

Long-term respiratory outcomes after COVID-19: a Brazilian cohort study

Nina Rocha Godinho dos Reis Visconti,¹ Michelle Cailleaux-Cezar,¹ Domenico Capone,¹ Maria Izabel Veiga dos Santos,¹ Nadja Polisseni Graça,¹ Luiz Paulo Pinheiro Loivos,¹ Alexandre Pinto Cardoso,¹ and Fernanda Carvalho de Queiroz Mello¹

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ABSTRACT

Objective. To investigate the prevalence and risk factors for persistent symptoms up to 12 months after hospital discharge in COVID-19 survivors.

Methods. This prospective cohort study included patients with COVID-19 discharged from a university hospital in Brazil. Follow-up was performed 2, 6, and 12 months after discharge. Lung function tests and chest computed tomography (CT) were performed 2 months after discharge and were repeated if abnormal. The primary outcomes were the symptoms present, work status, and limitations in daily activities.

Results. Eighty-eight patients were included. Dyspnea (54.5%), fatigue (50.0%), myalgia, and muscle weakness (46.6%) were the most common symptoms, which decreased over time. Anxiety was frequent (46.6%) and remained unchanged. One year after discharge, 43.2% of the patients reported limitations in daily activities, and 17.6% had not returned to work. Corticosteroid use was significantly associated with dyspnea and limitations in daily activities. Females had an increased risk of fatigue at the 12-month assessment, with marginal significance after multivariable adjustment. Young age and bronchial wall thickening on admission CT were also risk factors for dyspnea at follow-up. The most common lung function abnormalities were reduced diffusion capacity and small airway disease, which partially improved over time.

Conclusions. One year after hospital discharge, more than one-third of patients still had persistent COVID-19-related symptoms, remarkable dyspnea, fatigue, and limitations in daily activities, regardless of acute disease severity. Age, female sex, corticosteroid use during hospitalization, and bronchial thickening on admission CT were associated with an increased risk of sequelae.

Keywords

COVID-19; follow-up studies; respiratory function tests; Brazil.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for the coronavirus disease 2019 (COVID-19) pandemic, continues to pose a global threat and has caused an enormous disease burden since its emergence (1). As of March 2022, there have been more than 440 million cases and 5.9 million deaths from COVID-19 worldwide (2). Brazil has been particularly affected, with more than 28.5 million notified cases and 650 000 deaths from COVID-19 (3).

The clinical characteristics, pathogenesis, and complications of the acute phase of COVID-19 have been extensively studied (4). However, the long-term consequences of the infection remain under investigation and have become an increasing concern.

Previous studies have shown the persistence of symptoms, tomographic abnormalities, and pulmonary function impairment in SARS and Middle East respiratory syndrome survivors

¹ Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil ✉ Nina Visconti, ninavisconti@gmail.com

many years after disease onset (5). Initial evidence suggests similar long-term consequences for COVID-19. Reports describe a high prevalence of symptoms such as dyspnea, fatigue, and psychological distress up to 12 months after discharge (6–11). The term post-acute COVID-19 syndrome was proposed to define symptoms and complications that are present beyond 12 weeks of disease onset (12).

Although SARS-CoV-2 infection affects almost all systems, the lungs are the main organs affected, and injury may occur through inflammatory mechanisms and through a direct action of the virus, leading to diffuse alveolar damage and pulmonary vascular thrombosis (12). Recent studies have reported pulmonary function abnormalities following COVID-19, particularly a reduction in diffusion capacity, which can be observed for up to 12 months after infection (9, 10, 13). Persistence of tomographic abnormalities is also commonly reported, consisting of fibrous stripes, ground-glass opacities, reticular lesions, and parenchymal bands (10, 14, 15).

The full range of long-term consequences of COVID-19 and its impact on individual, public health, and economic aspects in Brazil remain to be established.

This study aimed to investigate the prevalence and risk factors for persistent symptoms up to 12 months after hospital discharge in COVID-19 survivors from a Brazilian cohort.

MATERIAL AND METHODS

Study design

This prospective cohort study was conducted at the Instituto de Doenças do Tórax of the Universidade Federal do Rio de Janeiro (UFRJ), located at Hospital Universitário Clementino Fraga Filho (HUCFF), in Rio de Janeiro, Brazil. HUCFF is a university tertiary public hospital that is a reference center for COVID-19 treatment.

Patients admitted from March 2020 to January 2021 with laboratory-confirmed COVID-19 and discharged before February 2021 were eligible for follow-up at the post-COVID-19 outpatient clinic. Follow-up appointments two months after hospital discharge were offered over the telephone. For patients that attended the first visit, follow-up appointments were scheduled six and 12 months after discharge.

Procedures

Baseline information and clinical data of the acute phase of COVID-19 were obtained through a review of medical records. Patients were stratified into groups according to acute disease severity based on the World Health Organization classification (16). Chest computed tomography (CT) performed during hospitalization was reviewed, and the extent of parenchymal involvement was classified as <25%, 25%–50%, 50%–75%, and >75%.

During follow-up, a systematic assessment of symptoms was performed, including the modified Medical Research Council (mMRC) score (17). Symptoms were recorded as present if they appeared after COVID-19 or worsened due to the infection. Complete lung function tests (LFT) and chest CT were performed 2 months after discharge and were repeated at the 6- and 12-month follow-up consultations if there were persistent abnormalities or new-onset symptoms.

Chest high-resolution CT was performed in the supine position during end-inspiration, with image reconstruction in a 1 mm slice thickness. The images taken during the hospital stay and follow-up were cross-compared and evaluated for the resolution of parenchymal abnormalities.

LFTs were done using the Master Screen Body and impulse oscillometry (IOS) (Vyair Medical GmbH, Hoechberg, Germany) according to the American Thoracic Society and European Respiratory Society guidelines (18–22). The obstructive pattern was defined as a reduction of the forced expiratory volume in the first second (FEV1) to the forced vital capacity (FVC) ratio (FEV1/FVC under the lower limit) (23). A restrictive pattern was defined as a reduction in the total lung capacity (TLC) (TLC under the lower limit) (24). Diffusing lung capacity for carbon monoxide (DLCO) was corrected for hemoglobin and was defined as reduced when inferior to the lower limit (25). Small airway disease was defined by IOS when reactance at 5 Hz (X5) predicted - X5 ≥ 0.15 kPa.s.L⁻¹ or the Delta of resistance at 5–20 Hz ($\Delta R5\text{--}20\%$) > 35% (26).

Statistical analysis

Characteristics are presented as medians with interquartile range (IQR) for continuous variables and absolute values and percentages for categorical variables. As appropriate, categorical variables were compared using the chi-squared or Fisher's exact test, and continuous variables were compared using the Kruskal–Wallis or Mann–Whitney U test.

The primary outcomes investigated were the symptoms present, mMRC score, work status, and limitations in daily activities in COVID-19 survivors at 2, 6, and 12 months after hospital discharge. Risk factors were explored for the most common symptoms and limitations in daily activities using a univariate analysis by estimating the risk ratios. Multivariable adjusted logistic regression models were used to estimate the odds ratios and 95% confidence intervals (CI). All tests were two-sided, and statistical significance was set at $p < 0.05$.

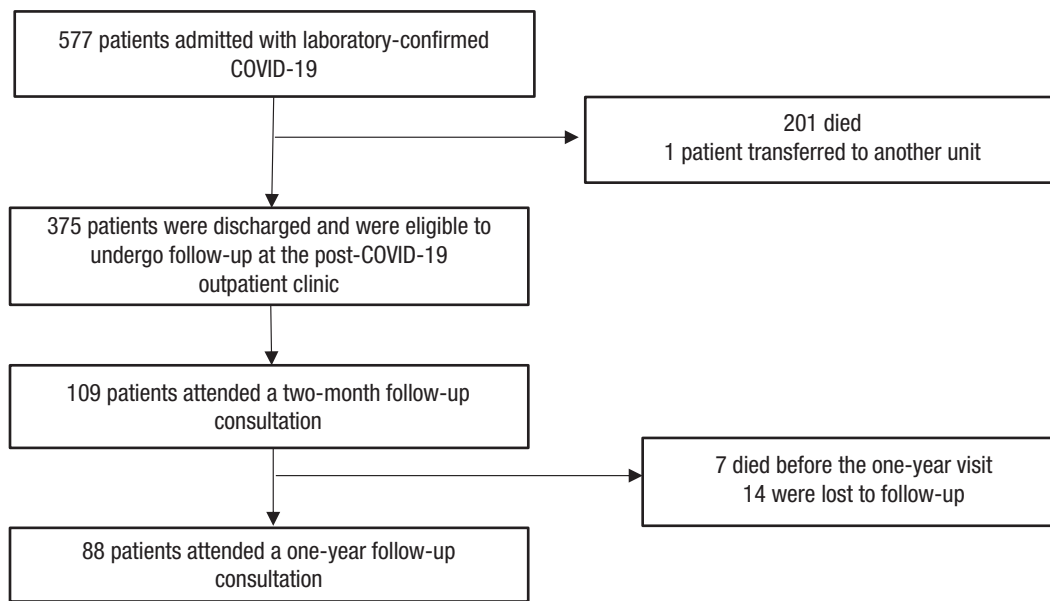
The secondary outcomes were lung function, and tomographic abnormalities present two months after discharge, and their temporal behavior. Functional characteristics were also described in patients who presented with persistent symptoms at the 12-month follow-up.

Written informed consent was obtained from all study participants. Measures were taken to guarantee the anonymity of the data. This study was approved by the Research Ethics Commission of the UFRJ (CAAE: 35177220.2.0000.5257).

RESULTS

A total of 577 patients were admitted to the university hospital with laboratory-confirmed COVID-19 from 11 March 2020 to 26 January 2021, of whom 375 were discharged and 201 died. One hundred and nine patients attended a two-month visit at the post-COVID-19 outpatient clinic, and 88 patients were included in the study having completed the one-year follow-up. Seven patients died before the 12-month follow-up visit, and 14 were lost to follow-up (Figure 1).

The demographic and clinical characteristics of the participants are presented in Table 1. The median age was 60.5 (53–69) years, and 46 (52.3%) were female. Comorbidities were present in 82 (93.2%) patients, including hypertension (73.9%), diabetes

FIGURE 1. Flow chart of patients with confirmed COVID-19 admitted and discharged from Hospital Universitário Clementino Fraga Filho between March 2020 and January 2021.

Source: Prepared by the authors using the study results.

mellitus (31.8%), and obesity (20.5%). Pulmonary diseases at baseline were uncommon: five patients were asthmatic, five had chronic obstructive pulmonary disease, and two had interstitial lung disease. Forty-six (52.3%) patients were current or former smokers.

Considering acute disease severity, 1 (1.1%), 21 (23.9%), 51 (58%), and 15 (17%) patients had mild, moderate, severe, and critical disease, respectively (Table 1).

The median length of the hospital stay was nine days. Seventy-five percent of the patients required supplemental oxygen, 17% required mechanical ventilation, and 27.3% were admitted to the intensive care unit. Antibiotics and corticosteroids were prescribed to 89.8% and 39.8% of patients, respectively. Oseltamivir was used in 48.9% of the patients, and no other antiviral or antibody treatments were used. Most patients (60.2%) received a prophylactic dose of anticoagulants. Seventy-eight baseline CT examinations were available for analysis, and the extent of parenchymal involvement is summarized in Table 1.

Demographic and baseline clinical characteristics of 206 patients admitted to HUCFF with confirmed COVID-19 in 2020 who were discharged but were not included in this study (could not be contacted or did not attend follow-up visits) were compared to the included population. The use of supplemental oxygen and invasive mechanical ventilation was significantly more frequent in the enrolled population (information available from the authors upon request).

The median time from discharge to the follow-up consultations was 72, 199, and 369 days for the 2, 6, and 12-month assessments, respectively (Table 2).

Dyspnea (54.5%) and fatigue (50%) were the most common symptoms at the first visit and decreased in frequency over time. The number of patients with an mMRC score of 0 increased, and the number of patients with an mMRC score of 2 decreased by the 12-month evaluation (Figure 2). Myalgia

and muscle weakness were present in 46.6% of the patients at the two-month assessment and further decreased to 35.2% and 28.4%, respectively, during the 12 months follow-up. However, anxiety and headache frequency did not change over time, and cough frequency increased to 35.2% at the 12-month follow-up.

On the impact of symptoms on daily life, during the first assessment, 69.3% of the patients reported at least some limitation in the performance of their daily activities. One year after being diagnosed with COVID-19, 43.2% of patients still had persistent limitation of their daily activities. For patients who worked before being infected with COVID-19, 65.7% and 82.4% returned to work two months and 12 months after discharge, respectively.

In relation to clinical complications after discharge, one patient presented with deep venous thrombosis, one had pulmonary embolism, one had ischemic stroke, and two had acute coronary syndrome. Seven patients died before completing the 12-month follow-up visit and were not included in this cohort: one from acute coronary syndrome, one from pulmonary sepsis, one from pulmonary embolism, one from gastrointestinal bleeding due to colon carcinoma, two suddenly died at home, and one had no defined cause.

LFT were performed in 73 patients two months after discharge. The most common findings were reduced diffusing lung capacity, observed in 22 (34.9%) patients, and small airway disease, observed in 20 (30.3%) patients. Restrictive and obstructive pattern were observed in seven (10.8%) and 10 (14.5%) patients, respectively (Table 3).

Of the 22 patients with reduced DLCO, 17 repeated the test: 12 at the six-month assessment and 11 at the 12-month assessment (because the six-month examination was abnormal or missing). At the end of the follow-up, 12 patients had normalized DLCO and five had reduced DLCO. Of the 20 patients with small airway disease at the two-month evaluation, 13 repeated

TABLE 1. Demographic and baseline clinical characteristics of patients with confirmed COVID-19 discharged from Hospital Universitário Clementino Fraga Filho

Characteristics	Total (n = 88)
Age, years	60.5 (53–69)
Median (IQR)	
Sex, n (%)	
Female	46 (52.3%)
Male	42 (47.7%)
Smoking history, n (%)	
Never smoked	42 (47.7%)
Current or former smoker	46 (52.3%)
Comorbidities, n (%)	82 (93.2%)
Hypertension	65 (73.9%)
Diabetes	28 (31.8%)
Obesity	18 (20.5%)
Cancer	12 (13.6%)
Coronary artery disease	10 (11.4%)
Arrhythmia	9 (10.2%)
Chronic kidney disease	8 (9.1%)
Autoimmune disease	7 (8.0%)
Asthma	5 (5.7%)
COPD	5 (5.7%)
Interstitial lung disease	2 (2.3%)
Characteristics during hospitalization for acute COVID-19	
Length of hospitalization, days	9 (6–15)
Median (IQR)	
Acute disease severity, n (%)	
Mild	1 (1.1%)
Moderate	21 (23.9%)
Severe	51 (58.0%)
Critical disease	15 (17.0%)
Treatment received, n (%)	
Admission to the ICU	24 (27.3%)
Use of supplemental oxygen	66 (75.0%)
Invasive mechanical ventilation	15 (17.0%)
Antibiotics	79 (89.8%)
Oseltamivir	43 (48.9%)
Corticosteroids	35 (39.8%)
Anticoagulation, prophylactic dose	53 (60.2%)
Anticoagulation, intermediate dose	17 (19.3%)
Anticoagulation, therapeutic dose	14 (15.9%)
Extension of tomographic involvement on baseline CT, n/N (%)^a	
<25%	24/78 (30.8%)
25%–50%	33/78 (42.3%)
50%–75%	15/78 (19.2%)
>75%	6/78 (7.7%)

Notes: IQR, interquartile range; COPD, chronic obstructive pulmonary disease; CT, computed tomography; ICU, intensive care unit.
^aN refers to the total number of patients evaluated, and n refers to the number of patients with abnormal results.
Source: Prepared by the authors using the study results.

the exam: 12 at the six-month assessment and 7 at the 12-month assessment (because the six-month exam was abnormal or missing). At the end of the follow-up, eight had normalized and five persisted with small airway disease. Five patients with restrictive pattern repeated the test during follow-up, and four

TABLE 2. Symptoms and limitations present during the follow-up of COVID-19 survivors 2, 6, and 12 months after hospital discharge from Hospital Universitário Clementino Fraga Filho

Variable	2-month assessment n = 88	6-month assessment n = 77	12-month assessment n = 88
Time from discharge to visit, days	72 (59–88)	199 (187–213)	369 (354–390)
Median (IQR)			
Symptoms, n (%)			
Dyspnea	48 (54.5%)	39 (44.3%)	29 (33.0%)
Fatigue	44 (50.0%)	34 (44.2%)	28 (31.8%)
Myalgia	41 (46.6%)	28 (36.4%)	31 (35.2%)
Muscle weakness	41 (46.6%)	28 (36.4%)	25 (28.4%)
Arthralgia	41 (46.6%)	34 (44.2%)	41 (46.6%)
Anxiety	41 (46.6%)	42 (55.3%)	42 (47.7%)
Chest pain	28 (31.8%)	22 (28.6%)	22 (25.0%)
Headache	27 (30.7%)	23 (29.9%)	27 (30.7%)
Cough	22 (25.0%)	23 (29.9%)	31 (35.2%)
Limitations in daily activities, n (%)			
No limitation	27 (30.7%)	38 (50.0%)	50 (56.8%)
Limitation	61 (69.3%)	38 (50.0%)	38 (43.2%)
Returned to work, n (%)^a			
Yes	23 (65.7%)	19 (73.1%)	28 (82.4%)
No	12 (34.3%)	7 (26.9%)	6 (17.6%)

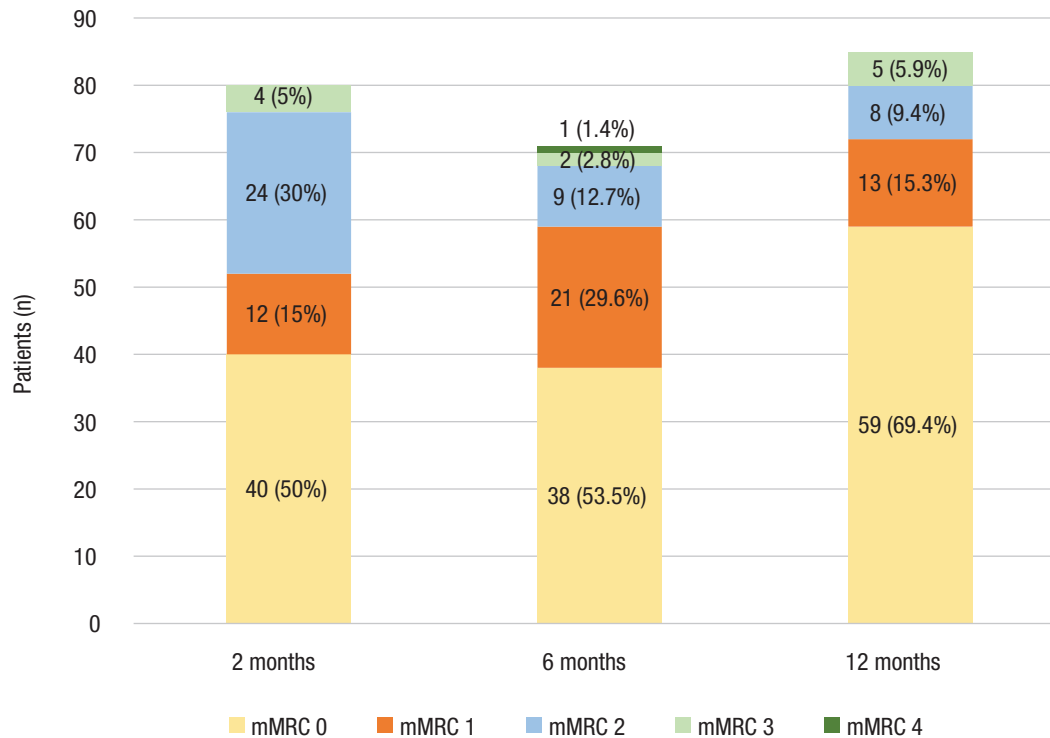
Notes: mMRC, modified Medical Research Council score.
^aData are related to patients that worked before COVID-19.
Source: Prepared by the authors using the study results.

had normalized lung volumes. Of the 10 patients with obstruction, only 4 had new spirometry during follow-up, and 2 had normalized.

CT was performed in 77 patients two months after discharge, and 73 patients underwent baseline CT for comparison (Table 3). At this time, only 26% of the patients had complete resolution of CT abnormalities. The most common findings were architectural distortions (61%), ground-glass opacities (54.5%), peripheral reticulation (48.1%), traction bronchiectasis (42.9%), and parenchymal bands (41.6%). Only 26 patients underwent CT at the six-month follow-up and 20 at the 12-month follow-up, impairing the temporal analysis.

Univariate analysis was performed to identify the risk factors for the most frequent symptoms and limitations at the 12-month assessment (Table 4). Obesity (RR 2.04; 95% CI [1.16, 3.60]), corticosteroid use during hospitalization (RR 1.86; 95% CI [1.03, 3.38]), dyspnea at admission (RR 2.61; 95% CI [1.11, 6.17]), and bronchial wall thickening on baseline CT (RR 2.62; 95% CI [1.02, 6.71]) were risk factors for dyspnea at 12 months. Young age was also significantly associated with dyspnea ($p = 0.046$). Female sex (RR 2.28; 95% CI [1.13, 4.63]) and ageusia at admission (RR 2.12; 95% CI [1.19, 3.77]) were associated with fatigue at 12 months. The use of corticosteroids (RR 1.87; 95% CI [1.16, 3.01]) was significantly associated with limitations in daily activities.

After multivariable adjustment, age (OR 0.92; 95% CI [0.86, 0.99]), use of corticosteroids (OR 6.61; 95% CI [1.34, 32.68]), and bronchial thickening on baseline CT (OR 7.57; 95% CI [1.46, 39.26]) remained significant factors for dyspnea 12 months

FIGURE 2. mMRC dyspnea score 2, 6, and 12 months after COVID-19*

Notes: mMRC: modified Medical Research Council.

*Data were missing for 8 patients at the two-month assessment, 17 patients at the six-month assessment (11 patients did not attend the follow-up visit), and 3 patients at the 12-month assessment.

Source: Prepared by the authors using the study results.

after discharge. Female sex (OR 2.44; 95% CI [0.86, 6.91]) had marginal significance as a risk factor for fatigue. The use of corticosteroids (OR 4.39; 95% CI [1.42, 13.64]) remained associated with limitations in daily activities.

Of the 29 patients with persistent dyspnea at the 12-month evaluation, 16 had LFT at the same time point. None had restriction, three (18.8%) had obstruction, two (12.5%) had reduced DLCO, and eight (50%) had small airway disease. Nineteen patients (65.5%) reported limitations in their daily activities. Two of the six patients with reduced DLCO at 12 months had dyspnea and limitations in daily activities. Eight of the 12 patients with small airway disease at 12 months had dyspnea, and 6 had limitations in daily activities.

DISCUSSION

A prospective study with follow-up assessments at 2, 6, and 12 months after hospital discharge for COVID-19 in a Brazilian cohort was conducted. To the best of our knowledge, this is the most extended follow-up study of COVID-19 survivors in Brazil with clinical and complete lung function evaluations. The pandemic has particularly affected Brazil with an enormous disease burden. The long-term consequences of COVID-19 are an important concern, as they may have a huge impact on public health and the economy in the coming years.

A high prevalence of symptom persistence was found one year after discharge. At the 12-month assessment, 33.0% of the patients still presented with dyspnea, 31.8% fatigue, 35.2% myalgia, and 28.4% muscle weakness. This finding is consistent

with previous publications that reported respiratory symptoms in 10%–58% and fatigue and muscle weakness in 32%–61% of patients after one year (10, 27–30).

Similar to recently published data, some symptoms, such as fatigue and muscle weakness, decrease over time, while anxiety symptoms persist (10). In our cohort, dyspnea improved over time, as shown by other authors (31). In contrast, some studies have reported an increase in the frequency of dyspnea during follow-up (10, 11). Patients followed up at our outpatient clinic received psychological and physiotherapy support, which could explain the better outcomes in our cohort. This emphasizes the importance of integrated care using a multidisciplinary approach for COVID-19 survivors.

Limitations in daily activities decreased during follow-up, but at the 12-month assessment, 43.2% of the patients still reported some limitations. A group that studied health-related quality of life using a 15-dimension instrument observed an increase in quality of life over time, especially due to an increase in the physical dimensions, with mental dimensions substantially unchanged (28). Other authors showed that COVID-19 patients had lower self-assessment scores for quality of life than the control group (10). In our study, 82.4% of patients had returned to work after one year, similar to the 88% previously reported (10). These data reinforce the need to develop strategies to address post-COVID-19 syndrome and mitigate its impact on health status and socioeconomic aspects.

Dyspnea was more frequently observed in younger patients, as previously reported (11). However, the reason for this finding remains unclear. One possible explanation is the greater

TABLE 3. Lung function and tomographic abnormalities present in COVID-19 survivors two months after hospital discharge from Hospital Universitário Clementino Fraga Filho

Variable	Two-month assessment <i>n/N (%)^a</i>
Lung function tests	
Total of patients	73
Time from discharge to LFT, days	75 (62–91)
Median (IQR)	
Lung function abnormalities, <i>n/N (%)</i>	
Obstructive pattern	10/69 (14.5%)
Restrictive pattern	7/65 (10.8%)
Reduced DLCO	22/63 (34.9%)
Small airway disease (IOS)	20/66 (30.3%)
Chest CT	
Total of patients	77
Time from discharge to CT, days	75 (60.5–92.5)
Median (IQR)	
Tomographic evolution, <i>n/N (%)</i>	
Complete resolution	19/73 (26.0%)
Partial resolution	54/73 (74.0%)
Unchanged	0/73 (0%)
Progression	0/73 (0%)
Tomographic abnormalities, <i>n/N (%)</i>	
Architectural distortion	47/77 (61.0%)
Ground-glass opacities	42/77 (54.5%)
Peripheral reticulation	37/77 (48.1%)
Traction bronchiectasis	33/77 (42.9%)
Parenchymal bands	32/77 (41.6%)
Septal thickening	31/77 (40.3%)
Emphysema	21/77 (27.3%)
Bronchial wall thickening	14/77 (18.2%)
Consolidation	6/77 (7.8%)
Crazy-paving	3/77 (3.9%)
Honeycombing	1/77 (1.3%)

Notes: LFT, lung function test; IQR, interquartile range; CT, computed tomography; DLCO, diffusing lung capacity for carbon monoxide; IOS, impulse oscillometry.

^a *N* refers to the total number of patients evaluated, and *n* refers to the number of patients with abnormal results.

Source: Prepared by the authors from the study results.

value placed on symptoms by totally active young patients. Obese patients also had a greater risk of dyspnea, although this was not significant after adjustment, as has been shown previously (32).

Corticosteroid use was considered a risk factor for persistent dyspnea and limitation in daily activities. A follow-up study also demonstrated that corticosteroid use was associated with an increased risk of post-sequelae and emerging sequelae, even after stratified analysis ($p < 0.001$) (27). Huang et al. (10) also demonstrated an increased risk of fatigue or muscle weakness with corticosteroid therapy. Therefore, this association may reflect the myopathic effects of corticosteroids, which may contribute to exercise limitations. This aspect deserves further study, as steroids are considered the standard treatment for COVID-19 patients with hypoxemia, and benefits versus long-term risks must be weighed.

Female sex is a risk factor for fatigue, which has been consistently reported in the literature (6, 10, 11, 29). In our cohort, the severity of the acute disease was not associated with the

presence of symptoms or limitations in daily activities during follow-up. There are conflicting data on this subject, with some groups showing a positive association (27, 28) and others showing no association (10, 29). This highlights the need to provide assistance to all patients after COVID-19, independent of acute disease severity.

Regarding lung function evaluation, the most common abnormalities were reduced DLCO and small airway disease. Reduced DLCO is consistently shown to be the main impairment post-COVID-19 and has been associated with acute disease severity (6, 13, 33, 34). COVID-19 may impair diffusion capacity through reduced alveolar volume, interstitial thickening, and pulmonary vascular involvement (18). Some studies have shown an association between reduced DLCO and persistent tomographic abnormalities, suggesting that interstitial thickening contributes, at least in part, to reduced diffusion capacity (7, 10, 31). In our study, 71% of patients with reduced DLCO had normalized repeated tests, suggesting that this alteration was significantly reversible.

IOS, a sensitive method for detecting small airway involvement (35), has not been widely used for COVID-19 follow-up. In this study, a significant prevalence of small airway disease (30.3%) was observed two months after infection, and among symptomatic patients at the 12-month assessment it was the main functional abnormality observed. Furthermore, most patients with small airway disease at 12 months presented with dyspnea. As seen with DLCO, 62% of patients with small airway disease had a normal examination result on repeated testing, suggesting potential reversibility. Further studies on small airway involvement in COVID-19 are needed to better characterize its prevalence, pathophysiological mechanisms, and therapeutic implications.

A restrictive ventilatory pattern was observed in 10.8% of patients, similar to previous reports and normalized in almost all patients who underwent repeated testing (13). This may be explained by interstitial fibrosis and respiratory muscle weakness, which could recover over time.

This study had some limitations. First, the patients included represent the profile of a tertiary hospital in terms of a higher prevalence of comorbidities and severe disease presentation. Second, although selection bias was limited by inviting all discharged patients, patients with fewer symptoms or who were too debilitated might have been less prone to attend follow-up visits. A comparison of the enrolled population with patients not included in the study showed that the enrolled population had a more severe presentation of acute disease. Third, a high rate of follow-up examinations was missing, probably due to pandemic waves, imposed restrictions, and fear of infection. Fourth, the absence of a pre-COVID-19 assessment limits the ability to conclude that all findings are directly related to COVID-19.

From a public health perspective, our results indicate that efforts should be directed toward creating services prepared to receive a significant number of patients with persistent symptoms after COVID-19 infection, with the capacity to perform multidisciplinary long-term follow-up. LFT should be performed to evaluate dyspnea and respiratory symptoms. However, other influencing factors should also be investigated. Rehabilitation programs should be encouraged to minimize limitations in daily activities and promote people's return to work to mitigate the socioeconomic impact of the pandemic.

TABLE 4. Evaluation of the risk factors for dyspnea, fatigue, and limitation in daily activities at the one-year assessment

Variables	Dyspnea at the one-year assessment				Fatigue at the one-year assessment		Limitation in daily activities at the one-year assessment			
	Univariate analysis		Multivariate analysis		Univariate analysis		Univariate analysis		Multivariate analysis	
	RR (95% CI)	p value	OR (95% CI)	p value	RR (95% CI)	p value	RR (95% CI)	p value	OR (95% CI)	p value
Female sex	1.49 (0.80, 2.79)	0.197	–	–	2.28 (1.13, 4.63)	0.014	1.25 (0.77, 2.05)	0.357	–	–
Age	–	0.046	0.92 (0.86, 0.99)	0.02	–	0.155	–	1.000	–	–
Obesity	2.04 (1.16, 3.60)	0.022	–	–	1.06 (0.51, 2.22)	0.877	1.21 (0.70, 2.07)	0.513	–	–
Corticosteroid use during hospitalization	1.86 (1.03, 3.38)	0.039	6.61 (1.34, 32.68)	0.02	0.72 (0.37, 1.40)	0.318	1.87 (1.16, 3.01)	0.010	4.39 (1.42, 13.64)	0.010
Bronchial wall thickening on baseline CT	2.62 (1.02, 6.71)	0.021	7.57 (1.46, 39.26)	0.016	1.75 (0.74, 4.10)	0.172	1.47 (0.79, 2.75)	0.195	–	–
Dyspnea at admission	2.61 (1.11, 6.17)	0.013	–	–	0.98 (0.52, 1.85)	0.948	1.75 (0.96, 3.22)	0.048	–	–
Ageusia at admission	1.27 (0.68, 2.38)	0.463	–	–	2.12 (1.19, 3.77)	0.015	1.30 (0.80, 2.13)	0.311	–	–

Notes: –, not determined; CI, confidence interval; CT, computed tomography; OR, odds ratio; RR, risk ratio.
Source: Prepared by the authors from the study results.

Conclusion

It was demonstrated that more than one-third of patients still had persistent COVID-19 related symptoms and at least some limitation to daily activities up to one year after hospital discharge, adding to the growing body of evidence on the post-COVID-19 syndrome. Dyspnea and fatigue were the most frequent symptoms during the follow-up period, with some improvement over time. Young age, use of corticosteroids during hospitalization, and bronchial wall thickening on CT at admission were significant risk factors for dyspnea at the 12-month follow-up assessment, and female sex was considered a risk factor for fatigue with marginal significance. The use of corticosteroids in the acute phase increased the risk of having limitations in daily activities at 12 months.

The functional assessment identified a high prevalence of reduced diffusing lung capacity and small airway disease, which demonstrated at least some reversibility over time. Dyspnea at the 12-month assessment could not be completely explained by lung function impairment, with probable multifactorial contributions.

This study emphasizes the importance of long-term multidisciplinary follow-up after COVID-19, regardless of acute disease severity, to clarify the pathophysiological mechanisms of post-COVID-19 syndrome and mitigate its impact on individual and public health.

Author contributions. NRGRV and MCC conceived original idea, collected and analyzed the data, interpreted results, and

wrote the manuscript. DC and MIVS interpreted the results. NPS, LPPL, and APC conceived original idea. FCQM conceived the original idea, analyzed data, and reviewed the manuscript. All authors read and approved the final version of the manuscript for submission.

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Resultados respiratorios a largo plazo tras la COVID-19: estudio de cohorte en Brasil

RESUMEN

Objetivo. Investigar la prevalencia y los factores de riesgo de los síntomas persistentes de la COVID-19 hasta 12 meses después del alta hospitalaria en pacientes sobrevivientes de esta enfermedad.

Métodos. Este estudio prospectivo de cohorte incluyó pacientes con COVID-19 que recibieron el alta de un hospital universitario en Brasil. El seguimiento se hizo a los 2, 6 y 12 meses del alta. Se realizaron pruebas de función pulmonar y tomografía computarizada de tórax dos meses después del alta y se repitieron si los resultados eran anormales. Los resultados primarios investigados fueron síntomas presentes, situación laboral y limitaciones en las actividades diarias.

Resultados. Se incluyeron 88 pacientes. Los síntomas más comunes fueron disnea (54,5%), fatiga (50,0%), mialgia y debilidad muscular (46,6%), que disminuyeron con el tiempo. La ansiedad fue frecuente (46,6%) y se mantuvo sin cambios. Un año después del alta, 43,2% de los pacientes notificaron limitaciones en las actividades diarias, y 17,6% no se había reincorporado al trabajo. El consumo de corticosteroides se asoció significativamente con disnea y limitaciones en las actividades diarias. Las mujeres tuvieron un mayor riesgo de fatiga en la evaluación a los 12 meses, con una importancia marginal después del ajuste multivariable. También fueron factores de riesgo de disnea en el seguimiento: edad temprana y engrosamiento de las paredes bronquiales en la tomografía computarizada al momento del ingreso hospitalario. Las anomalías más comunes de la función pulmonar fueron la reducción de la capacidad de difusión y la enfermedad de las vías respiratorias pequeñas, que mejoraron parcialmente con el tiempo.

Conclusiones. Un año después del alta hospitalaria, más de un tercio de los pacientes todavía tenían síntomas persistentes relacionados con la COVID-19, disnea notable, fatiga y limitaciones en las actividades diarias, independientemente de la gravedad aguda de la enfermedad. La edad, el sexo femenino, el uso de corticosteroides durante la hospitalización y el engrosamiento bronquial en la tomografía computarizada al momento del ingreso hospitalario se asociaron con un mayor riesgo de secuelas.

Palabras clave COVID-19; estudios de seguimiento; pruebas de función respiratoria; Brasil.

Desfechos respiratórios de longo prazo pós-COVID-19: estudo de coorte brasileiro

RESUMO

Objetivo. Investigar a prevalência e os fatores de risco para sintomas persistentes por até 12 meses após a alta hospitalar entre sobreviventes da COVID-19.

Métodos. Este estudo de coorte prospectivo incluiu pacientes com COVID-19 que receberam alta de um hospital universitário do Brasil. O acompanhamento foi realizado 2, 6 e 12 meses após a alta. Testes de função pulmonar e tomografia computadorizada (TC) do tórax foram realizados 2 meses após a alta hospitalar e repetidos em caso de resultados alterados. Os desfechos primários foram os sintomas presentes, a situação de trabalho e as limitações nas atividades diárias.

Resultados. Foram incluídos 88 pacientes. Dispneia (54,5%), fadiga (50,0%), mialgia e fraqueza muscular (46,6%) foram os sintomas mais comuns, que diminuíram com o tempo. A ansiedade era frequente (46,6%) e permaneceu inalterada. Um ano após a alta, 43,2% dos pacientes relatavam limitações nas atividades diárias e 17,6% não haviam retornado ao trabalho. O uso de corticosteroides estava significativamente associado à dispneia e a limitações nas atividades diárias. Pacientes do sexo feminino tinham um risco maior de fadiga na avaliação de 12 meses, com significância marginal após ajuste multivariado. A idade jovem e o espessamento da parede brônquica na TC de admissão também eram fatores de risco para dispneia no acompanhamento. As alterações mais comuns da função pulmonar foram capacidade de difusão reduzida e doença das pequenas vias aéreas, que melhoraram parcialmente com o tempo.

Conclusões. Um ano após a alta hospitalar, mais de um terço dos pacientes ainda apresentava sintomas persistentes relacionados à COVID-19, dispneia marcante, fadiga e limitações nas atividades diárias, independentemente da gravidade da doença aguda. A idade, o sexo feminino, o uso de corticosteroides durante a internação e o espessamento brônquico na TC de admissão estavam associados a um maior risco de sequelas.

Palavras-chave COVID-19; seguimentos; testes de função respiratória; Brasil.