/10.1186/s12877-020-01729-y.
41. Marando M, Fusi-Schmidhauser T, Tamburello A, et al. 1-year radiological, functional and quality-of-life outcomes in patients with SARS-CoV-2 pneumonia: a prospective observational study. *NPJ Prim Care Respir Med*. 2022;32(1):8. https://doi.org/10.1038/s41533-022-00273-z.
42. Liao T, Meng D, Xiong L, et al. Long-term effects of COVID-19 on health care workers 1-year post-discharge in Wuhan. *Infect Dis Ther*. 2022;11(1):145–163. https://doi.org/10.1007/s40121-021-00553-0.
43. do Amaral CMSSB, da Luz Goulart C, da Silva BM, et al. Low handgrip strength is associated with worse functional outcomes in long COVID. *Sci Rep*. 2024;14(1): 2049. https://doi.org/10.1038/s41598-024-52401-z.
44. Kohn L, Dauvrin M, Detollenaere J, et al. Long COVID and return to work: a qualitative study. *Occup Med (Lond)*. 2024;74(1):29–36. https://doi.org/10.1093/occmed/kqac119.

45. Cohen J, Rodgers YVM. Long COVID prevalence, disability, and accommodations: analysis across demographic groups. *J Occup Rehabil.*. 2024 https://doi.org/10.1007/s10926-024-10173-3 [Online ahead of print].
46. Rigo S, Barbic F, Khalaf K, et al. The Long-COVID autonomic syndrome in hospitalized patients: a one-year prospective cohort study. *Eur J Intern Med*. 2024; 120:38–45. https://doi.org/10.1016/j.ejim.2023.08.018.
47. Kuodi P, Gorelik Y, Zayyad H, et al. Association between BNT162b2 vaccination and reported incidence of post-COVID-19 symptoms: cross-sectional study 2020-21, Israel. *NPJ Vaccines*. 2022;7(1):101. https://doi.org/10.1038/s41541-022-00526-5.