Review Article

ISSN: 2966-4837

Brazilian Journal of Respiratory, Cardiovascular and Critical Care Physiotherapy
Jornal Brasileiro de Fisioterapia Respiratória, Cardiovascular e em Terapia Intensiva

Lung function in post-covid 19 survivors: an integrative review

Função pulmonar em sobreviventes pós-covid 19: uma revisão integrativa

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Abstract

Background: Coronavirus is a systemic viral infection that affects the airways and has a high transmission potential. Due to its severe damage to the lung parenchyma, it is necessary to perform outpatient follow-up and lung function tests, including spirometry, diffusion capacity, and lung volumes, to assess possible changes. **Aim**: To synthesize the scientific evidence regarding the deleterious effects on lung function post-COVID-19. **Methods**: This study is an integrative literature review. A search was conducted for articles in databases from 2020 to 2022, including studies in Portuguese and English, and involving patients over 18 years old. Duplicate articles, case reports, literature reviews, rehabilitation/treatment studies, and those that did not answer the guiding question were excluded. **Results**: Through the search strategy, 548 articles were found, of which 23 studies were included, with a total of 4,421 participants, 2,834 of whom underwent pulmonary function tests. There was a predominance of spirometry evaluations, with the main alterations being a decrease in carbon monoxide diffusion capacity and a restrictive ventilatory pattern. **Conclusion**: The present studies reveal that symptomatic patients exhibited greater changes in lung function compared to asymptomatic patients. The main deficits were reduced diffusion capacity and restrictive ventilatory changes from hospital discharge up to 12 months. Diffusion capacity showed greater sensitivity for detecting pulmonary alterations.

Keywords: Adult. Respiratory Function Tests. Coronavirus.

Resumo

Introdução: O Coronavírus é uma infecção viral sistêmica que causa lesão nas vias aéreas e têm amplo poder de transmissão. Devido à sua severa destruição do parênquima pulmonar faz-se necessário realizar acompanhamento ambulatorial e testes de função pulmonar através da espirometria, capacidade de difusão e volumes pulmonares para avaliar as possíveis alterações. **Objetivo**: Sintetizar as evidências científicas com relação aos efeitos deletérios na função pulmonar dos pacientes pós-covid 19. **Métodos**: Este estudo é uma revisão de literatura integrativa. Realizou-se a busca de artigos nas bases de dados no período de 2020 a 2022, incluídos nos idiomas portugues e inglês, e com pacientes maiores de 18 anos. Foram excluídos artigos duplicados, relatos de casos, revisão de literatura, estudos de reabilitação/tratamento e que não responderam à pergunta norteadora. **Resultados:** Foram encontrados por meio da estratégia de busca 548 artigos, sendo incluídos 23 estudos, com total de 4.421 participantes, e 2.834 realizaram os testes de função pulmonar. Houve predominância na avaliação pela espirometria, tendo como principais alterações a diminuição na capacidade de difusão do monóxido de carbono e padrão ventilatório restritivo. **Conclusão**: Os estudos incluídos apontam que pacientes sintomáticos apresentaram maiores alterações na função pulmonar em comparação com assintomáticos. Os principais déficits são as alterações ventilatórias restritivas e a redução da capacidade de difusão dos gases, sendo esta a que apresentou a maior sensibilidade para as disfunções pulmonares, no momento da alta hospitalar em até 12 meses.

Palavras-chave: Adulto. Testes de Função Respiratória. Coronavírus.

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How to cite: Mesquita AC, Mendes AFL, Rocha BLS, França ALN. Lung function in post-covid 19 survivors: an integrative review. Brazilian Journal of Respiratory, Cardiovascular and Critical Care Physiotherapy. 2024;15:e00082023. https://doi.org/10.47066/2966-4837.2024.0005en

Submitted on: December 01, 2023
Accepted on: October 31, 2024

Study carried out at: Regional Hospital of Mato Grosso do Sul, Campo Grande, MS, Brazil.

Ethical approval: Not applicable

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INTRODUCTION

The first cases of Coronavirus (COVID-19) occurred in December 2019 in Wuhan, China, being declared a global pandemic with widespread transmission power.

The disease spread in a few months, and the World Health Organization reported more than 624 million confirmed cases by October 2022[1].

COVID-19 is a systemic viral infection that can cause damage to the airways, mainly to the epithelial, alveolar, and endothelial cells, causing exudation of fluid rich in cells and plasma proteins, with an increase in the permeability of the membrane between the alveoli and the capillaries. This process induces a local inflammatory response with the presence of leukocytes, platelets, and fibrin, contributing to the formation of the hyaline membrane and thus alveolar fibrosis, resulting in a loss of aerated tissue[2].

In patients with severe destruction of the lung parenchyma, suffering from a subsequent mortality risk, longer hospitalization, and mechanical ventilation, pulmonary function tests (PFTs) should be assessed using spirometry, diffusion capacity, and lung volumes[3].

The British Thoracic Society guidelines[4] recommend that PFTs be carried out three months after discharge, in patients with persistent respiratory symptoms and no significant improvement on chest X-ray. The Sociedad Española de Neumalogía y Cirurgía Torácica[5] suggests that spirometry and DLCO measurement (carbon monoxide diffusing capacity) should be the first choice if interstitial lung disease is suspected, and that, if necessary, body plethysmography should be included for evaluation.

It is crucial to detect changes in lung function to diagnose and monitor patients with respiratory sequelae caused by COVID-19. Therefore, it is now essential to conduct research aimed at synthesizing the scientific evidence on the deleterious effects on lung function in post-COVID-19 patients.

METHODS

This study is an integrative literature review, which consists of searching for, analyzing, and synthesizing results already produced on a subject in a systematic, orderly, and comprehensive method. We included original articles published in the Latin American and Caribbean Health Sciences Literature (LILACS), Scientific Electronic Library Online (SciELO), and Library of Medicine National Institutes of Health (PubMed) databases from January 2020 to August 2022, available in Portuguese and English, and involving patients over the age of 18.

The following controlled descriptors were searched in the Health Sciences Descriptors (Decs) and Medical Subject Headings (Mesh): Adult; Respiratory Function Tests; and Coronavirus. The terms were combined using the Boolean operators "AND" and/or "OR". Duplicate articles, case reports, literature reviews, studies comparing with other pathologies, articles that did not answer the guiding question and rehabilitation/intervention studies were excluded.

This research followed six phases to compile the integrative review: defining the guiding question, searching the literature, collecting data, critically analyzing the studies included, discussing the results, and presenting the integrative review.

The research question was formulated according to the PICOD[6] strategy, an acronym. The population consisted of patients affected by COVID-19; Intervention consisted of lung function assessments; Control/Comparison consisted of symptomatic and asymptomatic patients; Outcome consisted of a survey of the deleterious effects of COVID-19 on lung function; and Study Design consisted of an integrative review. The following guiding question was posed: "What are the deleterious effects on lung function in patients affected by COVID-19?"

The level of evidence of the included articles was assessed using the model suggested by Galvão et al.[7], which considers the following levels: level I, studies from systematic reviews, meta-analysis, and randomized controlled clinical trials; level II, evidence from randomized controlled clinical trials; level III, evidence from non-randomized clinical trials; level IV, evidence from cohort and case-control studies; level V, evidence from systematic reviews of descriptive and qualitative studies; level VI, evidence from a single descriptive or qualitative study; and level VII, evidence from expert opinion and/or expert committee reports.

RESULTS

This study was conducted based on the data described in Figure 1. The search strategies found 548 articles, out of which 23 formed the final sample after applying the exclusion criteria. The sum of the samples of the studies included amounted to 4421 individuals. Of these, 2834 underwent pulmonary function tests (PFTs). Table 1 shows the characteristics of the samples.

All the articles were published in English, and most of them used spirometry and DLCO as methods of assessing lung function. The restrictive pattern was the main ventilatory disorder found, along with a reduction in diffusion capacity. Table 1 shows the main findings of the studies.

All studies were classified as level IV, corresponding to cohort studies when assessing the level of evidence based on the methodological approach to study design.

The studies analyzed in this review were classified and stored according to the main author and the year of publication, the country, the type of study, the level of evidence, the sample, the results of the pulmonary function assessments, and the conclusions.

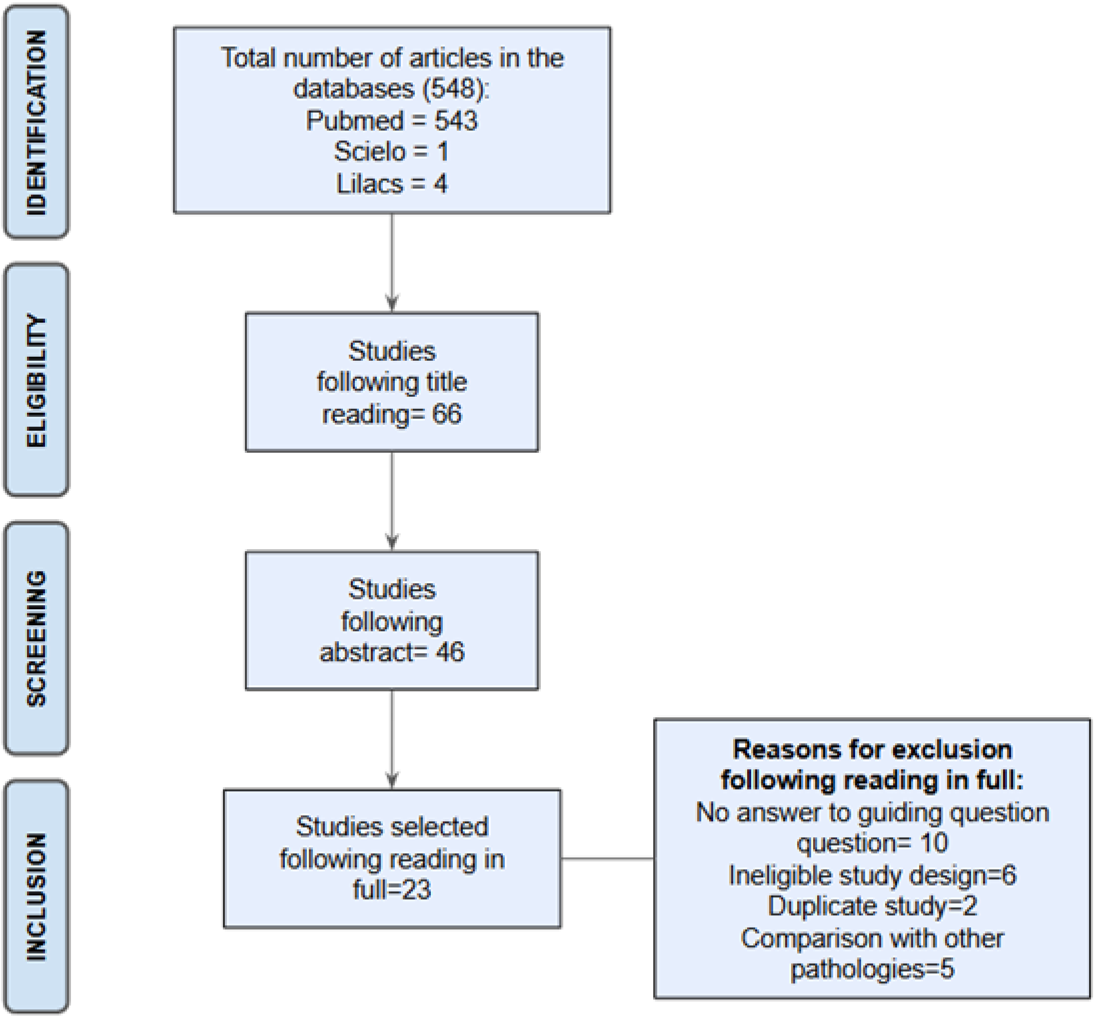

Figure 1. Flowchart of study selection. Campo Grande, MS – 2022.
Source: Elaborated by the authors.

Table 1. Synthesis of the evidence on impaired lung function in post-COVID-19 individuals (N=23). Campo Grande, MS - 2022.

Author (Year)	Country	Type of study/ Level of evidence	Sample	Main results	Conclusion of the study
Cortés-Telles et al. (2021)[9]	Mexico	Observational Study/Level 4	Total sample (n=186), with dyspnea (n=70) and without dyspnea (n=116); 30 to 90 days after the onset of symptoms; average age of 47 years; 61% male.	Pulmonary function was assessed by spirometry and DLCO. Patients with dyspnea had significantly lower FVC, FEV1, and DLCO, and 47% showed a restrictive ventilatory pattern.	Patients with persistent dyspnea mainly showed a restrictive pattern, lower DLCO, and lower FVC compared to patients without dyspnea.
González et al. (2021)[15]	Spain	Descriptive observational study/Level 4	Total sample (n=62); 3 months after hospital discharge; average age of 60; 74.2% (n=46) male.	Pulmonary function was assessed by spirometry and DLCO. 82% (n=50) had an abnormal DLCO (< 80% predicted) and 37.1% (n=23) had altered TLC.	The main finding of the study concerned the high proportion of patients with impaired DLCO.

Caption: DLCO: carbon monoxide diffusion capacity; TLC: total lung capacity; FEV1: forced expiratory volume in 1s; FVC: forced vital capacity; FEV1/FVC: ratio of forced expiratory volume in 1s and forced vital cavity; PEF: peak expiratory flow; ICU: intensive care unit; IMV: invasive mechanical ventilation; PFT: pulmonary function tests; FU: follow-up; KCO: transfer coefficient for carbon monoxide; LLN: lower limit of normal; AV: alveolar volume; HFNC: high-flow nasal cannula; LLN: lower limit of normal; CPAP: Continuous Positive Airway Pressure; FeNO: fractional exhaled nitric oxide. **Source:** Elaborated by the authors.

Table 1. Continued...

Author (Year)	Country	Type of study/ Level of evidence	Sample	Main results	Conclusion of the study
Guler et al. (2021)[17]	Switzerland	Observational Prospective multicenter cohort study/ Level 4	Total sample (n=113); 4 months after symptom onset, with mild/ moderate symptoms (n=47) and severe/ critical symptoms (n=66); average age from 52 to 60 years; 59.2% (n=67) male.	Pulmonary function was assessed by spirometry and DLCO. In the mild/ moderate group, the FEV1/FVC ratio was lower than in the severe/critical group, along with the TLC, FVC, FEV1, and DLCO variables. In the severe/ critical group, (n=39) required IMV, of whom DLCO and TLC showed a negative correlation with ventilation time.	They identified DLCO predicted at 4 months as the most significant factor associated with severe/critical respiratory COVID-19.
Huang et al. (2021)[16]	China	Ambi-directional cohort study/ Level 4	Total sample (n=1,276); within 6 to 12 months of symptom onset; (n=349) received PFT; average age of 59; 53% (n=681) male. In the severity scales, (n=318) scored on Scale 3; (n=864) on Scale 4; and (n=94) on Scales 5-6.	Pulmonary function was assessed by spirometry and DLCO. At 12 months, DLCO was found in 23% (n=13) of patients in the severity scale 3 group, 31% (n=36) in the scale 4 group, and 54% (n=38) in the scale 5-6 group. The proportion of TLC below 80% predicted in the scale 5-6 group decreased significantly from 39% (n=27) at 6 months to 29% (n=20) at 12 months.	At 12 months, there was a high prevalence of pulmonary diffusion impairment in patients with varying disease severity.
Froidure et al. (2021)[30]	Belgium	Single-center cohort study/ Level 4	Total sample (n=134); after 3 months of hospital discharge; (n=122) received PFT; average age of 60; 59% male.	Pulmonary function was assessed by spirometry and DLCO. DLCO was impaired in 47% (n=58), with 27% (n=33) showing a DLCO <60% of predicted values.	Severe and critical cases of COVID-19 have been shown to recover almost completely, with PFT close to normal.
Steinbeis et al. (2022)[31]	Germany	Prospective observational study/Level 4	Total sample (n=180); 12 months after COVID-19; average age of 56 years; 37.78% (n=68) female.	Pulmonary function was assessed by body plethysmography and DLCO. 32% (n=55) patients had pulmonary restriction and 61% (n=104) had reduced DLCO. TLC and FVC measurements were lower in patients with a higher level of respiratory support.	The relevance of the initial severity of the disease was demonstrated, with greater pulmonary functional impairment at 12 months after COVID-19.
Shah et al. (2021)[14]	Canada	Consecutive prospective cohort study/ Level 4	Total sample (n=60); 12 weeks after symptom onset; (n=57) received PFT; average age of 67; 68% male.	Pulmonary function was assessed by spirometry and DLCO. PFT was abnormal in 58% of patients. Altered DLCO appeared in 52% and 45% had an abnormal TLC, indicating a restrictive ventilatory deficit. Flow obstruction occurred in 11% of patients.	Over half of people hospitalized for COVID-19 are shown to have abnormalities in lung function 12 weeks after the onset of symptoms.

Caption: DLCO: carbon monoxide diffusion capacity; TLC: total lung capacity; FEV1: forced expiratory volume in 1s; FVC: forced vital capacity; FEV1/FVC: ratio of forced expiratory volume in 1s and forced vital cavity; PEF: peak expiratory flow; ICU: intensive care unit; IMV: invasive mechanical ventilation; PFT: pulmonary function tests; FU: follow-up; KCO: transfer coefficient for carbon monoxide; LLN: lower limit of normal; AV: alveolar volume; HFNC: high-flow nasal cannula; LLN: lower limit of normal; CPAP: Continuous Positive Airway Pressure; FeNO: fractional exhaled nitric oxide. **Source:** Elaborated by the authors.

Table 1. Continued...

Author (Year)	Country	Type of study/ Level of evidence	Sample	Main results	Conclusion of the study
Bellan et al. (2021)[32]	Italy	Prospective observational cohort study/ Level 4	Total sample (n=200); 12 months after COVID-19; (n=196) received PFT; average age of 62; 61% (n=122) male.	Pulmonary function was assessed by DLCO, of which 49% (n=96) was below 80% of the predicted value. The most severe impairment (DLCO <60% of predicted) occurred in 10.2% (n=20).	Abnormal respiratory function persisted over 12 months, and female gender was strongly associated with DLCO <80% of predicted.
Bardakci et al. (2021)[18]	Turkey	Prospective observational case study/ Level 4	Total sample (n=65); 6 months after hospital discharge; (n=59) received PFT; 75.4% (n=49) male.	Pulmonary function was assessed by spirometry, 30.5% (n=18) patients had low FEV1 values, and 45.8% (n=27) patients had lower FVC values.	A decrease in the participants' spirometry measurements was detected in the sixth month.
Miwa et al. (2021)[19]	Japan	Retrospective cohort study/ Level 4	Total sample (n=17); 100 days after the onset of symptoms; average age of 63 years; 82% (n=14) male.	Pulmonary function was assessed by spirometry and DLCO. Of these, 47% (n=8) patients showed abnormal lung function, with DLCO <80% for 35% (n=6) patients; VC <80% for 24% (n=4); and abnormalities in FEV1, DLCO, and VC for 6% (n=1) patient.	Approximately half of the patients showed altered lung function at the 100-day follow-up. DLCO reduction represented the most common alteration.
Stockley et al. (2021)[22]	United Kingdom	Retrospective cohort study/ Level 4	Total sample (n=92); 3 months after hospital discharge; average age of 56 years; (n=64) male; 45 treated on the wards and 47 admitted to the ICU.	Pulmonary function was assessed by spirometry and body plethysmography. Pulmonary restriction occurred in 55.3% (n=52) and 34% (n=32) showed a reduction in TLCO. KCO was relatively preserved/ increased in most patients (78.1%) and significantly higher in ICU patients.	Both groups had similar changes in lung function at 3 months, but the ICU group had a statistically significant increase in KCO.
Stylemans et al. (2021)[27]	Belgium	Real-life Follow-up Study/Level 4	Total sample (n=220); 10 weeks after COVID 19 (FU1, n=92); after 6 months (FU2; (n=79) received TPF. FU2 was divided into restrictive (n=39) and non-restrictive (n=40); average age of 56 and 57 years; 74% (n=29) and 37% (n=29) were male, respectively.	Pulmonary function was assessed by spirometry. The restriction in patients with FU2 restriction improved significantly over time but remained unresolved at 6 months. The median TLC in FU2 in the two subgroups was 95% and 74% predicted, respectively. Both showed significant improvements in TLCO.	Lung function continues to improve up to 6 months after COVID-19 pneumonia.

Caption: DLCO: carbon monoxide diffusion capacity; TLC: total lung capacity; FEV1: forced expiratory volume in 1s; FVC: forced vital capacity; FEV1/FVC: ratio of forced expiratory volume in 1s and forced vital cavity; PEF: peak expiratory flow; ICU: intensive care unit; IMV: invasive mechanical ventilation; PFT: pulmonary function tests; FU: follow-up; KCO: transfer coefficient for carbon monoxide; LLN: lower limit of normal; AV: alveolar volume; HFNC: high-flow nasal cannula; LLN: lower limit of normal; CPAP: Continuous Positive Airway Pressure; FeNO: fractional exhaled nitric oxide. **Source:** Elaborated by the authors.

Table 1. Continued...

Author (Year)	Country	Type of study/ Level of evidence	Sample	Main results	Conclusion of the study
Lindahl et al. (2021)[35]	Finland	Cohort study/ Level 4	Total sample (n=20); 3 to 6 months after hospital discharge; average age of 56; 14 males.	Pulmonary function was measured using spirometry, IOS, and exhaled NO. One patient had a slightly reduced FEV1. 39% (n=7) had slightly increased FENO of 25 to 50 ppb, indicating potential inflammation.	The small airways do not appear to be affected in COVID-19 survivors three to six months after the initial infection.
Ordinola Navarro et al. (2021)[23]	Mexico	Retrospective cohort study/ Level 4	Total sample (n=115); less than 30 days after COVID-19 positive; average age of 40 years; 57% (n=65) female.	Pulmonary function was assessed by spirometry, with alterations in PFT present in 17% (n=20) of patients. All had restrictive disabilities.	There was a high proportion of restrictive impairment.
Smet et al. (2021)[26]	Belgium	Cross-sectional study/Level 4	Total sample (n=220); 10 weeks after COVID-19; average age of 55; 62% male.	Pulmonary function was measured by spirometry and TLCO. 28% (n=84) had restrictive lung function and TLCO below LLN in 22% of patients. The hospital stays of restrictive patients were longer, requiring ICU and evolving to VMI more often.	Restriction was the most prevalent lung function impairment 10 weeks after COVID-19 pneumonia.
Trinkmann t al. (2021)[10]	Germany	Prospective cross-sectional study/Level 4	Total sample (n=246); average age of 48 years; 41 males, divided into symptomatic (n=113) and asymptomatic (n=133) patients.	Pulmonary function was assessed by spirometry, body plethysmography, and TLCO. The symptomatic patients had an FEV1 of 17% of the predicted, a CV of 15% of the predicted, and a TLCO of 15% of the predicted.	Compromised lung function was common even in younger SARS convalescents with few comorbidities.
Lehmann et al. (2022)[12]	Austria	Prospective cohort study/ Level 4	Total sample (n=135); 6 months after COVID-19; 48.8% male; average age of 48.9 years; divided into (n=96) symptomatic and (n=39) asymptomatic.	Pulmonary function was measured by spirometry and DLCO. Patients with persistent respiratory symptoms after COVID-19 had significantly lower FVC, TLC, and DLCO compared to asymptomatic patients.	Patients with respiratory symptoms were younger and had more compromised lungs compared to asymptomatic patients.
Eroglu et al. (2022)[11]	Turkey	Single-center prospective observational study/Level 4	Total sample (n=219); 1st and 6th months after hospital discharge; average age of 49 years; 39.7% female; divided into respiratory distress (n=178) and asymptomatic (n=41).	Pulmonary function was measured by spirometry. A comparison between groups indicated lower PFT values in patients who described respiratory distress. Obstructive lung disease was found in 7 patients, restrictive disease in 15, and small airway obstruction in 28.	PFTs can reveal reduced lung function even after the non-critical course of the disease.

Caption: DLCO: carbon monoxide diffusion capacity; TLC: total lung capacity; FEV1: forced expiratory volume in 1s; FVC: forced vital capacity; FEV1/FVC: ratio of forced expiratory volume in 1s and forced vital cavity; PEF: peak expiratory flow; ICU: intensive care unit; IMV: invasive mechanical ventilation; PFT: pulmonary function tests; FU: follow-up; KCO: transfer coefficient for carbon monoxide; LLN: lower limit of normal; AV: alveolar volume; HFNC: high-flow nasal cannula; LLN: lower limit of normal; CPAP: Continuous Positive Airway Pressure; FeNO: fractional exhaled nitric oxide. **Source:** Elaborated by the authors.

Table 1. Continued...

Author (Year)	Country	Type of study/ Level of evidence	Sample	Main results	Conclusion of the study
Compagnone et al. (2020)[24]	Italy	Cohort study/ Level 4	Total sample (n=49); 3 months after hospital discharge; 41 received PFT; after 58 years; 89.8% male. All patients received an MV for an average of 11 days.	Pulmonary function was assessed by spirometry and DLCO. DLCO impairment <75% of predicted occurred in 59% (n=29) patients and 46% (n=19) patients exhibited restrictive impairment.	Mechanical ventilation seems to play a role in lung injury, with time on invasive mechanical ventilation emerging as an independent predictor of changes in PFT.
Van Gassel et al. (2021)[33]	Netherlands	Observational Study/Level 4	Total sample (n=48); mechanically ventilated within 3 months of hospital discharge; average age of 63 years; 68.8% male; 43 underwent Pulmonary Function Tests.	Pulmonary function was assessed by spirometry and DLCO. A decreased TLC and diffusion capacity were found in 23 and 36 participants, respectively.	Most of the COVID-19 survivors on invasive mechanical ventilation had abnormal pulmonary function tests with a prevalence in the reduction of DLCO and TLC.
Faverio et al. (2021)[25]	Italy	Prospective, multicenter observational cohort study/ Level 4	Total sample (n=287); 12 months after hospital discharge; divided into oxygen-only group (n=61); “CPAP” group (n=136); “IMV” group (n=90); 74% male; average age of 60.7 years.	Pulmonary function was assessed by body plethysmography, DLCO, and spirometry. DLCO showed a statistically significant improvement between 6 and 12 months only for the CPAP and IMV groups. Patients treated with prophylactic heparin showed a statistically significant trend (p=0.06) towards a reduction in DLCO. Only 20.7% had a restrictive pattern, with an obstructive pattern observed in only 3.8%, among whom the comorbidities were asthma (n=1), active smoking (n=1), and previous smoking (n=3).	DLCO was the most sensitive parameter for identifying pulmonary sequelae, showing improvement between 6 and 12 months.
Mancuzo et al. (2021)[20]	Brazil	Multicenter Prospective Descriptive and Analytical Study/ Level 4	Total sample of 242 patients; after 45 days in the hospital; average age of 59; 52.1% male; divided into 58.3% ward group; 28.9% did not require IMV (ICU/VM-) and 12.8% required IMV (ICU/VM+).	Pulmonary function was assessed using spirometry, DLCO, and body plethysmography. Only the ICU/VM+ group had a mean TLC <80% below predicted, as well as CVL and FVC below LLN. DLCO was below LLN in 21% of the cohort, but in 50% of the patients in the ICU/VM+ group, DLCO was significantly lower.	High frequency of changes in lung function in patients hospitalized for COVID-19, especially in those who underwent MV. The main changes were restrictive disorders and reduced DLCO.
Baldini et al. (2021)[21]	Argentina	Analytical cross-sectional observational study/Level 4	Total sample (n=55) patients; 8 to 12 weeks after COVID-19 diagnosis; 73% (n=40) male; average age of 54 years; 45% required MV; 38% required oxygen therapy; 16% were treated with a nasal cannula.	Pulmonary function was assessed using spirometry and DLCO. Spirometry revealed that 27.3% had ventilatory deficits suggesting restriction. DLCO showed that 51% of patients had values below 80% of predicted. DLCO, KCO, and AV values recorded gas exchange disturbances in 58% of the patients.	The presence of abnormal gas exchange is the main characteristic of patients with pulmonary sequelae from COVID-19.

Caption: DLCO: carbon monoxide diffusion capacity; TLC: total lung capacity; FEV1: forced expiratory volume in 1s; FVC: forced vital capacity; FEV1/FVC: ratio of forced expiratory volume in 1s and forced vital cavity; PEF: peak expiratory flow; ICU: intensive care unit; IMV: invasive mechanical ventilation; PFT: pulmonary function tests; FU: follow-up; KCO: transfer coefficient for carbon monoxide; LLN: lower limit of normal; AV: alveolar volume; HFNC: high-flow nasal cannula; LLN: lower limit of normal; CPAP: Continuous Positive Airway Pressure; FeNO: fractional exhaled nitric oxide. **Source:** Elaborated by the authors.

DISCUSSION

According to the studies featured in this research, symptomatic patients had altered PFTs compared to asymptomatic patients. The main deficits found involved a restrictive pattern and a decrease in carbon monoxide diffusing capacity (DLCO). These findings are consistent with the meta-analysis by Ahmed et al.[8], who reported that although lung function has shown signs of recovery over time, a reduction in DLCO may still occur in 11 to 45% of COVID-19 survivors after 12 months.

The studies included in this research[9-12] showed that as compared to asymptomatic patients, after the acute phase of the disease, symptomatic patients had spirometric changes in the variables forced vital capacity (FVC), total lung capacity (TLC), forced expiratory volume in the first second (FEV1), and vital capacity (VC). These findings were corroborated by Albu et al.[13], who reported that patients with persistent symptoms had impaired lung function, sleep disorders, cognitive impairment, and neurological sequelae. Lehmann et al.[12] also found that DLCO was significantly reduced in symptomatic patients compared to asymptomatic patients, confirming the impaired gas diffusion capacity in these patients.

Spirometry was predominant in terms of PFTs. Shah et al.14 reported that at least one pulmonary function variable was altered in 58% of patients. Other studies[14-21] found abnormalities in TLC, FVC, and FEV1, and Guler et al.[17] reported reductions in these variables, especially in severe or critically ill patients, compared to those with mild or moderate symptoms.

Several studies [22-25] have highlighted the restrictive pattern as one of the main pulmonary disorders, and it was observed in patients who had longer hospital stays and a greater need for invasive ventilation[26]. In Stylemans et al.[27], despite the significant improvement in the restrictive pattern after six months, there was no complete resolution of the alteration.

Fibrotic complications after COVID-19 could explain the restrictive spirometric changes. The most likely pathophysiology involves the recruitment and activation of fibroblasts, leading to pulmonary fibrosis and decreased parenchymal compliance[28].

Some studies have observed airflow obstruction[11,14,15]. Faverio et al.[25] reported that four of the 11 patients who presented this alteration were smokers, one of whom was active, and three were former smokers, as well as one patient with asthma as a comorbidity. The systematic review by Torres-Castro et al.[29] showed that 7% of patients had flow obstruction; however, the authors of the ICU studies used different cut-off points to define obstruction, which may have caused the results to be heterogeneous.

Other studies assessed DLCO[12,14-17,19-21,25,30-33], suggesting this to be the most sensitive measure for predicting pulmonary impairment. Guler et al.[17] and Mancuzo et al.[20] reported a strong correlation between the necessity and duration of mechanical ventilation and the lower DLCO in severe/critical patients.

Froidure et al.[30] and Bellan et al.[32] showed that patients of moderate to severe severity had a DLCO lower than 60% of predicted. Bellan et al.[32] found that 29.3% (n=27) of patients showed no significant improvement after 12 months of follow-up, with females strongly associated with a DLCO of less than 80%. In terms of pulmonary function, Faverio et al.[25] and Stylemans et al.[27] reported significant improvement in DLCO at 6 and 12 months of follow-up. Interestingly, Faverio et al.[25] observed that in participants treated with prophylactic heparin, the chances of DLCO alteration were reduced with a tendency towards statistical significance; however, further studies are still needed to substantiate this finding.

Steinbeis et al.[31] found reductions in TLC and FVC via body plethysmography in patients who required greater ventilatory support, which persisted for up to 12 months. Stockley et al.[22] confirmed a reduction in DLCO in 34% of patients and an increase in KCO (carbon monoxide transfer coefficient) in 78.1% of them. In the same study, although DLCO showed no difference between the groups admitted to the ward compared to the intensive care unit (ICU), there was a significant increase in KCO in patients admitted to the ICU, confirming Mo et al.[34] who observed a change in this same variable in critically ill patients compared to those with mild to moderate COVID-19.

Only one study by Lindahl et al.[35] assessed pulse oscillometry and extended measurements of exhaled nitric oxide (NO) and found that seven (39%) patients had slightly raised FENO (fractional exhaled nitric oxide), indicating a potential inflammation of the small airways. However, the study concluded that the small airways do not seem to be affected in COVID-19 survivors three to six months after the initial infection.

This integrative review was carried out based on low-level evidence studies, representing a limitation of the research. No extensive searches were carried out in other databases, nor was the list of references of the included studies checked. In addition, the absence of PFTs before COVID-19 in the patients assessed is also a limiting factor.

CONCLUSION

Even after hospital discharge, survivors of severe acute respiratory syndrome (SARS) caused by COVID-19 present changes in lung function. Symptomatic patients showed greater changes in PFTs than asymptomatic patients, suggesting that outpatient monitoring of these patients is required. DLCO showed the highest correlation with pulmonary alterations; however, further research is needed to statistically support this evidence and reduce heterogeneity between samples.

FUNDING

Nothing to declare.

CONFLICT OF INTEREST

Nothing to declare.

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