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The assessment of pulmonary impairment and clinical correlations in patients survived from SARS-CoV-2 infection

A 3-month follow-up study

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Abstract

During the coronavirus disease 2019 (COVID-19), the extent of pulmonary impairment associated with initial clinical parameters remained controversial. The notion is valuable for the recovery and prognosis of COVID-19. This study investigated the long-term pulmonary sequelae of severe acute respiratory syndrome coronavirus 2 infection, focusing on pulmonary function and clinical parameters during the 3 months after diagnosis. This is a retrospective, single-center observational study of 229 patients who tested positive for COVID-19 and made the 3rd-month follow-up visit between June 2020 and May 2021. The demographic and clinical characteristics of patients and treatment outcomes were recorded. The obstructive, restrictive pulmonary dysfunction patterns were analyzed to associate with the radiological findings, disease severity, and clinical parameters. The median age of the patients was 46 years. The most common residual symptoms were dyspnea (38%), dry cough (34.5%), and fatigue (29.4%). The obstructive and restrictive pulmonary dysfunction patterns were observed in 38.9% and 2.2% of the patients, respectively. Two-fifth of patients had some form of pulmonary dysfunction. A significant rate (35.8%) of patients had reduced diffusing capacity for carbon monoxide values. Obstructive pulmonary dysfunction was more common among older patients, whereas hypertension was more common among patients with extended hospital stays. Long-term pulmonary dysfunction was a frequent complication in patients recovering from severe severe acute respiratory syndrome coronavirus 2 infection. Understanding these long-term effects is essential for providing appropriate medical care for COVID-19 survivors. Therefore, further research is needed to elucidate the postinfection changes in the lung.

Abbreviations: COVID-19 = coronavirus disease 2019, CT = computed tomography, DLCO = diffusing capacity for carbon monoxide, FEV_1 = forced expiratory volume in 1 s, FVC = forced vital capacity, LoS = length of hospital stay, MEF25–75% = mid-expiratory flow 25–75%, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, TLC = total lung capacity.

Keywords: obstructive, pulmonary diseases, pulmonary function tests, respiratory system, restrictive, severe acute respiratory syndrome coronavirus 2

1. Introduction

Pulmonary impairment due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is a well-documented condition characterized by acute fibrinous and organizing pneumonia, resulting in extensive intra-alveolar fibrin deposition.[1] This acute injury, accompanied by damage to alveolar epithelial and endothelial cells, triggers secondary fibroproliferation, indicating chronic vascular and alveolar remodeling that can lead to pulmonary fibrosis and hypertension.[1] Patients often present with secondary consolidation of pneumonic lesions, manifesting as pulmonary diffusion dysfunction and restrictive or obstructive ventilatory defects after discharged from the hospital.[2] Fibrotic changes and varying degrees of interstitial thickening were reported; however, pulmonary interstitial fibrosis remains unresolved, warranting closer attention.[3,4]

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The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

This study was designed as a single-center, retrospective, observational study. The study protocol was approved by Acıbadem University and Acıbadem Healthcare Institutions, Medical Research Ethics Committee – ID number: 2023-14/479. The study was carried out in accordance with the principles outlined in the Declaration of Helsinki. Due to the retrospective design and unanimous nature of the collected information, written informed consent was not obtained from the patients.

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Recovery of patients with SARS-CoV-2 infection-associated pneumonia has been investigated in the context of short- and medium-term pulmonary sequelae.[3,5] Exertional dyspnea and fatigue due to impaired carbon monoxide diffusion capacity and reduced alveolar volume were frequently detected in the SARS-CoV-2 survivors.[3,6] However, the extent of cardiopulmonary improvement, influenced by disease-related factors, varies among patients.[3,4] It has been reported that the chronic fibrotic changes in residual pulmonary lesions tend to become symptomatic approximately 3 months after the diagnosis.[7] Thus, the duration of the recovery period, which can extend from months to years, emerges as a key factor resulting in variable outcomes.[1,4,6]

Given the functional impairment and persistence of radiological findings such as ground-glass opacities, crazy paving, and interstitial thickening after the diagnosis, several authors recommended that SARS-CoV-2 survivors should be closely followed up per optimal short- and midterm monitoring strategies involving in-person visits as early as 3 months after the diagnosis and by conducting respiratory investigations.[8,9] In sum, there is a compelling need to elucidate the extent and recovery of pulmonary impairment beyond the acute phase of SARS-CoV-2 infection. In light of this information, this study was carried out to assess the pulmonary functional status of SARS-CoV-2 survivors 3 months after diagnosis and its relationship with clinical parameters recorded at first admission.

2. Methods

2.1. Study design

This study was designed as a single-center, retrospective, observational study. The study protocol was approved by the local ethical committee (Acıbadem University and Acıbadem Healthcare Institutions, Medical Research Ethics Committee – ID number: 2023-14/479). The study was carried out in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was not obtained from the patients due to the study's retrospective design and the collected data's anonymity.

2.2. Population and sample

The study population consisted of all consecutive patients who tested positive for coronavirus disease 2019 (COVID-19) based on the real-time reverse transcription-polymerase chain reaction test conducted using the nasopharyngeal swab specimens and made the 3rd-month follow-up visit at Altunizade Acibadem Hospital, Department of Chest Diseases, Istanbul, Turkey, between June 2020 and May 2021. The study inclusion criteria were having had computed tomography (CT) scans at first admission and pulmonary function and diffusion tests at the 3rd-month follow-up visit. Patients who died during their stay in the hospital, who had coexisting pulmonary comorbidities, including chronic obstructive pulmonary disease, emphysema, pulmonary fibrosis, and/or bronchiectasis, who could not have spirometry due to chronic neurological disorders, pregnancy or breastfeeding, and patients with incomplete data were excluded from the study.

2.3. Follow-up procedures

All patients' oxygen saturation (SpO_2) levels were measured at the first admission, and thorax CT scans were performed. The imaging findings, including ground-glass opacity, crazy paving, consolidation, and signs suggestive of fibrosis, were recorded.[10] The severity of the lung involvement was graded using Michael et al's method described in the literature.[5,11] World Health Organization's ordinal scale of clinical improvement was used to stratify the patients as a) nonhospitalized patients without supplemental oxygen therapy, b) hospitalized patients without supplemental oxygen therapy, c) hospitalized patients with supplemental low-flow oxygen therapy, d) hospitalized patients with high-flow oxygen therapy and with or without temporary noninvasive ventilation, e) hospitalized patients with invasive mechanical ventilation, and f) hospitalized patients with extracorporeal membrane oxygenation.[2,12] Patients received treatments per the relevant national guidelines of the Turkish Ministry of Health. Per institutional policy, all patients were called to make outpatient clinic follow-up visits at 3-month intervals after discharge to evaluate the presence of pulmonary sequelae. At the 3rd-month follow-up visit, patients were checked for any residual symptoms and the type of residual symptoms, if any. A spirometry technician performed the pulmonary function tests using a spirometry device (Care Fusion, Jaeger, Höchberg, Germany). In this context, patients' forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), total vital capacity, FVC/FEV_1 ratio, and forced mid-expiratory flow were measured in accordance with the American Thoracic Society (ATS)–European Respiratory Society (ERS) guidelines.[13,14] A minimum of 3 measurements were performed for each variable of pulmonary function to obtain the best measurements and ensure the reproducibility of the data. All values were expressed as a percentage of predicted values adjusted for patients' gender, age, weight, and height.[15]

Patients' diffusing capacity for carbon monoxide (DLCO) ($mol \times min^{-1} \times kPa^{-1}$) values were measured using a plethysmography device (Carefusion, Jaeger, Höchberg, Germany) per the American Thoracic Society/European Respiratory Society guidelines,[5] corrected for hemoglobin and expressed as mL/min/mm Hg.[16,17] The predicted DLCO/alveolar lung volume (carbon monoxide transfer coefficient [KCO]) was also calculated using the relevant values.[6] The DLCO/KCO values measured as <80% of the predicted value were considered abnormal.[1,5,18,19]

The pulmonary function test results were interpreted according to the guidelines of the leading societies and experts. Accordingly, patients' final pulmonary statuses were assessed as normal, restrictive, or obstructive.[2,6,15–17] Cases with reduced FEV_1/FVC ratios were reported to be diagnosed with an obstructive respiratory pattern after using a bronchodilator.[20,21] Reduced FVC and/or FEV_1, normal FEV_1/FVC, and reduced total lung capacity (TLC) were deemed to indicate restrictive respiratory patterns.[20] FEV25–75% values below the lower limit of normal were deemed to indicate small airway disease.[21]

2.4. Data collection

The medical records of the patients were obtained from the hospital information system. Patients' demographic (age, gender) and clinical characteristics (body mass index, smoking history, comorbidities) were recorded. The treatment outcomes of the patients, including length of hospital stay (LoS), were obtained from their hospitalization charts. The results of the pulmonary function tests were also recorded.

2.5. Statistical analysis

Several statistical analysis methods were used to provide a comprehensive understanding of the pulmonary sequelae of SARS-CoV-2 infection and the influencing factors. In this context, the study's primary outcome was the rate of patients with pulmonary function test findings that suggest obstructive or restrictive pathologies. In contrast, the secondary outcomes included the correlations between pulmonary function test results, the severity of lung involvement, and clinical improvement parameters.

Kruskal–Wallis H test was used to compare the nonparametric numerical variables between the study groups, namely the patient group with normal pulmonary function (n = 135), the

patient group with obstructive pattern (n = 89), and the patient group with restrictive pattern (n = 5). In cases where significant differences were determined between the groups, post hoc analyses were conducted using the Dwass-Steel-Critchlow-Fligner test to pinpoint specific differences.

The Fisher-Freeman-Halton test was used to compare the categorical variables between the groups where the expected number of cells in RxC tables was < 5.

Statistical analyses were performed using Jamovi project 2.3.28.0 (Jamovi, version 2.3.28.0, 2023, retrieved from https://www.jamovi.org) and JASP 0.17.3 (Jeffreys' Amazing Statistics Program, version 0.17.3, 2023, retrieved from https://jasp-stats.org) software packages. Probability (*P*) statistics of ≤ .05 were deemed to indicate statistical significance.

3. Results

The median age of the 229 patients in the study sample was 46 years (with a range of 18–77). Almost two-thirds (59.0%) of the patients were male. The most common comorbidities observed in the study group was hypertension (n = 46, 20.1%) followed by diabetes mellitus (n = 35, 15.3%). Patients' demographic and clinical characteristics are given in Table 1.

Thorax CT scans of 32 (14.0%) patients taken at first admission were normal. Nevertheless, the ground-glass opacity was still the most frequent (66.4%) imaging finding. Based on CT findings, lung involvement was present in < 25% of the lobes of the lungs in most (87.8%) patients. Patients' imaging findings are given in Table 2.

The most common treatment method applied to hospitalized patients with supplemental low-flow oxygen therapy (n = 102, 44.5%), followed by hospitalized patients with high-flow oxygen therapy and with or without temporary noninvasive ventilation (n = 82, 35.8%) (Table 2).

The distribution of the residual symptoms identified during the 3rd-month follow-up visit is given in Table 3. Accordingly, more than half (56.3%) of the patients had at least one residual symptom. The most frequent residual symptom was dyspnea (38.0%), followed by dry cough (34.5%) and fatigue (29.4%) (Table 3).

Patients' pulmonary function test results and diffusion capacity values assessed during the 3rd-month follow-up visit are given in Figure 1. Accordingly, the median values of the predicted FEV_1/FVC ratio, mid-expiratory flow 25–75% (MEF25–75%), and DLCO were 81.0% [56.0–100.0], 84.0% [22.0–165.0], and 85.0% [45.0–305.0], respectively.

Based on the results of the measurements, we detected obstructive and restrictive patterns in 89 (38.9%) and 5 (2.2%) patients, respectively (Table 4). In addition, 82 (35.8%) patients had reduced DLCO values.

Significant correlations were found between parameters such as age, presence of hypertension, LoS, and disease severity assessed at the 3rd-month follow-up visit (Table 5). There was no significant correlation between patients' other demographic and clinical characteristics at admission and pulmonary dysfunction patterns ($P > .05$). The patients with obstructive pulmonary dysfunction were significantly older and hypertensive than those with restrictive and normal pulmonary dysfunction ($P = .004$ and $P = .021$, respectively). LoS was significantly longer in patients with restrictive pulmonary dysfunction patterns than in those with obstructive and normal pulmonary dysfunction ($P = .027$). There was also a significant difference in disease severity between the patient groups ($P = .002$) (Table 5).

Table 1

Demographic and clinical characteristics of the patients.

Parameter	Overall (n = 229)
Age (*year*)*	46.0 [18.0–77.0]
Sex†	
Female	94 (41.0)
Male	135 (59.0)
BMI (kg/m^2)*	27.0 [18.0–47.0]
Smoking†	50 (21.8)
Cigarette (*packages/year*)*	15.0 [1.0–50.0]
Comorbidities†	
Hypertension	46 (20.1)
Diabetes mellitus	35 (15.3)
Coronary artery disease	23 (10.0)
Malignancy	6 (2.6)

BMI = body mass index.
*Median [min–max].
†n (%).

4. Discussion

Our findings showed that almost two-fifths of the patients had obstructive or restrictive respiratory dysfunction in the 3rd-month follow-up after SARS-CoV-2 infection. Dyspnea and dry cough were seen in nearly one-third of the patients. The obstructive pulmonary dysfunction was more common than the restrictive pulmonary dysfunction. There was no significant difference in demographic and clinical characteristics between the patients with obstructive and restrictive pulmonary dysfunction patterns.

Several studies in the literature predicted the pulmonary sequelae up to 24 months after the SARS-CoV-2 infection.[4,6,7,12,18,20,22–25] Chen et al[2] reported the first 3 months after COVID-19 as the critical recovery period for diffusion capacity. Baldini et al[5] could not find any parameter that can significantly predict the pulmonary sequelae or any relationship between pulmonary sequelae and the severity of the disease 3 months after diagnosis, contrary to others who determined age, prolonged LoS, and endotracheal intubation as independent risk factors for abnormal pulmonary dysfunction 3 months after diagnosis.[1,9] Diffusion dysfunction of the lungs lasting > 6 months after SARS-CoV-2 infection may suggest long-term sequela in coronavirus pneumonia. However, the exact nature of the relationship between the underlying pathophysiology and postinfection symptoms remains unclear.[2] The first 3 months after being infected with SARS-CoV-2 are considered the most critical period for the resolution of post-COVID symptoms.[25] Therefore, patients' complaints, such as fatigue or muscle weakness, sleep difficulties, anxiety, or depression that occur after the expected recovery period, i.e., 3 to 6 months, should prompt physicians to investigate underlying pathologies.[24,26] Although long-term respiratory complaints and pathological changes are expected after SARS-CoV-2 infection, several studies with different sample characteristics and study designs have reported slow but progressive improvement in patients' pulmonary function test results.[25]

No significant difference was reported in the spirometry findings between the 6th and 24th months of follow-up or during the close follow-up period of 6 months after acute COVID-19. The recovery in the pulmonary functions was reportedly more prominent and faster during the 1st months of follow-up than between the 3rd and 6th months and vanished after the first 12 months.[2,4,6,8,27,28] Vander Sar-vander Brugge et al[25] observed that the resolution of most of the abnormalities, including dyspnea, DLCO measurements, and tomography findings, occurred within the first 3 months after diagnosis. The fact that COVID-19 sequelae are still unpredictable creates a need for accurate prognostic markers after discharge.[1] We suspect that adaptive respiratory mechanisms play a role in overcoming respiratory impairment in patients with previous SARS-CoV-2 infection, notably in the first 3 months.

There are conflicting outcomes on the results of spirometry and diffusion tests.[3] It has been reported that findings of impaired pulmonary function suggest restrictive lung functions rather than volume-adjusted diffusion capacity failure.[5–7,12,20,29] Functional abnormalities of the lungs in patients who recovered from severe COVID-19 in the 6th week after discharge were reportedly associated with the overexpression of inflammatory biomarkers, including neutrophil-to-lymphocyte ratio and C-reactive protein levels.[22] The pulmonary changes in the recovery period may be associated with chronic parenchymal and vascular damage depending on the degree of inflammation experienced in the acute period. We categorized the patients in our sample into normal, obstructive, and restrictive pulmonary dysfunction groups.[20,21,30] The rate of patients with obstructive or restrictive respiratory patterns at the 3rd-month follow-up (41.1%) was comparable to that reported in Frija-Masson study featuring the same follow-up interval.[1] However, the rate of patients with obstructive pathology was significantly higher than the rate of patients with restrictive pathology. We also detected significant decreases in FEV_1/FVC ratio, MEF25–75%, and DLCO values. The relatively low number of patients with invasive ventilation might be the reason for our study's low rate of patients with restrictive patterns. Parenchymal destruction and altered diffusion capacity may be unrelated pathological events.[6,9] All these changes may be related to sequential changes in lung parenchyma and vasculature after SARS-CoV-2 infection. Prospective studies are needed to clarify such complex relationships.

Isolated reduced DLCO values during the postinfection recovery period have been frequently considered an impaired indicator for persistent alveolar–capillary damage in SARS-CoV-2 patients.[1,2,6,7,12,20,28,31] Several authors considered DLCO

Table 2

Clinical characteristics of initial SARS-CoV-2 infection in the study group.

Parameter	Definition/explanation	Overall (n = 229)
Computed tomography findings*	Normal imaging	32 (14.0)
	Ground glass appearance	152 (66.4)
	Crazy paving	30 (13.1)
	Consolidation	15 (6.6)
Severity of lung involvement based on computed tomography*	Normal imaging	32 (14.0)
	<25%	169 (73.8)
	25%–<50%	24 (10.5)
	50%–<75%	4 (1.7)
	75%–100%	0 (0.0)
Length of hospital stay (*day*)†		10.0 [1.0–53.0]
Severity of disease*	NOO and NOH	45 (19.7)
	LFO	102 (44.5)
	HFO	82 (35.8)

HFO = hospitalized patients with high-flow oxygen therapy with or without temporary noninvasive ventilation, LFO = hospitalized patients with supplemental low-flow oxygen therapy, NOH = hospitalized patients without supplemental oxygen therapy, NOO = nonhospitalized patients without supplemental oxygen therapy, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
*n (%).
†Median [min–max].

Table 3

Oxygen saturation measurements and the distribution of the residual symptoms in the 3rd-month follow-up of the patients.

	Overall (n = 229)
Oxygen saturation (SpO_2) (%)*	98.0 [90.0–100.0]
Residual symptoms†	129 (56.3)
Dyspnea	87 (38.0)
Dry cough	79 (34.5)
Fatigue	67 (29.4)
Sleep disturbances	17 (7.4)

*Median [min–max].
†n (%).

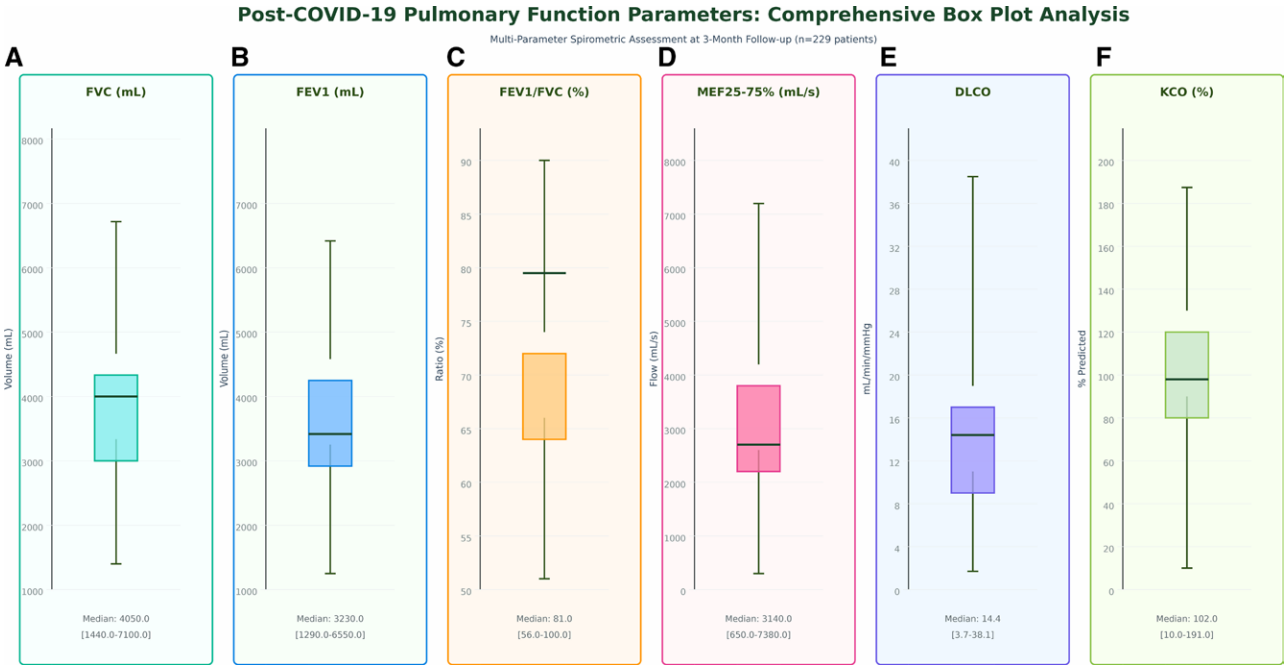

Figure 1. Multi-parameter pulmonary function assessment at 3-month post-COVID-19 follow-up. Box plot analysis demonstrating spirometric parameter distributions in COVID-19 survivors (n = 229). Each panel represents median values, interquartile ranges, and extreme distributions for: (A) Forced vital capacity (FVC, mL), (B) forced expiratory volume in 1 s (FEV_1, mL), (C) FEV_1/FVC ratio (%), (D) mid-expiratory flow 25–75% (MEF25–75%, mL/s), (E) diffusion capacity for carbon monoxide (DLCO, mL/min/mm Hg), and (F) transfer coefficient (KCO, %). Data illustrate heterogeneous respiratory recovery patterns with significant inter-parameter variability, supporting individualized therapeutic strategies in post-COVID respiratory sequelae management. Whiskers represent minimum-maximum ranges; boxes denote 25th to 75th percentiles; horizontal lines indicate median values.

values < 80% of the predicted value abnormal.[1,5,18,20] It has been shown that mechanical ventilation led to significantly lower TLC% and DLCO% values than continuous positive airway pressure or only oxygen.[3] It has also been stated that restriction-related changes in diffusion capacity were due to invasive ventilation or disease severity.[1,6] Then again, an average value of DLCO/KCO reportedly indicated normal diffusing capacity and membrane function in the alveolar units participating in gas exchange, even in patients with severe-to-extremely-severe radiological pneumonia.[7] In this study, almost one-third of the patients had reduced DLCO. A reduction in DLCO may also occur in patients without restrictive or obstructive respiratory dysfunction due to impaired gas exchange efficiency. Interstitial lung disease characterized by alveolar destruction, alveolar thickening, ventilation/perfusion mismatch without mechanical abnormalities, or pulmonary vascular diseases might be the underlying pathologies in patients with long-standing respiratory problems.[20] Therefore, we think that low DLCO values may be of more critical importance than the importance attributed to them. Hence, studies with more extended follow-up periods are needed to shed light on the subject.

Table 4

Final evaluation of the respiratory system in the 3rd-month follow-up.

	Overall (n = 229)
Normal pulmonary function*	135 (59.0)
Obstructive pattern*	89 (38.9)
Restrictive pattern*	5 (2.2)
Reduced DLCO (<80%)*	82 (35.8)

DLCO = diffusing capacity for carbon monoxide.
*n (%).

The literature data on the correlation between pulmonary function test results and residual CT lesions are contradictory.[1,7,9,12] Tuncer et al[32] investigated the correlation between persistent symptoms and pulmonary sequelae indicated by chest CT. They concluded that patients with post-COVID CT findings were more prone to long-term pulmonary dysfunctions than those without post-COVID CT findings. Impaired pulmonary function was significantly associated with higher CT scores and impaired TLC and DLCO values at the 3rd-month follow-up.[33] The differences in patient characteristics, such as severity of inflammation or mechanical ventilation use, might be the reason for the lack of correlations between the radiological abnormalities and the degree of pulmonary impairment.

Benedetto et al[20] reported that a restrictive ventilatory defect associated with impaired gas exchange led to patient-centered outcomes, including exertional and daily-life dyspnea and reduced exercise capacity. Other studies, including ours, found that dyspnea still existed in more than half of the patients.[3,12,34] Dyspnea was the most common complaint in our study group, even though the rate of patients with restrictive pulmonary dysfunction was considerably lower than those reported in the literature. Dyspnea, which was common in the patients included in our study, may also be caused by other factors, such as anemia.

The study's primary limitation was its retrospective, single-center design which may have introduced selection bias or limited the generalizability of the results to the broader population. The relatively short follow-up period may be deemed another limitation as it may have hindered reaching more robust and reliable conclusions regarding long-term outcomes. In addition, the lack of patients' pulmonary function data in the pre-COVID-19 period may be considered another limitation as it prevented analyzing the longitudinal lung changes and assessing the rate of patients with impaired lung function directly

Table 5

Association between the demographic and initial clinical characteristics and the respiratory pattern in the 3rd-month follow-up.

	Normal pulmonary function (n = 135)	Obstructive pattern (n = 89)	Restrictive pattern (n = 5)	*P*
Age (*year*)*	43.0 [18.0–73.0]	50.0 [24.0–77.0]	42.0 [34.0–62.0]	**.004**
Sex†				
Female	55 (40.7)	37 (41.6)	2 (40.0)	.999
Male	80 (59.3)	52 (58.4)	3 (60.0)	
BMI (kg/m^2)*	27.0 [18.0–47.0]	26.8 [19.3–43.3]	26.0 [25.0–27.0]	.756
Smoking†	25 (18.5)	25 (28.1)	0 (0.0)	.147
Cigarette (*packages/year*)*	0.0 [0.0–35.0]	0.0 [0.0–50.0]	0.0 [0.0–0.0]	.147
Comorbidities†				
Hypertension	20 (14.8)	26 (29.2)	0 (0.0)	**.021**
Diabetes mellitus	20 (14.8)	15 (16.9)	0 (0.0)	.816
Coronary artery disease	14 (10.4)	8 (9.0)	1 (20.0)	.512
Malignancy	3 (2.2)	3 (3.4)	0 (0.0)	.740
Computed tomography findings†				
Normal imaging	17 (12.6)	15 (16.9)	0 (0.0)	.293
Ground glass appearance	92 (68.1)	55 (61.8)	5 (100.0)	
Crazy paving	14 (10.4)	16 (18.0)	0 (0.0)	
Consolidation	12 (8.9)	3 (3.4)	0 (0.0)	
Severity of lung involvement based on computed tomography†				
Normal	17 (12.6)	15 (16.9)	0 (0.0)	.450
<25%	97 (71.9)	67 (75.3)	5 (100.0)	
25%–<50%	17 (12.6)	7 (7.9)	0 (0.0)	
50%–<75%	4 (3.0)	0 (0.0)	0 (0.0)	
Length of hospital stay (*day*)*	10.0 [1.0–53.0]	9.0 [3.0–33.0]	24.0 [8.0–42.0]	**.027**
Severity of disease†				
NOH + NOO	34 (25.2)	11 (12.4)	0 (0.0)	**.002**
LFO	54 (40.0)	48 (53.9)	0 (0.0)	
HFO	47 (34.8)	30 (33.7)	5 (100.0)	

The bold value indicate statistically significant $P < .05$.BMI = body mass index, HFO = Hospitalized patients with high-flow oxygen therapy with or without temporary noninvasive ventilation, LFO = hospitalized patients with supplemental low-flow oxygen therapy, NOH = hospitalized patients without supplemental oxygen therapy, NOO = nonhospitalized patients without supplemental oxygen therapy.
*Median [min–max].
†n (%).

attributable to SARS-CoV2 infection. The fact that we only evaluated the pulmonary changes contrary to the studies[20,25,35] that investigated cardiopulmonary system abnormalities following SARS-CoV-2 infection may be considered another limitation. Lastly, the lack of data on cardiac function changes was also a limitation. Future research could benefit from a multicenter, prospective design that includes patients with baseline pulmonary assessments. Extended follow-up periods combined with integrated cardio-pulmonary evaluations would be beneficial as well in offering a more comprehensive understanding of long-term outcomes.

5. Conclusion

In conclusion, we established that pulmonary dysfunction is a common consequence of SARS-CoV-2 infection. Of the spirometric pulmonary and lung diffusion parameters we investigated, FEV_1/FVC ratio, MEF25–75%, and DLCO values were the most commonly detected abnormalities of the pulmonary sequelae after SARS-CoV-2 infection. More comprehensive studies are needed to determine the optimum follow-up period to determine the extent of improvement in lung functions and the treatment methods that can be used to ensure improvement in lung functions.

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