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Relationship between functional capacity and reduced lung function in adults with long Covid: Sulcovid-19 Survey

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ABSTRACT

Introduction: Studies on lung capacity and functionality in people recovering from COVID-19 often focus on hospitalized patients and/or those who underwent mechanical ventilation, while research on mild cases of the disease is less common. **Objective:** To evaluate the relationship between functional capacity and reduced lung function in adults with long COVID. **Methods:** This was a cross-sectional study. The dependent variables were peripheral muscle strength, balance, functional mobility, exertional dyspnea, and reduced lung function as the exposure variable. The relationship between peripheral muscle strength, balance, and the independent variable was assessed. Poisson regression models with robust variance adjustment were used to calculate the crude and adjusted prevalence ratios (PR) with 95% confidence intervals (95% CI) and p-values. To analyze the association between functional mobility, exertional dyspnea, and the independent variable, linear regression was applied, both crude and adjusted, to calculate the β coefficient with corresponding 95% CIs and p-values. A significance level of 5% was adopted for two-tailed tests. **Results:** Individuals with reduced lung function were 2.69 times more likely (95% CI: 1.45-4.97) to have reduced peripheral muscle strength and 2.85 times more likely (95% CI: 1.29-6.30) to have reduced balance. Functional mobility decreased by an average of -2.85 points (95% CI: -4.66 to -1.04), while exertional dyspnea increased by 1.46 points (95% CI: 0.68-2.24) in people with reduced lung function. **Conclusion:** Individuals with mild acute infection and no pre-existing comorbidities experienced reduced lung function associated with decreased functional capacity.

Keywords: COVID-19; respiratory function tests; muscle strength; functional residual capacity.

INTRODUCTION

Infection with SARS-CoV-2 has presented a significant challenge to global public health, affecting individuals both in the acute phase of the infection and in the post-infection¹. Long COVID is defined by the persistence of symptoms for at least three months, with symptoms lasting at least two months that cannot be explained by an alternative diagnosis^{2,3}. Among non-hospitalized individuals, the prevalence of long COVID can reach up to 34.0%⁴.

The respiratory system is particularly vulnerable to the detrimental effects of COVID-19⁵. Inflammatory responses triggered by the virus can result in symptoms such as a dry cough, decreased oxygen levels, and dyspnea⁵. These changes can lead to impairments in lung and muscle function and might result in reduced tolerance for physical activity, consequently reducing functional capacity⁶.

Persistent respiratory symptoms and impaired pulmonary function have been increasingly recognized as sequelae of COVID-19⁷. A study with a median follow-up period of 75 days after diagnosis showed that pulmonary function impairment was significantly associated with worsening dyspnea, assessed through the modified Medical Research Council Dyspnea Scale (mMRC), and the score obtained in the 'functional capacity' domain of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) 45 days after hospital discharge⁸.

However, most studies on lung function and functional capacity in COVID-19 survivors typically focus on patients who were hospitalized and/or received mechanical ventilation, and studies involving mild cases of the disease are scanty⁹.

Therefore, this study aimed to assess the relationship between functional capacity and reduced lung function in adults experiencing long COVID symptoms.

METHODS

Data were analyzed from the Sulcovid-19 study, a longitudinal study that monitors the health of individuals infected with SARS-CoV-2 in the city of Rio Grande, in the state of Rio Grande do Sul, Brazil. Participants were required to be ≥ 18 years old, have received a COVID-19 diagnosis through RT-PCR testing between December 2020 and March 2021, have experienced COVID-19 symptoms during the acute phase, and have received medical care in Rio Grande. The study protocol was approved by the Health Research Ethics Committee (CEPAS) of the Federal University of Rio Grande (FURG) (CAAE: 39081120.0.0000.5324).

To identify adults who had been infected with SARS-CoV-2, we contacted the Epidemiological Health Surveillance department of the city of Rio Grande. Subsequently, a list consisting of 4,014 individuals who had tested positive for SARS-CoV-2 through RT-PCR, along with their corresponding information, such as name, address, telephone number, and presence of symptoms, was compiled. Subsequently, inclusion and exclusion criteria were applied, resulting in 3,822 individuals considered eligible for the study (Figure 1).

Data collection was conducted through telephone interviews carried out by trained interviewers who underwent a selection process and received training for questionnaire administration. When necessary, home visits were offered as an alternative for in-person data collection. Further information about the study design and recruitment process can be found elsewhere¹⁰.

Overall, 348 individuals aged between 18 and 59 were deemed eligible to participate: they had no pre-existing comorbidities, were non-smokers, and presented at least one persistent respiratory symptom such as fatigue, cough, or shortness of breath. Those with cognitive impairment, difficulties, or functional limitations that would hinder the evaluation process, as well as individuals diagnosed with diabetes mellitus, hypertension, asthma,

chronic obstructive pulmonary disease, heart disease, active smokers, obesity, and pregnant women, were excluded.

All eligible participants for functional capacity and pulmonary function assessment were contacted by telephone at least three times to provide information about the study and schedule the evaluation sessions. A trained professional conducted the appointments and evaluations, which took place at the participants' homes.

Functional capacity was defined as participants' balance, strength, and perceived effort. We used four tests to assess functional capacity, as follows: Timed Up and Go (TUG - balance), handgrip strength, Berg Balance Scale (BBS) (functional balance in task performance), and the Modified Borg Scale (assessment of perceived effort and dyspnea).

To perform the TUG test, the participant was instructed to sit in a chair with lateral arm support. Subsequently, the evaluator asked the participant to stand up without leaning on the sides of the chair, walk three meters, turn 180°, return to the starting point, and sit down again. Normal values were in accordance with¹¹: less than 10 seconds for completely free and independent individuals; 10-19 seconds for independent individuals with reasonable balance; and 20-29 seconds for subjects with significant difficulties in performing daily tasks. For analysis purposes, the results of this test were dichotomized into “normal balance” and “reduced balance”.

Handgrip strength was assessed using a dynamometer (Saehan dynamometer). Participants were seated with their arms positioned parallel to the trunk, shoulder in a neutral position, and elbow flexed at 90°. Additionally, the wrist was maintained in hyperextension of up to 30° and ulnar deviation of up to 15°. Three measurements were taken for both hands, with a minimum 30-second interval between each. The tests alternated between the dominant and non-dominant sides to minimize the impact of muscle fatigue. The highest value obtained

for each hand was subjected to data analysis¹². For analysis purposes, the results were categorized into reduced and non-reduced peripheral muscle strength¹².

The Berg Scale consists of 14 common items from daily life, with a maximum score of 56 points to be achieved, and each item has an ordinal scale comprising 5 options ranging from 0 to 4 points based on the level of difficulty. The overall score can range from 0 (severely impaired balance) to 56 (excellent balance); a score lower than 45 points was predictive of recurrent falls¹³. We chose to present this outcome in the form of mean and standard deviation, as it is a discrete numerical variable, with higher values representing better conditions of functional balance^{13,14}.

Modified Borg Scale allows the measurement of exercise intensity, providing an individualized assessment of dyspnea, fatigue, or pain during exercise¹⁵. Numeric values were used in accordance with¹⁶, where 0 represents an absence of fatigue/dyspnea sensation; 0.5 very, very slight; 1 very slight; 2 slight; 3 moderate; 4 somewhat intense; 5 intense; 6 and 7 very intense; 8 and 9 very, very intense, and 10 maximum. Self-reported sensations of fatigue and dyspnea were collected using a printed visual scale at the beginning of the tests and after their completion. At the initial moment of the tests, the individual was asked to report their sensation of dyspnea using the printed Modified Borg Scale. Following this, pulmonary function testing, peripheral muscle strength testing, balance testing, and functional mobility assessments were conducted. Finally, the individual was asked to report their sensation of dyspnea after the tests using this printed material. Dyspnea on exertion is a numerical scale, and we chose to present the results as mean and standard deviation. However, this outcome was constructed considering the difference between the score before and after exertion¹⁷.

Pulmonary function was assessed through spirometry using a portable spirometer from the Minispir brand. The Minispir portable spirometer is a compact and easy-to-use device designed to measure respiratory functions, such as forced vital capacity (FVC), forced

expiratory volume in the first second (FEV1), and other important pulmonary parameters. It is ideal for monitoring in clinical settings or for home use, allowing healthcare professionals to perform quick and accurate spirometry tests. Participants were seated upright without back support and wore a nose clip. Subsequently, the participant was instructed to breathe calmly, completely inhaling to reach full lung capacity, followed by an explosive and steady exhalation. This maneuver was repeated three times, and the highest recorded value was selected, according to recommendations from the literature¹⁸. The results obtained were initially categorized as (0) normal, (1) obstructive, and (2) restrictive¹⁸. For analysis purposes, we dichotomized this variable into reduced pulmonary function (No/Yes). Therefore, those individuals with obstruction and/or restriction were considered to have reduced lung function, regardless of the degree of impairment.

The control variables used were: sex (female; male), age group (tertile), skin color (white; black/brown), marital status (with and without a partner), education (no education/ 1st grade or elementary school; 2nd grade or high school; 3rd grade or higher education) and monthly income (no income; less than R\$500.00 to R\$1.000.00; between 1.001.00 to R\$2.000.00; between 2.001.00 to R\$4.000.00; more than R\$4.001.00).

Data were analyzed using the Stata 16.1 statistical package. Univariate analysis was performed to describe the sample, using absolute and relative frequency for each variable of interest. To examine the relationship between exposure and outcome variables, a Poisson regression model with robust adjustment for variance was used. Crude and adjusted prevalence ratios (PR) were calculated, along with their corresponding 95% confidence intervals (95% CI) and p-values. For assessing the association between outcome and functional capacity, as well as dyspnea on exertion, crude and adjusted linear regression models were used. The β coefficients, along with their respective 95% confidence intervals

(95%CI) and p-values, were calculated. The significance level was set at 5% for two-tailed tests.

RESULTS

Overall, 348 individuals were eligible, and 166 were interviewed, resulting in a response rate of 47.7%. Most of the participants were women (65.7%), white (77.0%), lived with a partner (72.1%), and had completed high school (83.5%). The mean age was 41.1 ± 8.7 , ranging from 18 to 59 years (Table 1). Among the participants assessed, 0.99% (95% CI: 0.68% – 1.43%) were underweight, while 25.73% (95% CI: 24.16% – 27.38%) had a normal weight. The overweight category was observed in 40.35% (95% CI: 38.55% – 42.17%) of the participants, and 32.93% (95% CI: 31.23% – 34.69%) were classified as obese. Regarding physical activity, 73.04% of individuals did not engage in physical activity (95% CI: 71.39% – 74.62%), while 26.96% do (95% CI: 25.38% – 28.61%). When analyzing physical activity in categorized terms, considering a minimum of 150 minutes per week, 84.01% of participants are inactive (95% CI: 82.63% – 85.29%), and 15.99% are active (95% CI: 14.71% – 17.37%).

In the group of participants assessed, 89.21% (95% CI: 87.91% – 90.39%) reported being reinfected with COVID-19, while 9.94% (95% CI: 8.89% – 11.10%) stated they were not reinfected. Additionally, 0.85% (95% CI: 0.57% – 1.26%) reported reinfection confirmed by testing. Regarding COVID-19 vaccination, 14.42% (95% CI: 13.19% – 15.76%) of participants reported having received no doses. In contrast, 35.51% (95% CI: 33.78% – 37.27%) indicated they had received both doses, while 50.07% (95% CI: 48.24% – 51.89%) reported having received only one dose.

Table 2 shows the prevalence of residual respiratory symptoms and functional capacity outcomes. Briefly, 82.4% reported fatigue, and 28.6% pain/discomfort in breathing.

Abnormal spirometric pattern was observed in 19.9% of the participants, reduced peripheral muscle strength in 27.9%, and reduced balance in 17.5% (Table 2).

Participants with reduced pulmonary function were more likely to have reduced peripheral muscle strength (PR 2.69, 95% CI: 1.45; 4.97) and reduced balance (PR 2.85, 95% CI: 1.29–6.30). Also, functional mobility decreased (β -2.85; 95% CI -4.66; -1.04), and dyspnea on exertion increased (β 1.46, 95% CI 0.68; 2.24) (Table 3).

DISCUSSION

Fatigue was highly reported by participants with reduced lung function, as expected. We found that experiencing reduced lung function due to COVID-19 infection was associated with reduced muscle strength, balance, and functional mobility. Additionally, dyspnea was positively associated with reduced pulmonary function.

We revealed that even after six months of infection, 19.9% of individuals with mild infection and long COVID had reduced pulmonary function. A meta-analysis involving 380 individuals after SARS-CoV-2 infection found that 15.0% of participants assessed exhibited a restrictive pattern of pulmonary function, and 7.0% exhibited an obstructive pattern¹⁹. SARS-CoV-2 infection promotes diffuse destruction of the alveolar epithelium, capillary damage/bleeding, hyaline membrane formation, fibrous proliferation of the alveolar septum, and lung consolidation, which might result in reduced pulmonary function²⁰. Our results are relevant to raise awareness among healthcare professionals about the importance of monitoring not only individuals hospitalized due to SARS-CoV-2 but also those who were not hospitalized and continue to experience residual symptoms of COVID-19, such as fatigue, cough, and shortness of breath. These individuals must have their lung function assessed even

after three months of infection, as these symptoms can lead to changes in pulmonary function^{21,22}.

A study demonstrated that 6 months after intensive care unit discharge, grip strength values were significantly lower in the COVID-19 patients compared to healthy controls²³. The vulnerability of skeletal muscle to the SARS-CoV-2 virus through the angiotensin-converting enzyme-2 (ACE-2) might explain strength reductions²⁴. With the coronavirus active in the lungs, leukocytes infiltrate lung tissue, and cytokines (especially IL-6) are secreted by these leukocytes, disrupting metabolic homeostasis and causing muscle loss²⁴. This may result in reduced exercise tolerance and increased susceptibility to fatigue, impairing the quality of life²⁴.

A meta-analysis showed that individuals affected by COVID-19 presented prevalence rates of 26.4% dizziness, which is related to the loss of balance²⁵. SARS-CoV-2 affects the central nervous system through the olfactory bulb, causing neuroinflammation that damages neurons, and since neurons rarely regenerate, results in long-lasting neuronal dysfunction²⁶. Furthermore, the virus's action on the brain can trigger transient or long-term orthostatic intolerance syndrome, leading to balance impairments²⁷.

The reduction in peripheral muscle strength is a common effect observed in restrictive respiratory diseases such as chronic obstructive pulmonary disease, resulting in a decreased state of health, reduced ability to perform daily activities, poorer quality of life, and a higher risk of mortality^{28,29}. These findings can be extrapolated to individuals infected with SARS-CoV-2, given the similarity of symptoms between these respiratory diseases.

Reduced lung function affects functional capacity due to the reduction of physical activity and increases exertional dyspnea³⁰. The chronic dyspnea experienced by individuals with long COVID may be a consequence of residual lung involvement³¹. Even asymptomatic COVID-19 patients can develop lung involvement that can result in fibrosis, leading to

persistent dyspnea³². Additionally, these patients may have pulmonary scarring resulting from the acute phase of COVID-19, which can also explain the dyspnea³³.

This study has limitations and strengths. It is necessary to mention that the sample size restricts the generalization of the results, and it is also important to consider the possibility of reverse causality. We sought to minimize this possibility by applying exclusion criteria. To the best of our knowledge, no studies have investigated that have investigated pulmonary function, peripheral muscle strength, exertional dyspnea, and functional mobility in adults with long COVID symptoms who were not hospitalized during the acute phase of the infection and had no previous comorbidities. It is important to highlight that we used instruments considered gold standards to collect the main outcomes.

Conclusion

Individuals with long COVID symptoms who had a mild acute infection with SARS-CoV-2 and no pre-existing comorbidities exhibited a reduction in peripheral muscle strength and balance. Furthermore, those with decreased lung function had an increased likelihood of experiencing reduced functional capacity. These findings may inform public health policy and direct future research efforts to understand the long-term implications of this condition, emphasizing the importance of surveillance and follow-up for individuals infected with SARS-CoV-2, including those who were not hospitalized. Additionally, our findings can contribute to the adaptation of specific treatments for long COVID and the effective management of healthcare services to meet the evolving demands associated with this condition.

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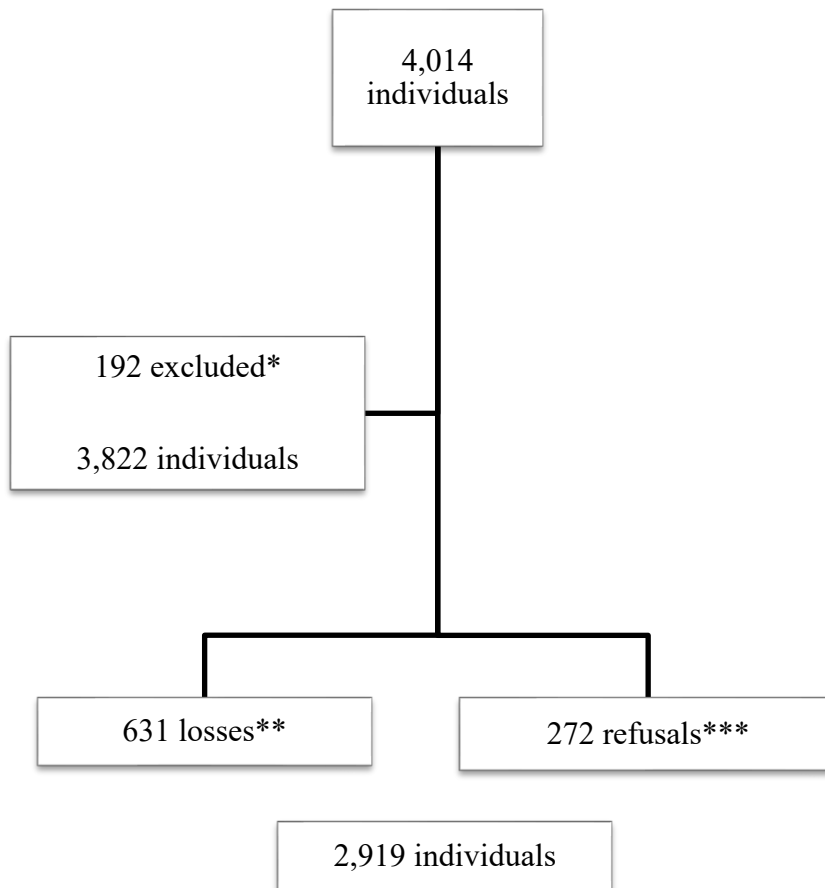
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Figure 1: Recruitment and exclusion process of individuals infected with SARS-CoV-2. Sulcovid-19 Survey.



*Excluded due to lack of information, such as address and telephone.

**Individuals who did not respond to the three telephone contacts and who were not found at home during home visits were considered losses. Individuals whose addresses could not be found were also considered lost.

***Individuals' refusals included, among others, a lack of time and interest in talking about their infection.

Table 1: Characteristics of the sample with long COVID residents of southern Brazil. 2021 (n=166)

Variable	n	%
Gender (n=166)		
Male	57	34.3
Female	109	65.7
Age group (tertiles) (n=166)		
1 tertile 18-36 years	60	36.1
2 tertile 37-41 years	52	31.3
3 tertile 42-59 years	54	32.5
Marital status (n=165)		
With partner	119	72.1
Without partner	46	27.9
Skin color (n=165)		
White	127	77.0
Black/brown	38	23.0
Education (n=164)		
No study / 1st grade or elementary school	27	16.5
2nd grade or high school	70	42.7
3rd degree or higher education	67	40.8
Income (n=148)		
No income	20	13.5
Less than BRL 500,00 to BRL 1,000.00	19	12.8
Between BRL 1,001.00 to BRL 2,000.00	45	30.4
Between BRL 2,001.00 and BRL 4,000.00	42	28.4
More than BRL 4,001.00	22	14.9

Table 2: Residual respiratory symptoms and functional capacity outcomes (n=166).

Variable	n	%
Shortness of breath (n=93)		
No	55	59.1
Yes	38	40.9
Cough with phlegm (n=28)		
No	16	57.1
Yes	12	42.9
Dry cough (n=99)		
No	76	76.8
Yes	23	23.2
Pain/discomfort to breathe (n=77)		
No	55	71.4
Yes	22	28.6
Fatigue/ Tiredness (n=159)		
No	28	17.6
Yes	131	82.4
Abnormal spirometric pattern (n=166)		
No	133	80.1
Yes	33	19.9
Reduced peripheral muscle strength (n=166)		
No	119	72.1
Yes	46	27.9
Reduced balance (n=166)		
No	137	82.5
Yes	29	17.5
Functional mobility		
	Mean	SD
	53.2	4.2
Dyspnea on exertion		
	Mean	SD
Initial	1.5	2.0
End	3.2	2.8

SD= standard deviation

Table 3: Adjusted analysis between pulmonary function and functional capacity in individuals with long COVID, residents of southern Brazil.

2021 (n=166).

	Crude Analysis			Adjusted analysis*		
	Effect measure (Prevalence Ratio)	95% CI	p-value	Effect measure (Prevalence Ratio)	CI95%	p-value
Outcome: Reduced peripheral muscle strength	PR=3.36	(1.88;6.00)	<0.001	PR=2.69	(1.45;4.97)	0.002
Outcome: Reduced balance	PR=3.27	(1.57;6.80)	0.001	PR=2.85	(1.29;6.30)	0.009
	Effect measure (beta coefficient)			Effect measure (beta coefficient)		
Outcome: Functional balance	β =-2.64	(-4.20; -1.09)	0.001	β =-2.85	(-4.66; -1.04)	0.002
Outcome: Dyspnea on exertion	β =1.37	(1.07-1.67)	<0.001	β =1.46	(0.68;2.24)	<0.001

PR: Prevalence Ratio; β = beta coefficient

*Adjust for sex, age group, skin color, marital status, education, and income.