
Impact of COVID-19 Severity on Sleep Parameters, Exercise Tolerance, Respiratory Muscle Strength, Pulmonary Function, and Quality of Life: A cross-sectional study

Impacto da gravidade da COVID-19 nos parâmetros do sono, tolerância ao exercício, força muscular respiratória, função pulmonar e qualidade de vida: um estudo transversal

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Jose Carlos Nóbrega Júnior

ORCID: <https://orcid.org/0000-0003-3908-9260>
Federal University of Pernambuco, Brazil.
E-mail: c10carlo@gmail.com

Anna Myrna Jaguaribe de Lima

ORCID: <https://orcid.org/0000-0002-4224-4009>
Federal Rural University of Pernambuco, Brazil.
E-mail: annamyrna@uol.com.br

Daiara Xavier

ORCID: <https://orcid.org/0000-0002-8806-8151>
Federal University of Pernambuco, Brazil.
E-mail: daiara.xavier@ufpe.br

Roberta Torres

ORCID: <https://orcid.org/0000-0002-2950-3408>
Federal University of Pernambuco, Brazil.
E-mail: roberta.crisitiane@ufpe.br

Magno Formiga

ORCID: <https://orcid.org/0000-0003-0327-9695>
Federal University of Ceará, Ceará, Brazil.
E-mail: magno.formiga@ufc.br

Daniella Brandão

ORCID: <https://orcid.org/0000-0001-8805-6815>
Federal University of Pernambuco, Recife, Pernambuco, Brazil.
E-mail: daniella.brandao@ufpe.br

Shirley Campos

ORCID: <https://orcid.org/0000-0003-3079-8300>
Federal University of Pernambuco, Recife, Pernambuco, Brazil.
E-mail: shirley.campos@ufpe.br

Armèle Dornelas de Andrade

ORCID: <https://orcid.org/0000-0001-9430-4395>
Federal University of Pernambuco, Recife, Pernambuco, Brazil.
E-mail: arnele.andrade@ufpe.br

ABSTRACT

To investigate the impact of post-COVID-19 infection severity on lung function, exercise tolerance, sleep parameters, and quality of life. A cross-sectional study with 30 individuals (age 44.27 ± 14.88 years; 70% women) affected by COVID-19 (23.37 ± 3.49 months after acute infection) was divided into 3 groups: control, mild, and moderate/severe. Evaluations included: submaximal aerobic capacity, respiratory muscle strength, lung function, sleep parameters and quality of life. The moderate/severe group showed lower results for the predicted percentage of FEV1/FVC ($p=0.004$) and significant differences in sustained maximum inspiratory pressure (SMIP) and fatigue index (FIT) ($p<0.05$). They also showed reduced exercise tolerance with shorter walking distances ($p<0.001$), poorer sleep quality, excessive daytime sleepiness, lower sleep efficiency ($p=0.032$), longer sleep latency ($p<0.001$), and more awakenings ($p=0.006$). Quality of life was reduced in three of the eight domains assessed. Individuals with moderate/severe COVID-19 exhibited impaired pulmonary function, reduced sleep efficiency, more awakenings, and lower quality of life compared to those with asymptomatic or mild cases.

Keywords: exercise tolerance; sleep quality; long-COVID-19; quality of life; lung function;

RESUMO

Investigar o impacto da gravidade da infecção pós-COVID-19 na função pulmonar, tolerância ao exercício, parâmetros do sono e qualidade de vida. Um estudo transversal com 30 indivíduos (idade $44,27 \pm 14,88$ anos; 70% mulheres) acometidos pela COVID-19 ($23,37 \pm 3,49$ meses após infecção aguda) foram divididos em 3 grupos: controle, leve e moderado/grave. As avaliações incluíram: tolerância ao esforço, força muscular respiratória, função pulmonar, parâmetros de sono e qualidade de vida. O grupo moderado/grave apresentou resultados inferiores para o percentual previsto de VEF1/CVF ($p=0,004$) e diferenças significativas na pressão inspiratória máxima sustentada (SMIP) e no índice de fadiga (FIT) ($p<0,05$). Eles também mostraram menor tolerância ao exercício com distâncias curtas de caminhada ($p<0,001$), pior qualidade do sono, sonolência diurna excessiva, menor eficiência do sono ($p=0,032$), maior latência do sono ($p<0,001$) e mais despertares ($p=0,006$). A qualidade de vida foi reduzida em três dos oito domínios avaliados. Indivíduos com COVID-19 moderada/grave apresentaram função pulmonar prejudicada, redução da eficiência do sono, mais despertares e menor qualidade de vida em comparação com os casos assintomáticos ou leves.

Palavras-chave: tolerância ao exercício; qualidade do sono; COVID-19 longa; qualidade de vida; função pulmonar;

INTRODUÇÃO

The COVID-19 infection is responsible for several sequelae, mainly in the cardiovascular and respiratory systems even after the active phase of the disease, with thrombosis, myocarditis, diffuse alveolar damage or interstitial pulmonary fibrosis being possible to observe (Liu et al., 2020; Besnier et al., 2022). Regarding the severity of the disease, in cases of mild disease, fever, sore throat, dry cough, malaise, body aches, nausea and vomiting were observed. Moderate cases had symptoms of pneumonia and significant lesions on chest CT. Severe cases, acute respiratory distress syndrome, along with shock, coagulation disorders, encephalopathy, heart failure and acute kidney injury (Parasher, 2021).

In this context, COVID-19 came to be seen as an aggressive agent capable of triggering negative psychological effects that can raise levels of anxiety, depression and stress in infected individuals, remaining even after the acute period of the disease. These negative emotions contribute to affect the quality of sleep, leading to the emergence of sleep disorders (Özlü et al., 2021; Souza et al., 2021).

Many patients still have symptoms related to COVID-19 even after 1 year of infection. This impact can still be observed through changes in chest computed tomography with ground-glass opacities and interstitial fibrosis as the most frequent findings, changes in exercise tolerance and difficulty in performing activities of daily living (ADLs) (Zhan et al., 2021; Morrow et al., 2022). The mid- and long-term repercussions of COVID-19 infections and the consequences of disease severity on patients' general health, well-being, physical function and ability to return to work are still considered a gap in the literature (Jacobs et al., 2021; Daynes et al., 2021; Nakanishi et al., 2021). In view of the above, the present study aims to investigate the impact of the severity of COVID-19 on lung function, exercise tolerance, sleep quality and quality of life of individuals after infection.

MATERIALS AND METHODS

Sample

This is a cross-sectional study, carried out from January 2021 to October 2022 with a convenience sampling considered individuals attending the main reference centers due to the persistence of post-infection symptoms; invitations occurred via direct disclosure or social media.

Volunteers of both sexes, aged over 18 years, who were not engaged in any form of physical activity and were diagnosed with COVID-19 after the acute phase of infection, with the first infection confirmed by RT-PCR testing, were included. As for the exclusion criteria, individuals with reporting disorders of before COVID-19 (i.e., orthopedic, neurologic), pregnancy, or during the active infection phase were excluded.

Individuals were classified according to the severity of the post-COVID-19 syndrome, based on the severity, intensity, and persistence of symptoms after the acute infection. The patients were divided into three groups: asymptomatic (control), mild, and moderate/severe. The asymptomatic group consisted of individuals who did not experience any flu-like symptoms despite testing positive for the virus. Mild post-COVID-19 syndrome included individuals with mild fatigue, mild symptoms of anxiety and depression, and poor sleep quality, but without impairment in their daily activities. Moderate/severe post-COVID-19 syndrome: besides the symptoms of the mild group, individuals from this group could also present moderate or severe dyspnea, muscle pain, difficulty concentrating and chronic pain that hindered their ability to function independently (Appel et al., 2024).

The project was submitted to evaluation and approval by the Research Ethics Committee for Human Beings of the Universidade Federal de Pernambuco – UFPE, having been approved under protocol number 4.983.173 (CAAE 50483621.1.0000.5208, approval date 17/09/2021), respecting Resolution No. 466/12. All volunteers were informed about the research and signed the free and informed consent form prepared by the responsible researcher.

Measures of inspiratory muscle performance

Inspiratory muscle performance was evaluated using the Test of Incremental Respiratory Endurance (TIRE) (Formiga et al., 2019). TIRE includes measurements of MIP (MIP), maximum sustained inspiratory pressure (SMIP) and fatigue index (FIT). These variables are obtained using the PrO2 (PrO2Fit Health, Smithfield, RI, USA), a portable and wireless pressure gauge, synchronized with a smartphone through an application to provide users with graphical biofeedback while performing the test. All inspiratory maneuvers were performed in accordance with the American Thoracic Society (ATS) standards for testing the respiratory muscles (ATS, 2002).

Objective assessment of sleep parameters

The Actrust 2 actigraph (Copyright© 2014, Condor Instruments Ltda, Brazil) was used to evaluate sleep. Participants wore the device for 7 days on a bracelet on the non-dominant arm, were instructed to remain with the device on the arm at the usual sleep-wake time, and were free to self-select their bedtime and wake times throughout the assessment period. The information was stored on the device and later transmitted to a computer on a second visit after the 7 days in the laboratory. All actigraphies recorded sleep efficiency (ratio of total sleep time to total duration of time in bed), sleep onset latency (time in minutes between bedtime and sleep onset), awakenings after sleep onset (number of minutes marked as awake during the sleep period after sleep onset), and total sleep time (sleep duration during the longest sleep period at night).

Subjective Assessment of Sleep Parameters

Assessment of Excessive Daytime Sleepiness

The Epworth Daytime Sleepiness Scale (EDSS) consists of a scale validated for the Brazilian population that assesses other everyday situations and asks the individual to self-assess the chance of sleeping while performing these activities, scoring from 0 to 3, where 0: no chance of nap, 1: low chance, 2: moderate chance, 3: high chance. When the sum of two components of the scale reaches a value ≥ 10 , it means that the patient has excessive daytime sleepiness that needs to be investigated (Bertolazi et al., 2009).

Sleep Quality Assessment

The Pittsburgh Sleep Quality Index (PSQI) was used considering nineteen individual items that give rise to seven scoring components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. The sum of scores obtained in the seven components generates a global score capable of classifying sleep quality as good (0 to 4 points), poor (>5 points) (Bertolazi; Barreto, 2008).

Lung function

Lung function assessment was performed using KoKo® Spirometer digital spirometry (nSpire Health, UK). The test was performed with the individual in a sitting position, with feet flat on the floor, spine erect and using a mouthpiece and nose clip. At least three forced vital capacity (FVC) and slow vital capacity (SVC) maneuvers were

performed, observing the two-minute interval between maneuvers, as recommended by the American Thoracic Society (ATS) and pulmonary function guidelines. Then, the average of the three measurements taken was performed and the values were expressed as a percentage of the normal predicted value for the Brazilian population (Duarte; Crapo; Rodrigues, 2007). FEV1 and the relationship between FEV1 and forced vital capacity (FEV 1 /FVC) were also analyzed.

Quality of life assessment

The Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), a questionnaire composed of 36 items that are divided into eight topics: functional capacity; mental health and general health status; pain and social aspects of the patient; the emotional aspects and the physical aspects and vitality. There is also a comparative assessment between current health conditions and those presented a year ago. The final score ranged from 0 to 100, where zero corresponded to the worst general state of health and 100, to the best state of health (Ciconelli et al., 1999).

Exercise Tolerance Assessment

The six-minute walk test (6MWT) was performed according to the criteria established by the American Thoracic Society (Crapo et al., 2002). Patients walked as fast as possible in a 30-meter corridor, without running, for 6 minutes. The distance traveled was expressed in absolute values and percentage of predicted for the Brazilian population according to the equation determined by Britto et al., (2014).

Statistical analysis

The data were stored and analyzed using the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, USA). Normality and homogeneity of variances were checked by the Shapiro-Wilk and Levene tests, respectively. Descriptive statistics are presented in absolute frequency and relative frequency (categorical variables) and mean \pm standard deviation. One-Way ANOVA with Tukey's post-hoc test was conducted to compare the effect of disease severity within each group. The significance level adopted in all analyzes was 5% ($p < 0.05$).

RESULTS

In total, 30 patients diagnosed with COVID-19 were evaluated. Table 1 shows the sample characterization data.

Table1. Sample characterization.

	Control (n=10)	Mild (n=9)	Moderate/severe (n=11)
Age (years)	41.40±15.37	41.89±14.32	48.82±15.15
BMI (kg/m²)	28.18±3.20	26.61±2.50	32.78±5.85
Post-covid time (months)	23.20±3.49	24.00±3.35	23.00±3.87
Sex, [n(%)]			
Female	6 (60%)	6 (66.7%)	9 (81.8%)
Male	4 (40%)	3 (33.3%)	2 (18.2%)
Hospitalization, [n(%)]			
Home treatment	10 (100%)	3 (33.3%)	1 (9.1%)
Nursery	0 (0%)	6 (66.7%)	5 (45.5%)
ICU	0 (0%)	0 (0%)	5 (45.5%)
BMI, [n(%)]			
Normal	2 (20%)	3 (33.3%)	2 (18.2%)
Overweight	5 (50%)	5 (55.6%)	1 (15%)
Obese	3 (30%)	1 (11.1%)	8 (72.7%)

Note: Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as frequencies (percentage). ICU=intensive care unit; BMI= body mass index.

Table 2 shows the variables related to lung function and respiratory muscle strength for the three groups. A reduction in the predicted percentage for the forced expiratory volume in the first second to forced vital capacity ratio (FEV1/FVC) is observed in the moderate/severe group compared to the control group. However, the other variables related to lung function did not show differences between the groups. Regarding the TIRE measures of inspiratory muscle performance, both sustained maximum inspiratory pressure (SMIP) and the fatigue index (FIT) showed lower values in the moderate/severe group compared to the asymptomatic group.

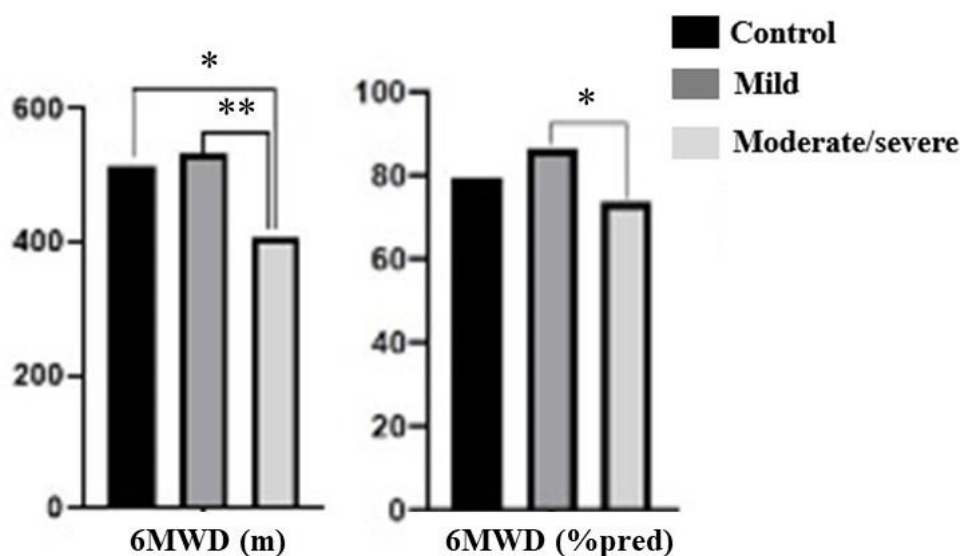
Table 2. Results of lung function, respiratory muscle strength and submaximal functional capacity.

	Groups			F	p-value between groups
	Control (n=10)	Mild (n=9)	Moderate/severe (n=11)		
	Mean (SD)	Mean (SD)	Mean (SD)		
FEV1(%pred)	80±19.12	84.11±5.60	69.45±11.97	3.169	0.058
FVC(%pred)	83±17.58	91.33±11.21	84.09±12.36	0.980	0.388
FEV1/FVC (%pred)	97.60±8.20	91.89±6.47	79.73±15.95*	6.802	0.004#
MIP	90±20.44	82±23.95	84.73±39.20	0.180	0.836
SMIP	637.80±114.46	527.44±154.75	448.91±162.91*	4.408	0.022#
FIT	27.34±8.23	23.78±8.03	16.51±11.39*	3.569	0.042#

Note: FEV1: forced expiratory volume in one second; FVC: forced vital capacity; MIP: maximum inspiratory pressure; SMIP: maximum sustained inspiratory pressure; FIT: fatigue index test; 6MWD: distance covered in the six-minute walk test; # significant difference from baseline between control, mild, and moderate/severe groups ($p < 0.05$). Continuous variables are expressed as mean \pm standard deviation. One-Way ANOVA and Tukey Test. $p < 0.05$. *Control; **Mild; ***Moderate/severe.

The comparison of the results related to the 6-minute walk test (6MWT) and the predicted percentage of the distance walked in the 6MWT is presented in figure 1. The moderate/severe group showed a shorter 6MWT distance compared to the control and mild groups, and a lower percentage of predicted values compared to the mild group.

Figura 1. Submaximal functional capacity results for the Control, Mild and Moderate/severe groups. One-Way ANOVA and Tukey Test. (*: $p < 0,05$; **: $p < 0,001$).



Regarding quality of life, the moderate/severe group showed worse scores in three of the eight domains assessed (functional capacity, physical role limitations, and general health) compared to the control group. However, the relatively low scores across all eight domains for the three groups suggest a decline in quality of life for patients after being affected by COVID-19. Additionally, the moderate/severe group had lower scores in the functional capacity domain compared to the mild group.

Table 3. Results related to quality of life (SF - 36).

	Groups			F	p-value between groups
	Control (n=10)	Mild (n=9)	Moderate/severe (n=11)		
Functional capacity	Mean (SD) 69.50±20.87	Mean (SD) 64.44±15.70***	Mean (SD) 39.64±20.01*	7.334	0.003#
Limitation by physical aspects	55.40±36.85	53.22±29.15	20.55±35.18*	3.436	0.047#
Pain	60.70±30.68	58.78±24.26	53.27±11.22	0.293	0.748
general state of health	65.80±21.70	62.33±16.23	45.09±19.12*	3.494	0.045#
Vitality	46.70±25.05	49.11±17.23	41.82±25.32	0.262	0.771
Social aspects	57.80±22.36	54.44±24.59	56.18±18.31	0.057	0.945
Limitation by emotional aspects	48.50±34.05	35.33±32.08	46.64±45.23	0.329	0.722
Mental health	59.30±20.55	60.56±13.77	68.36±23.76	0.624	0.543
Total score	463.70±144.41	438.22±133.56	371.55±125.96	1.318	0.284

Note: # significant difference from baseline between control, mild, and moderate/severe groups ($p < 0.05$). Continuous variables are expressed as mean \pm standard deviation. One-Way ANOVA and Tukey Test. $p < 0.05$. *Control; **Mild; ***Moderate/severe.

Table 4 presents the evaluation of sleep parameters. It can be observed that both the mild and moderate/severe groups had PSQI scores indicating poor sleep quality (>5), with the moderate/severe group showing the worst responses compared to the control group. Regarding excessive daytime sleepiness (EDS), the moderate/severe group had higher scores, indicating a greater presence of EDS in this group. In the objective evaluation of sleep parameters, the moderate/severe group showed worse performance in terms of sleep latency, sleep efficiency, and nocturnal awakenings compared to the control group.

Table 4. Sleep Quality (Direct and Indirect Measures) and Excessive Daytime Sleepiness.

	Groups			F	p-value between groups
	Control (n=10)	Mild (n=9)	Moderate/severe (n=11)		
	Mean (SD)	Mean (SD)	Mean (SD)		
Total time in bed (h)	7.10 \pm 1.17	8.31 \pm 2.07	8.48 \pm 1.52	2.182	0.132
Total sleep time (h)	6.40 \pm 1.48	7.74 \pm 2.11	7.21 \pm 1.27	1.619	0.217
Latency (min)	3.40 \pm 1.18	2.49 \pm 0.89***	4.84 \pm 0.88*	14.391	0.000#
Sleep efficiency (%)	84.83 \pm 4.75	83.35 \pm 5.44	79.25 \pm 4.08*	3.914	0.032#
Awakenings	8.51 \pm 3.27	7.19 \pm 3.21***	11.82 \pm 7.71*	6.191	0.006#
EDSS	4.20 \pm 2.20	7.33 \pm 4.63	10.91 \pm 4.23*	8.100	0.002#
PSQI	5.80 \pm 3.76	7.67 \pm 3.12	11.09 \pm 2.94*	7.006	0.004#

Note: EDSS: Epworth Daytime Sleepiness Scale; PSQI: Pittsburgh Sleep Quality Index. # Significant difference from baseline between control, mild, and moderate/severe groups ($p < 0.05$). Continuous variables are expressed as mean \pm standard deviation. One-Way ANOVA and Tukey Test. $p < 0.05$. *Control; **Mild; ***Moderate/severe.

DISCUSSION

The objective of this study was to evaluate the impact of COVID-19 severity on sleep parameters, exercise tolerance, respiratory muscle strength, lung function, and quality of life after the infection period, considering the severity of the disease at the time of infection. Among the most relevant findings, higher PSQI and ESS scores, lower sleep efficiency, longer sleep latency, and more nocturnal awakenings were observed in the moderate/severe group compared to the control group. Regarding quality of life, patients showed low scores across domains, with the moderate/severe group performing worse in

three of the eight assessed domains than the control group. Additionally, the moderate/severe group had a higher percentage of individuals with reduced lung function, lower inspiratory muscle strength, and poorer performance in the 6-minute walk test (6MWT) compared to the control and mild groups, and a lower percentage of predicted values compared to the mild group.

According to Liu et al. (2020), COVID-19 patients may develop residual pulmonary fibrotic lesions, which significantly impact their lung function. Our study supports these findings, as we observed poorer lung function performance in the group of patients with moderate/severe cases. According to Zhan et al. (2021), the infection does not lead to significant pulmonary changes in mild cases, and abnormalities are not observable on chest CT scans. However, 53% of severely ill patients may exhibit various abnormalities, with ground-glass opacities and interstitial fibrosis being the most frequent findings, even one year after infection. Additionally, Ojo et al. (2020) suggested that the extent of lung injury and the inflammatory response correlate with the extent of fibroblastic response required for the repair process of the lesion.

In relation to respiratory muscle strength, considering that sustained maximum inspiratory pressure (SMIP) can be regarded as a measure derived from maximum inspiratory pressure (MIP) over time, both variables are correlated (Formiga et al., 2019). In this context, we categorized the moderate/severe group as having lower endurance and a higher fatigue index compared to control group. Additionally, the three groups did not differ in terms of respiratory muscle strength, which was considered within the normal range, as maximum inspiratory pressure (P_Imax) values exceeded 60 mmHg for all groups. This may be related to the relatively younger age of the patients in this study and their activity profiles. The study by Sirayder et al. (2022), conducted with post-COVID adults and healthy individuals, found no difference between the groups in terms of respiratory muscle strength, with maintenance of strength observed in both groups.

In a cohort study conducted by Nopp et al. (2022), most patients included had mild to moderate COVID-19 and exhibited persistent symptoms even after the active phase of the disease, including reduced exercise capacity, dyspnea, fatigue, and functional impairment. In the initial assessment of patients in the present study, it was observed that patients achieved, on average, only 79% of the predicted distance in the 6-minute walk test. These findings are common among survivors of critical illnesses, especially those at risk of significant impairment due to post-intensive care syndrome (Kress; Hall, 2014).

In another 5-year follow-up study with survivors of acute respiratory distress syndrome (ARDS), it was observed that the sample achieved only 76% of the predicted capacity in the 6-minute walk test (Ahmed et al., 2020). Our results support these findings, as we observed differences in the performance of the 6-minute walk test among the control, mild, and moderate/severe COVID-19 groups. Additionally, we observed a difference of 109.02 meters between the control and moderate/severe groups, and 127.38 meters between the mild and moderate/severe groups in terms of distance covered in the test.

In the analysis of quality of life, we observed low scores across all eight domains of the SF-36 for the three groups, indicating a decline in the quality of life of patients after being affected by COVID-19. Additionally, it was noted that the moderate/severe group had worse scores in the domains of physical functioning, role limitations due to physical health, and general health perception compared to the control group. These findings suggest that more severe cases may be associated with greater physical and emotional limitations, hindering daily activities and altering the individual's perception of their own health condition. Ahmed et al. (2020), in their systematic review, found that SF-36 scores in COVID-19 survivors were notably lower compared to healthy individuals in the studies analyzed.

The study by Tanriverdi et al. (2022), conducted with COVID-19 patients post-infection, observes the persistence of symptoms such as anxiety, depression, and poor sleep quality in the medium term. Furthermore, the authors state that patients who recovered from moderate disease exhibit significant negative changes in peripheral muscle strength, physical performance, mood, and sleep quality compared to those who recovered from mild disease. These findings are consistent with those obtained in our study, where we observed lower sleep efficiency, increased nocturnal awakenings, and longer sleep latency in the moderate/severe disease group compared to those who were asymptomatic or had mild symptoms. Additionally, the moderate/severe group scored higher on the excessive daytime sleepiness scale, as fragmented sleep due to awakenings directly influences efficiency and thereby worsens sleep quality, contributing to daytime dysfunction.

When analyzing self-reported overall sleep quality, it's evident that patients perceive their sleep as negatively affected by COVID-19 infection, and poor sleep quality persisted even long after the active phase of the disease. These findings align with results from Nowakowski et al. (2022), where similar outcomes were observed, with an average

PSQI score of 9.69 reported by 82.3% of the analyzed sample. Furthermore, the authors linked overall self-reported sleep quality and daytime dysfunction with symptoms of depression, anxiety, and post-traumatic stress. Regarding excessive daytime sleepiness (EDS), the moderate/severe group scored higher, indicating a greater presence of excessive daytime sleepiness in this group.

Semyachkina-Glushkovskaya et al. (2021), observed an increase in sleep disorders related to COVID-19, termed as 'coronasomnia'. In this context, COVID-19-related sleep disturbances can lead to disruption of the blood-brain barrier, exposing the brain to the entry of viruses, bacteria, and toxins. Upon invasion, the immune system is immediately activated, producing inflammatory mediators that promote hyperinflammation of the central nervous system to eliminate pathogens from infected tissues. This inflammatory process is directly proportional to the severity of COVID-19. The findings presented justify the results obtained in our study, as infection caused by the virus has a greater potential to cause damage in the group with more severe COVID-19. This may reinforce the poorer outcomes found in the quality of life scores, excessive daytime sleepiness, number of awakenings, sleep latency, and sleep efficiency for the moderate/severe group compared to the other groups.

A limitation of the study is the heterogeneity of the sample regarding the duration of COVID-19. Another aspect is the sample size of our study; however, in the context of numerous long-term negative sequelae caused by a novel virus, it is crucial to address knowledge gaps in the field and identify potentially impactful factors that may contribute to understanding these changes, as well as guiding new treatment measures.

CONCLUSION

The findings of this study suggest that COVID-19 leaves significant sequelae on lung function, sleep quality, quality of life, and exercise tolerance in individuals who have recovered from moderate/severe cases compared to those who were control or had mild symptoms. A prospective cohort study is needed for future investigations to elucidate the connections between disease severity and repercussions post-COVID-19 onset. In clinical practice, our results highlight the necessity for a comprehensive evaluation involving all pulmonary and sleep parameters in post-COVID-19 patients to implement appropriate intervention strategies tailored to the severity of the disease.

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Conflict of interest

The author has no conflict of interest.

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