Changes in functional capacity after one year of hospitalization for COVID-19

Alterações da capacidade funcional após um ano de internação hospitalar por COVID-19

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Abstract

Introduction: Monitoring the long-term consequences of COVID-19 and its impact on different aspects is essential. **Objective:** To assess functional capacity and associated factors up to one year after hospital discharge in COVID-19 survivors. **Methods:** This cross-sectional study included individuals aged 18 years or older, residents of a medium city in Rio Grande do Sul, Brazil, with a laboratory diagnosis of COVID-19, who required hospitalization. Data collection was performed through home visits, face-to-face interviews, and physical tests, which assessed a set of sociodemographic, clinical, and health characteristics. The primary outcomes were functional status and muscle strength assessed by the Post-COVID-19 Functional Status Scale and the Medical Research Council Score. Analyses were performed using crude and adjusted logistic regression models. **Results:** Of the 160 individuals, the majority were female (53.1%), white (71.9%), with a mean age of 64 years. Functional limitations were identified in 67.5% (95%CI 46.2 - 70.2) of the sample, with 50.9% (95%CI: 41.8 - 60.0) presenting changes in muscle strength, 10% of which (95%CI 5.8 - 17.0) presented muscle weakness. An association was found between greater functional limitation and diagnosis of respiratory diseases (p = 0.002). Changes in muscle strength were associated with female gender (p = 0.009), diagnosis of sarcopenia (p = 0.036), smoking (p = 0.022) and need for orotracheal intubation (p = 0.009). **Conclusion:** It was observed that, within one year after hospital discharge, individuals presented signi ficant functional limitations, with more than half presenting some type of muscle strength impairment and a portion showing signs of muscle weakness.

Keywords: Health assessment. Hospitalization. Functional status. Acute post-COVID-19 syndrome.

Resumo

Introdução: *Monitorar as consequências a longo prazo da COVID-19 e seu impacto em diferentes aspectos é essencial.* ***Objetivo:*** *Avaliar a capacidade funcional e os fatores associados em até um ano após a alta hospitalar em sobreviventes da COVID-19.* ***Métodos:*** *Trata-se de um estudo transversal que incluiu indivíduos com 18 anos ou mais, residentes de uma cidade gaúcha de médio porte, com diagnóstico laboratorial de COVID-19, que necessitaram de internação hospitalar. A coleta de dados foi realizada por meio de visitas domiciliares, entrevistas presenciais e testes físicos, que avaliaram um conjunto de características sociodemográficas, clínicas e de saúde. Os desfechos primários foram o estado funcional e a força muscular avaliados pela escala de estado funcional pós-COVID-19 e pelo* Medical Research Council Score*. As análises foram realizadas por meio de modelos de regressão logística bruta e ajustada.* ***Resultados:*** *Dos 160 indivíduos, a maioria era do sexo feminino (53,1%), de cor branca (71,9%), com média de idade de 64 anos. Limitações funcionais foram identificadas em 67,5% (IC95% 46,2 - 70,2) da amostra, sendo que 50,9% (IC95%: 41,8 - 60,0) apresentaram alteração da força muscular e 10% destes (IC95% 5,8 - 17,0) apresentaram fraqueza muscular. Encontrou-se associação entre maior limitação funcional e diagnóstico de doenças respiratórias (p = 0,002). A alteração da força muscular foi associada ao sexo feminino (p = 0,009), diagnóstico de sarcopenia (p = 0,036), tabagismo (p = 0,022) e necessidade de intubação orotraqueal (p = 0,009).* ***Conclusão:*** *Observou-se que, em até um ano após a alta hospitalar, os indivíduos apresentaram limitações funcionais significativas, com mais da metade apresentando algum tipo de comprometimento da força muscular e uma parcela apresentando sinais de fraqueza muscular.*

Palavras-chaves: *Avaliação em saúde. Internação hospitalar. Estado funcional. Síndrome pós-COVID-19 aguda.*

Introduction

The COVID-19 pandemic, caused by the novel coronavirus (SARS-CoV-2), represents one of the greatest global health challenges of this century. By October 2023, more than 37 million confirmed cases and 700,000 accumulated deaths had been recorded due to COVID-19.[1] Although Brazil has one of the most robust healthcare systems in Latin America, capacity is quite uneven throughout the country.

Added to the existing challenges, after three years of the pandemic, the post-COVID-19 syndrome has been considered the post-pandemic pandemic. It is estimated that more than 65 million people worldwide may be suffering from persistent symptoms caused by COVID-19, showing that the virus has significant short- and long-term consequences.[2] Studies reveal that, in individuals who had more severe cases of the disease, including those who required hospitalization and admission to an intensive care unit (ICU), those impairments were observed for a long term, persisting for up to two years after the infection.[3,4] However, the magnitude of the sequelae produced by the disease is not yet well established in the literature. To date, more than 200 symptoms associated with the syndrome have been described.[2,5] The most commonly described symptoms involve the respiratory, neurological, and musculoskeletal systems, such as fatigue, dyspnea, weakness, and cognitive deficits, making it a complex syndrome that has a wide variety of symptoms and can affect all systems of the body.[5]

Musculoskeletal limitations and decreased cardiorespiratory capacity contribute to a worse quality of life, often making individuals functionally incapacitated.[2,6,7] Studies show a high prevalence of physical limitations, limited ability to perform activities of daily living, and changes in muscle strength after infection with the SARS-CoV-2 virus.[4,8-12]

In March 2023, the World Health Organization declared the end of the pandemic, but the impacts caused will likely be felt for a long time.[13] The literature indicates that functional limitations need to be explored not only after hospital discharge, but also throughout the recovery period. Within this context, it is essential to monitor the long-term consequences of COVID-19 and its impact on individual, public health, and economic aspects in Brazil in different contexts, given the existing inequalities. Thus, the aim of our study was to assess the functional status, peripheral muscle strength, as well as sociodemographic, clinical and health associated factors, within 12 months after hospital discharge, in individuals hospitalized due to COVID-19 in a medium-city in southern Brazil.

Methods

This was a cross-sectional study conducted from September 2022 to April 2023 in Passo Fundo, a

medium-sized city located in southern Brazil. The target population were reported and confirmed cases of severe acute respiratory syndrome (SARS) to the Influenza Epidemiological Surveillance System (SIVEP-Gripe), admitted to a hospital environment as a result of COVID-19. Male and female individuals, aged 18 or over, hospitalized and discharged between September 1, 2021 and September 15, 2022, with confirmed SARS due to COVID-19, residing in urban households in Passo Fundo (with telephone number or address available for contact) were considered eligible.

Subjects who had severe cognitive impairment (assessed using a dual approach: caregiver-reported information and clinical observation by the interviewer) that prevented them from participating in the study and those who died in the period after hospitalization due to COVID-19 were considered ineligible.

After defining those eligible, up to three phone contact attempts were made, at alternate times and days within a window of up to ten days, and, in cases of acceptance of the invitation to participate, the interview was scheduled according to the participant's availability. In cases where there was no response to our phone contact, up to three attempts were made to approach the address provided and, therefore, those who did not respond to both approaches were considered losses in the study. To carry out the face-to-face interview, a home visit was conducted. The data collection instrument was comprised of a questionnaire developed for the study itself, through an intelligent questionnaire built in the Research Electronic Data Capture (RedCap) application, being structured in 11 blocks, namely: A. Identification and sociodemographic characteristics; B. Health characteristics and lifestyle habits; C. Data related to symptoms and hospitalization due to COVID-19; D. Persistent symptoms after COVID-19; E. Use of post-COVID-19 health services; F. Assessment of functional status post-COVID-19; G. Assessment of health-related quality of life; H. Assessment of mental health; I. Sleep assessment; J. Muscle strength assessment; and K. Neurological assessment.

For this study, sociodemographic (sex, age, gender, education, socioeconomic position following Brazilian Economic Classification Criteria, occupation, self-reported skin color), clinical (number of times having had COVID-19, data on vaccination against COVID-19, ICU admission, use of oxygen therapy, need for invasive and non-invasive mechanical ventilation, and use of a physical therapy service after discharge), and health (practice of physical activities ,smoking, and presence of comorbidities - obesity, sarcopenia, osteoporosis, respiratory diseases) characteristics were analyzed.

Functional status was assessed using the Post-COVID-19 Functional Status Scale, translated and validated into Brazilian Portuguese by Machado et al.,[14] which is considered the standard scale for assessing functional limitations after COVID-19 infection. The scale is made up of several functional outcomes and focus on daily activities carried out, whether at home or at work, and changes in lifestyle. It is graded into five levels, namely: grades 0 (no functional limitations), 1 (negligible functional limitations), 2 (slight functional limitations), 3 (moderate functional limitations), and 4 (severe functional limitations).[14] To rule out cases of functional incapacity prior to hospitalization due to COVID-19, a question was asked regarding the ability to live alone before hospitalization, and if the answer was negative, the participant was classified as functionally dependent prior to hospitalization and was not eligible to answer the functional capacity scale.

In order to analyze the factors associated with the functional limitation outcome, the variable was dichotomized, in which individuals classified as having no functional limitations (0), and those with negligible (1) and slight (2) limitations were grouped and compared with those who had moderate (3) and severe results (4).

Peripheral muscle strength was assessed through the Medical Research Council (MRC) protocol, which consists of assessing and grading the strength of six muscle groups. The sum of the results varies from 0-60, with 60 points being considered normal muscle strength, while results below that value show changes in muscle strength, and results below 48 points are indicative of muscle weakness.[15] In this study, in order to analyze the outcomes, changes in muscle strength and presence of muscle weakness, two cutoff points were used in the MRC protocol. The cutoff point <48 points represented the standard test indicator for the presence of muscle weakness, while the cutoff point <60 points represented individuals who had some change in muscle strength.

Statistical analyses were performed using the software SPSS Statistics for Windows, version 26.0 (SPSS Inc., Chicago, Illinois, USA) and consisted of descriptive statistics, using absolute (n) and relative (%) frequencies and analytics.

For multivariate analysis, crude and adjusted (for all other variables) logistic regression models were performed to verify the association of the outcomes of interest with the independent variables. The level of statistical significance adopted was $p < 0.05$.

This research is an excerpt from the project *Analysis of the Post-COVID-19 Health Situation in Southern Brazil*, approved on June 7, 2022, by the Universidade Federal da Fronteira Sul Ethics Committee for Research with Human Beings – opinion no. 5,453,565. Individuals participated voluntarily, reading and signing the free and informed consent form prior to conducting the study.

Results

From September 1, 2021, to September 15, 2022, a total of 557 hospital admissions for confirmed cases of SARS due to COVID-19 were reported in Passo Fundo, Brazil. After applying the inclusion and exclusion criteria (Figure 1), a total of 160 participants were interviewed.

Sociodemographic data indicate that the majority of individuals were female (53.1%), under 65 years of age (54.1%), and self-identified as white (71.9%). Additional clinical and health characteristics of the sample are presented in Table 1.

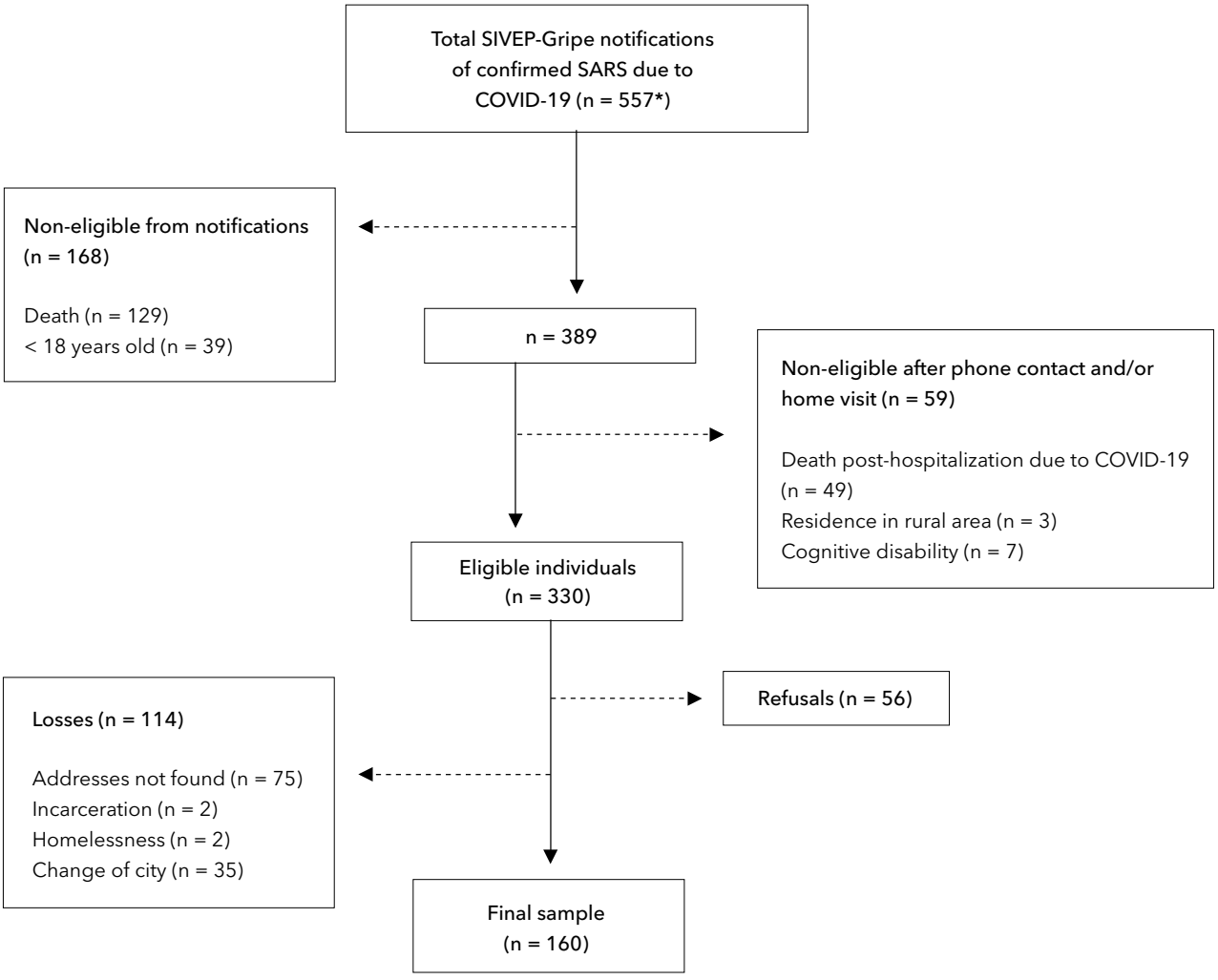

Figure 1 - Sample breakdown flowchart.

Note: SIVEP-Gripe = Influenza Epidemiological Surveillance System; SARS = Severe Acute Respiratory Syndrome. *Number of hospital admissions in Passo Fundo, RS, Brazil, from 09/01/2021 to 09/15/2022.

Table 1 - Sociodemographic, clinical, and health characteristics of individuals post-hospitalization due to COVID-19 (n = 160)

Characteristics	n (%)
Sex	
Male	75 (46.9)
Female	85 (53.1)
Age bracket (years)	
≥ 65	76 (45.9)
< 65	81 (54.1)
Skin color (self-reported)	
White	115 (71.9)
Black/brown	45 (28.1)
Socioeconomic position*	
A-B	71 (44.7)
C-D-E	89 (55.3)
Education level	
Never studied/Primary education	84 (53.2)
Secondary/Higher education	76 (46.8)
Active occupational activity	
No	120 (75.0)
Yes	40 (25.0)
Sarcopenia	
No	64 (40.0)
Yes	96 (60.0)
Osteoporosis	
No	86 (53.8)
Yes	74 (46.2)
Respiratory diseases	
No	94 (59.5)
Yes	66 (40.5)
Obesity	
No	89 (55.6)
Yes	71 (44.4)
Physical activity	
No	76 (47.5)
Yes	84 (52.5)
Smoking prior to hospitalization	
No	94 (58.8)
Yes/former smoker	66 (41.2)
COVID-19 frequency	
1	129 (80.6)
2 or more	31 (19.4)
Admission to intensive care unit	
No	128 (80.0)
Yes	32 (20.0)
Use of oxygen in hospital admission	
No	30 (18.9)
Yes	130 (81.1)
Intubation	
No	147 (91.9)
Yes	13 (8.1)
Vaccination prior to hospital admission	
No	25 (15.6)
Yes	135 (84.4)
Physical therapy after hospital discharge	
No	126 (78.7)
Yes	34 (21.3)

Note: *According to the Brazilian Economic Classification Criteria (ABEP).

The results of the functional capacity classification demonstrated that, of the 160 participants, 46 had been unable to live alone before hospitalization due to COVID-19, being classified as ineligible, and were therefore not included in the analysis. Thus, the total number for this variable was made up of 114 individuals. It was found that 67.5% (95%CI 46.2-70.2) of participants have some type of functional limitation as a result of COVID-19. Of those, the majority have moderate (31.6%) and severe (23.7%) limitations, meaning that they can no longer live alone or can no longer carry out certain activities spontaneously and require help from other people. In the analysis considering the dichotomized outcome, a prevalence of 55.3% of functional limitation was observed.

Individuals with the highest rates of functional status limitations were those with a low education level (66.1%), those who did not perform active occupational activities (62.5%), those who reported having sarcopenia (63.6%) and respiratory diseases (72.9%), those who required oxygen therapy during hospitalization (60.4%) and physiotherapy after discharge (75%) (Table 2).

Table 3 presents the analysis of the association of sociodemographic, clinical, and health characteristics with functional status. In the crude analysis, a low education level (OR: 0.40 95%CI: 0.19 - 0.85), not performing an active occupational activity (OR: 0.37 95%CI: 0.16 - 0.85), having diagnosis of sarcopenia (OR: 2.25 95% CI: 1.05 - 4.80) and respiratory diseases (OR: 3.65 95% CI: 1.63 - 8.15), having used oxygen therapy (OR: 3.97;

95%CI: 1.31 - 12.04) and undergone physical therapy after hospital discharge (OR: 3.00; 95%CI: 1.09 - 8.25) were significantly associated with functional status. After adjustment, those individuals with respiratory diseases (OR: 5.67; 95%CI: 1.93 - 16.68) were more likely to have moderate or severe limitations in functional status than those who did not have respiratory diseases. Participants who were obese were 72% (OR: 0.33; 95%CI: 0.12-0.91) less likely to have functional limitations than those who were not obese. The other variables did not remain statistically associated with functional status after the adjusted analysis model.

Table 2 - Sociodemographic, clinical, and health characteristics of individuals post-hospitalization due to COVID-19, according to functional status (n = 114)

Characteristics	Functional status		p
	Grades 0, 1, and 2 - n (%)	Grades 3 and 4 - n (%)	
Sex			
Male	25 (51.0)	24 (49.0)	0.241
Female	26 (40.0)	39 (60.0)	
Age bracket (years)			
<65	30 (53.6)	26 (46.4)	0.062
≥65	21 (36.2)	37 (63.8)	
Skin color (self-reported)			
White	34 (42.0)	47 (58.0)	0.353
Black/brown	17 (51.5)	16 (48.5)	
Education level			
Never studied/Primary education	20 (33.9)	39 (66.1)	**0.016**
Secondary/Higher education	31 (56.4)	24 (43.6)	
Socioeconomic position*			
A-B	27 (52.9)	24 (47.1)	0.113
C-D-E	24 (38.1)	39 (61.9)	
Active occupational activity			
No	30 (37.5)	50 (62.5)	**0.017**
Yes	21 (61.8)	13 (38.2)	
Sarcopenia			
No	27 (56.3)	21 (43.8)	**0.035**
Yes	24 (36.4)	42 (63.6)	
Osteoporosis			
No	33 (51.6)	31 (48.4)	0.097
Yes	18 (36.0)	32 (64.0)	
Respiratory diseases			
No	38 (57.6)	28 (42.4)	**0.001**
Yes	13 (27.1)	35 (72.9)	
Obesity			
No	24 (36.9)	41 (63.1)	0.053
Yes	27 (55.1)	22 (44.9)	
Physical activity			
No	19 (40.4)	28 (59.6)	0.438
Yes	32 (47.8)	35 (52.2)	

Note: *According to the Brazilian Economic Classification Criteria (ABEP). Bolds value = significant ratio ($p < 0.05$).

Table 2 - Sociodemographic, clinical, and health characteristics of individuals post-hospitalization due to COVID-19, according to functional status (n = 114) (continued)

Characteristics	Functional status		p
	Grades 0, 1, and 2 - n (%)	Grades 3 and 4 - n (%)	
Smoking			
No	34 (49.3)	35 (50.7)	0.228
Yes/Former smoker	17 (37.8)	28 (62.2)	
COVID-19 frequency			
1	39 (44.3)	49 (55.7)	0.869
2 or more	12 (46.2)	14 (53.8)	
Admission to intensive care unit			
No	43 (46.2)	50 (53.8)	0.498
Yes	8 (38.1)	13 (61.9)	
Use of oxygen in hospital admission			
No	13 (72.2)	5 (27.8)	**0.011**
Yes	38 (39.6)	58 (60.4)	
Intubation in hospital admission			
No	49 (46.7)	56 (53.3)	0.184*
Yes	2 (22.2)	7 (77.8)	
Vaccination prior to hospital admission			
No	9 (45.0)	11 (55.0)	0.979
Yes	42 (44.7)	52 (55.3)	
Physical therapy after hospital discharge			
No	45 (50.0)	45 (50.0)	**0.037**
Yes	6 (25.0)	18 (75.0)	

Note: *Fisher's exact test. Bolds value = significant ratio ($p < 0.05$).

In order to assess muscular strength, participants considered functionally dependent prior to hospitalization were excluded from the analysis of the muscular strength test as functional impairment could negatively influence the individual's muscular strength, thus the analyzed sample consisted of 114 participants.

The results indicate that 50.9% of individuals (95% CI: 41.8 - 60.0) have some change in peripheral muscle strength and, of these, 10.6% (95%CI: 5.8 - 17.0) have muscle weakness within 12 months of hospital discharge. Individuals who were female ($p = 0.009$), were not gainfully employed ($p = 0.003$), were diagnosed with sarcopenia ($p = 0.005$), and who required intubation during hospitalization ($p = 0.032$) had a higher ratio of change in muscle strength than their peers (Table 4).

Table 5 presents the analysis of the association of sociodemographic, clinical, and health characteristics with changes in muscle strength (MRC < 60 points). In the crude analysis, women (OR: 2.76; 95%CI: 1.28 - 5.92), those with sarcopenia (OR: 2.99; 95%CI: 1.38 - 6.48), and those intubated upon hospitalization (OR: 8.80; 95%CI: 1.06 - 72.86) were more likely to have changes in muscle strength than men, those without sarcopenia, and those not intubated, respectively. Participants who were gainfully employed were 0.72 times (OR: 0.28; 95%CI: 0.12 - 0.66) less likely to have changes in muscle strength than those who were not gainfully employed. After adjusting for all other variables, the female sex (OR: 5.09; 95%CI: 1.63 - 15.84), sarcopenia (OR: 2.93; 95%CI: 1.07 - 8.03), and intubation (OR: 34.97; 95%CI: 2.47 - 495.75) remained significantly associated with changes in muscle strength. In this adjusted model, smoking was also significantly associated with changes in muscle strength, where former and current smokers were more likely to have muscle weakness compared to those who had never smoked (OR: 3.90; 95%CI: 1.21 - 12.54).

Table 3 - Crude and adjusted analysis in relation to associated factors and the functional status of an individual post-hospitalization due to COVID-19 (n =114)

Characteristics	Crude		Adjusted	
	Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Sex				
Male	1	0.242	1	0.515
Female	1.56 (0.73-3.30)		0.69 (0.23-2.08)	
Age bracket (years)				
<65	1	0.064	1	0.799
≥65	2.03 (0.96-4.30)		1.17 (0.35-3.87)	
Skin color (self-reported)				
White	1	0.354	1	0.314
Black/brown	0.68 (0.30-1.53)		0.56 (0.18-1.74)	
Education level				
Never studied/Primary education	1	**0.017**	1	0.516
Secondary/Higher education	0.40 (0.19-0.85)		0.68 (0.21-2.20)	
Socioeconomic position*				
A-B	1	0.114	1	0.620
C-D-E	1.82 (0.86-3.87)		1.32 (0.44-3.95)	
Active occupational activity				
No	1	**0.019**	1	0.183
Yes	0.37 (0.16-0.85)		0.44 (0.13-1.48)	
Sarcopenia				
No	1	**0.036**	1	0.570
Yes	2.25 (1.05-4.80)		1.33 (0.50-3.56)	
Osteoporosis				
No	1	0.099	1	0.331
Yes	1.89 (0.89-4.04)		1.70 (0.58-5.00)	
Respiratory diseases				
No	1	**0.002**	1	**0.002**
Yes	3.65 (1.63-8.15)		5.67(1.93-16.68)	
Obesity				
No	1	0.055	1	**0.033**
Yes	0.48 (0.22-1.01)		0.33 (0.12-0.91)	
Physical activity				
No	1	0.439	1	0.068
Yes	0.74 (0.35-1.58)		0.36 (0.12-1.08)	
Smoking				
No	1	0.229	1	0.395
Yes/Former smoker	1.60 (0.74-3.44)		0.62 (0.20-5.08)	
COVID-19 frequency				
1	1	0.869	1	0.514
2 or more	0.93 (0.39-2.23)		1.50 (0.43-5.08)	
Admission to intensive care unit				
No	1	0.499	1	0.589
Yes	1.40 (0.53-3.69)		1.50 (0.36-6.48)	

Note: *According to the Brazilian Economic Classification Criteria (ABEP). Bolds value = significant ratio ($p < 0.05$). CI = confidence interval.

Table 3 - Crude and adjusted analysis in relation to associated factors and the functional status of an individual post-hospitalization due to COVID-19 (n =114) (continued)

Characteristics	Crude		Adjusted	
	Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Use of oxygen in hospital admission				
No	1	**0.015**	1	0.073
Yes	3.97 (1.31-12.04)		4.11 (0.88-19.29)	
Intubation in hospital admission				
No	1	0.175	1	0.482
Yes	3.06 (0.61-15.45)		2.27 (0.23-22.41)	
Vaccination prior to hospital admission				
No	1	0.979	1	0.818
Yes	1.01 (0.38-2.67)		0.87 (0.26-2.87)	
Physical therapy after hospital discharge				
No	1	**0.033**	1	0.101
Yes	3.00 (1.09-8.25)		2.8 1(0.82-9.66)	

Note: Bolds value = significant ratio ($p < 0.05$). CI = confidence interval.

Table 4 - Sociodemographic, clinical, and health characteristics of individuals post-hospitalization due to COVID-19, according to changes in muscle strength (n = 114)

Characteristics	Muscle weakness			Changes in muscle strength		
	≤ 48 pts	> 48 pts	p	< 48 pts	> 48 pts	p
Sex						
Male	47 (95.9)	2 (4.1)	0.066**	31 (63.3)	18 (36.7)	**0.009**
Female	55 (84.6)	10 (15.4)		25 (38.5)	40 (61.5)	
Age bracket (years)						
<65	53 (94.6)	3 (5.4)	0.125**	30 (53.6)	26 (46.4)	0.351
≥65	49 (84.5)	9 (15.5)		26 (44.8)	32 (55.2)	
Skin color (self-reported)						
White	71 (87.7)	10 (12.3)	0.504	38 (46.9)	43 (53.1)	0.460
Black/brown	31 (93.9)	2 (6.1)		18 (54.5)	15 (45.5)	
Education level						
Never studied/Primary education	52 (88.1)	7 (11.9)	0.630	25 (42.4)	34 (57.6)	0.135
Secondary/Higher education	50 (90.9)	5 (9.1)		31 (56.4)	24 (43.6)	
Socioeconomic position*						
A-B	45 (88.2)	6 (11.8)	0.698	28 (54.9)	23 (45.1)	0.267
C-D-E	57 (90.5)	6 (9.5)		28 (44.4)	35 (55.6)	
Active occupational activity						
No	69 (86.3)	11 (13.8)	0.105**	32 (40.0)	48 (60.0)	**0.003**
Yes	33 (97.1)	1 (2.9)		24 (70.6)	10 (29.4)	

Note: Data presented as n (%). *According to the Brazilian Economic Classification Criteria (ABEP). **Fisher's exact test. Bolds value = significant ratio ($p < 0.05$). pts = points.

Table 4 - Sociodemographic, clinical, and health characteristics of individuals post-hospitalization due to COVID-19, according to changes in muscle strength (n = 114) (continued)

Characteristics	Muscle weakness			Changes in muscle strength		
	< 48 pts	> 48 pts	p	< 48 pts	> 48 pts	p
Sarcopenia						
No	42 (87.5)	6 (12.5)	0.558	31 (64.6)	17 (35.4)	**0.005**
Yes	60 (90.9)	6 (9.1)		25 (37.9)	41 (62.1)	
Osteoporosis						
No	56 (87.5)	8 (12.5)	0.546**	34 (53.1)	30 (46.9)	0.334
Yes	46 (92.0)	4 (8.0)		22 (44.0)	28 (56.0)	
Respiratory diseases						
No	59 (89.4)	7 (10.6)	0.974	35 (53.0)	31 (47.0)	0.328
Yes	43 (89.6)	5 (10.4)		21 (43.8)	27 (56.3)	
Obesity						
No	57 (87.7)	8 (12.3)	0.551**	33 (50.8)	32 (49.2)	0.685
Yes	45 (91.8)	4 (8.2)		23 (46.9)	26 (53.1)	
Physical activity						
No	41 (87.2)	6 (12.8)	0.514	23 (48.9)	24 (51.1)	0.973
Yes	61 (91.0)	6 (9.0)		33 (49.3)	34 (50.7)	
Smoking						
No	61 (88.4)	8 (11.6)	0.761**	38 (55.1)	31 (44.9)	0.116
Yes/Former smoker	41 (91.1)	4 (8.9)		18 (40.0)	27 (60.0)	
COVID-19 frequency						
1	76 (86.4)	12 (13.6)	0.065**	45 (51.1)	43 (48.9)	0.429
2 or more	26 (100)	0 (0.0)		11 (42.3)	15 (57.7)	
Admission to intensive care unit						
No	84 (90.3)	9 (9.7)	0.461**	48 (51.6)	45 (48.4)	0.263
Yes	18 (85.7)	3 (14.3)		8 (38.1)	13 (61.9)	
Use of oxygen in hospital admission						
No	16 (88.9)	2 (11.1)	1.000**	12 (66.7)	6 (33.3)	0.105
Yes	86 (89.6)	10 (10.4)		44 (45.8)	52 (54.2)	
Intubation in hospital admission						
No	96 (91.4)	9 (8.6)	0.053**	55 (52.4)	50 (47.6)	**0.032****
Yes	6 (66.7)	3 (33.3)		1 (11.1)	8 (88.9)	
Vaccination prior to hospital admission						
No	19 (95.0)	1 (5.0)	0.689**	13 (65.0)	7 (35.0)	0.118
Yes	83 (88.3)	11 (11.7)		43 (45.7)	51 (54.3)	
Physical therapy after hospital discharge						
No	82 (91.1)	8 (8.9)	0.275**	48 (53.3)	42 (46.7)	0.082
Yes	20 (83.3)	4 (16.7)		8 (33.3)	16 (66.7)	

Note: Data presented as n (%). **Fisher's exact test. Bolds value = significant ratio ($p < 0.05$). pts = points.

Table 5 - Crude and adjusted analysis in relation to sociodemographic, clinical, and health characteristics associated with changes in muscle strength (MRC < 60 points) of individuals post-hospitalization due to COVID-19 (n = 114)

Characteristics	Crude		Adjusted	
	Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Sex				
Male	1	**0.010**	1	**0.005**
Female	2.76 (1.28-5.92)		5.09 (1.63-15.84)	
Age bracket (years)				
< 65	1	0.351	1	0.859
≥ 65	1.42 (0.68-2.97)		0.90 (0.28-2.91)	
Skin color (self-reported)				
White	1	0.460	1	0.809
Black/brown	0.73 (0.32-1.65)		1.15 (0.37-3.56)	
Education level				
Never studied/Primary education	1	0.137	1	0.570
Secondary/Higher education	0.57 (0.27-1.20)		0.71 (0.22-2.32)	
Socioeconomic position*				
A-B	1	0.268	1	0.567
C-D-E	1.52 (0.72-3.20)		0.72 (0.23-2.21)	
Active occupational activity				
No	1	**0.004**	1	0.102
Yes	0.28 (0.12-0.66)		0.36 (0.11-1.22)	
Sarcopenia				
No	1	**0.005**	1	**0.036**
Yes	2.99 (1.38-6.48)		2.93 (1.07-8.03)	
Osteoporosis				
No	1	0.334	1	0.444
Yes	1.44 (0.69-3.03)		0.66 (0.23-1.90)	
Respiratory diseases				
No	1	0.329	1	0.782
Yes	1.45 (0.69-3.07)		0.86 (0.31-2.41)	
Obesity				
No	1	0.686	1	0.116
Yes	1.1 7(0.55-2.45)		2.27 (0.82-6.35)	
Physical activity				
No	1	0.973	1	0.660
Yes	0.99 (0.47-20.8)		1.26 (0.44-3.60)	
Smoking				
No	1	0.117	1	**0.022**
Yes/Former smoker	1.83 (0.85-3.94)		3.90 (1.21-12.54)	
COVID-19 frequency				
1	1	0.430	1	0.940
2 or more	1.42 (0.59-3.45)		1.05 (0.31-3.53)	
Admission to intensive care unit				
No	1	0.266	1	0.409
Yes	1.73 (0.65-4.57)		0.55 (0.13-2.26)	

Note: *According to the Brazilian Economic Classification Criteria (ABEP). Bolds value = significant ratio (p < 0.05). CI = confidence interval.

Table 5 - Crude and adjusted analysis in relation to sociodemographic, clinical, and health characteristics associated with changes in muscle strength (MRC < 60 points) of individuals post-hospitalization due to COVID-19 (n = 114) (continued)

Characteristics	Crude		Adjusted	
	Odds ratio (95%CI)	p	Odds ratio (95%CI)	p
Use of oxygen in hospital admission				
No	1	0.111	1	0.637
Yes	2.36 (0.82-6.81)		1.38 (0.36-5.26)	
Intubation in hospital admission				
No	1	**0.044**	1	**0.009**
Yes	8.80 (1.06-72.86)		34.97 (2.47-495.75)	
Vaccination prior to hospital admission				
No	1	0.123	1	0.405
Yes	2.20 (0.87-6.01)		1.73 (0.48-6.27)	
Physical therapy after hospital discharge				
No	1	0.086	1	0.353
Yes	2.27 (0.88-5.88)		1.75 (0.54-5.73)	

Note: Bolds value = significant ratio ($p < 0.05$). CI = confidence interval.

Discussion

This study showed that, within 12 months of hospital discharge, individuals hospitalized due to COVID-19 had significant functional limitations and considerable signs of changes in muscle strength and muscle weakness. Important sociodemographic, clinical, and health characteristics were related to the analyzed outcomes.

The prevalence of functional limitation was 67.5% (95%CI: 46.2 - 70.2). A systematic review conducted by Almeida et al.[8] involving 35 studies showed similar results to our study by indicating a reduction in physical function and the ability to perform activities of daily living after a SARS-CoV-2 infection. A longitudinal study that assessed more than a thousand survivors also found that more than half remained with functional limitations 24 months after hospital discharge.[4] A similar result was found in a Danish study which observed functional status limitations in 49% of the sample eight months after hospital discharge.[9] When assessing functional limitations nine months after hospital discharge, a study showed that 94% of individuals had slight and moderate functional limitations, and the authors further reported that 56% of the sample were on medical leave away from their work activities after COVID-19.[10]

When assessing the associated factors, our findings showed that participants diagnosed with obesity were the ones with better functional capacity, a result opposite to that found in the literature, which noted a relationship between worse functional levels and obesity.[4,8,11,16] Potential mechanisms to explain our discovery may be related to what the literature presents as the paradox of obesity and chronic diseases. Obese patients with those conditions have better medium and long-term prognoses than thinner patients. It is worth noting that those conditions are often associated with a state of cachexia and frailty, as observed in post-COVID-19 syndrome, therefore, having greater weight and more body mass could be protective or a marker associated with maintaining vigor.[17]

Another association highlighted in our study was related to a greater probability of moderate and severe levels of functional limitation in individuals diagnosed with respiratory diseases. In this same direction, Genecand et al.[18] assessed patients with COVID-19 diagnosed with respiratory changes and showed that this population lives with a high burden of symptoms, and that 97% of the sample had some type of functional change after seven months of acute infection, with functional impact being considered high in 73% of participants.

Our data also showed that over 50% of participants showed decreased muscle strength after COVID-19, with 10% remaining with muscle weakness. The presence of decreased muscle strength was associated with the female sex, sarcopenia diagnosis, and smoking habit. Having required orotracheal intubation during hospitalization due to COVID-19 was also associated with lower muscle strength. Our results are in line with the research carried out in the largest health center in Brazil that evaluated the muscular strength of the upper limbs and found values below normal in more than half of the sample.[11]

A population-based study that assessed more than two thousand people, up to eighteen months post-infection, also observed lower muscle strength in the upper limbs and physical deconditioning.[12] The literature suggests that the musculoskeletal symptoms caused by the virus are linked to mitochondrial dysfunction, oxidative stress, and reduced antioxidants. Mitochondria play an important role in muscle sequelae, as mitochondrial bioenergetic dysfunction can lead to anaerobic glycolysis to offset dysfunctional oxidative phophorylation, leading to an increase in glycolysis that can cause cell damage, changes in lactate levels, and other metabolic pathways leading to muscle weakness and fatigue.[19,20] Sex differences can be explained by variations in the immune response. In women, the innate and adaptive immune response is rapid and aggressive to combat invading pathogens, while men have an attenuated immune response and are more susceptible to viral infections. Hormonal differences and the expression and regulation of ACE 2 must also be considered.[21-26] The fact that women suffer more from prolonged symptoms is explored by Ganesh et al.[25] in their study that showed elevated levels of interleukin 6 in survivors with post-COVID-19 syndrome. In the study, high levels of the cytokine were associated with the female sex, suggesting that it is one of the explanations for the sex difference in the chronic phase of the disease. Interleukin 6 is elevated in other autoimmune syndromes, which occur more in women, such as fibromyalgia and chronic fatigue syndrome, indicating the presence of a common pathway between those conditions and encouraging this assumption.[25]

Our results confirmed that those who did not require orotracheal intubation at the time of hospitalization are less likely to have changes in muscle strength post-COVID-19.

The literature indicates that patients admitted to the ICU and who required mechanical ventilation, i.e., those with the most severe form of the disease, are those who suffer most from sequelae.[6,7,27,28] ICU-acquired weakness is a common, incident, and known issue in intensive care, with its prevalence being higher in patients who have been mechanically ventilated.[29]

A systematic review conducted by Domingo et al.[30] points out that it will be hard to identify whether the functional impairments found in post-COVID-19 syndrome are directly caused by the infection, whether they are consequences of hospitalization for severe illness, or even an exacerbation of a pre-existing condition. It is hypothesized that the infection may act as an immune trigger, and the persistent symptoms may be an immune response.[31,32] Explanations for functional impairment further include persistent symptoms themselves such as dyspnea, fatigue syndrome, cardiorespiratory changes, and muscle weakness.[7,31,33]

To our knowledge, this is one of the first population-representative studies to assess the consequences of COVID-19 in those individuals affected by the most severe forms of the disease, in a region in southern Brazil. However, some limitations must be mentioned. The assessment of functional capacity and muscle strength was carried out using subjective and/or self-reported methods, therefore, it is recommended that future research use objective methods ensuring detailed and accurate information. Furthermore, it is assumed that, for some of the relationships investigated between functional status and muscle strength outcomes and sociodemographic, clinical, and health characteristics, there may have been a lack of statistical power.

Conclusion

In summary, a significant ratio of individuals with functional limitations and changes in muscle strength was observed after COVID-19. The prevalence of functional limitation was higher in people with a low education level, who did not perform active occupational activities, with a diagnosis of sarcopenia and respiratory diseases, who required oxygen therapy during hospitalization and physiotherapy after discharge. Also, people diagnosed with respiratory diseases were more likely to have functional limitations post-COVID-19.

The prevalence of changes in muscle strength was more observed in women, in those who did not perform active occupational activities, with a diagnosis of sarcopenia and who required orotracheal intubation. The probability of presenting changes in peripheral muscle strength was higher in women, smokers, individuals with a diagnosis of sarcopenia and those who required orotracheal intubation were more likely to present changes in muscle strength. No association was found between muscle weakness and the other variables analyzed.

Population-wide studies, in low- and middle-income countries such as Brazil, are necessary to assess and monitor the consequences of COVID-19. In addition to estimating the magnitude of sequelae, these studies are able to identify the risk groups most vulnerable to the disease's sequelae.

Authors' contributions

TSP drafted the manuscript. SGS, GOA, JP lead the conception and design of the study. SGS led the analysis and collaborated with the critical revision of the manuscript. BZP, DCBB, RSS, ILL, GOA, JP read, revised, and approved the final version of the manuscript.

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