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Oximetry at admission as a predictor of tomographic and functional impairment after 3–6 months in hospitalized patients with COVID-19

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Abstract

Objective: To investigate characteristics that may be associated with radiologic and functional findings following discharge in patients with severe coronavirus disease 2019 (COVID-19).

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Methods: This single-center, prospective, observational cohort study comprised patients aged >18 years who were hospitalized with COVID-19 pneumonia, between May and October 2020. After 3 to 6 months of discharge, patients were clinically evaluated and underwent spirometry, a 6-minute walk test (6MWT), and chest computed tomography (CT). Statistical analysis was performed using association and correlation tests.
Results: A total of 134 patients were included (25/114 [22%] were admitted with severe hypoxemia). On the follow-up chest CT, 29/92 (32%) had no abnormalities, regardless of the severity of the initial involvement, and the mean 6MWT distance was 447 m. Patients with desaturation on admission had an increased risk of remaining CT abnormalities: patients with SpO_2 between 88 and 92% had a 4.0-fold risk, and those with $SpO_2 < 88\%$ had a 6.2-fold risk. The group with $SpO_2 < 88\%$ also walked shorter distances than patients with SpO_2 between 88 and 92%.
Conclusion: Initial hypoxemia was found to be a good predictor of persistent radiological abnormalities in follow-up and was associated with low performance in 6MWT.

Keywords
COVID-19, lung function, oximetry, 6MWT, chest CT, hypoxemia

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Introduction

Since December 2019, the coronavirus disease 2019 (COVID-19) pandemic has increased in magnitude, with increased morbidity and mortality rates, becoming a public health emergency with a global impact. A total of 548 066 834 confirmed cases and 6 336 909 deaths had been recorded worldwide by 1 July 2022, and in Brazil, alarming numbers were recorded, with 32 358 018 confirmed cases, including 671 416 deaths by this time.[1]

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) infection exhibits great variability in clinical presentation, from the asymptomatic patient to patients with severe pneumonia that can progress to respiratory distress syndrome and death.[2–5] Thus far, the extent to which the initial severity of COVID-19 impacts or predicts the persistence of structural and functional abnormalities in the respiratory system remains unclear.

Most previously published studies on the follow-up of post-covid patients have focused on evaluation until the 6th or 12th month after hospital discharge.[6–16] Some studies have shown that individuals with severe disease may still present with radiological changes, such as mosaic attenuation, thickening of interlobular septa and reticulations, and functional abnormalities, such as impairment in diffusing capacity of the lungs for carbon monoxide (DLCO), walking distance in the 6-minute walk test (6MWT), and total lung capacity.[6–16]

The present study aimed to investigate whether there were correlations between a patient's baseline clinical and demographic data, hospital admission features, and ventilatory management with the persistence of tomographic, lung function, and functional capacity (6MWT and dyspnea assessment) impairment after 3–6 months from hospital discharge in patients with moderate to severe COVID-19.

Patients and methods

Study population

This single-center, prospective, observational cohort study included consecutive

patients aged >18 years who were admitted to Hospital de Clínicas da Unicamp (Campinas, São Paulo, Brazil) for treatment of COVID-19 pneumonia, with a diagnosis confirmed by real-time polymerase chain reaction, in the period between May and October 2020. The Research Ethics Committee of the Faculty of Medical Sciences of University of Campinas approved this study (ruling 31783420.7.0000.5404). Patients who did not attend a follow-up assessment until 3 months after hospital discharge, those who declined to participate, and those who were elderly or had comorbidities or disabilities that prevented them from performing the functional tests were excluded.

Patients were evaluated in outpatient care and invited to be followed until 3 months after hospital discharge. Those who agreed to participate provided written informed consent prior to study inclusion. At this time, clinical evaluation, spirometry, and 6MWT were performed, and a high-resolution chest computed tomography (CT) scan was scheduled. All patient details were de-identified for the study, and the reporting of this study conforms to STROBE guidelines.[17]

Hospitalization data were collected by reviewing online medical records. All medical procedures were performed by the attending team. Saturation of peripheral oxygen (SpO_2) was assessed by pulse oximetry at hospital admission. Two experienced pulmonologists (PV and MP) evaluated CT scans performed during hospitalization and follow-up, and doubtful cases were resolved by consensus. The severity stratification of initial CT results was based on Radiological Society of North America (RSNA) guidelines.[18] CT images were classified, by subjective visual analysis, as typical for COVID-19, atypical, indeterminate, and negative (no abnormalities). The degree of lung involvement on CT was classified as mild (<25%), moderate (between 25 and 50%), or severe (>50%). For statistical analysis, follow-up high resolution CT (CT performed at 3–6 months following discharge) was classified as normal or abnormal.

Physical therapists (BV, LR, LO, and AL) performed the 6MWT according to international recommendations,[19] in a 30-m corridor, with an assessment of vital signs (SpO_2, heart rate, and respiratory rate) and Borg scale immediately prior to testing and at the end of the 6MWT. The distance walked (6MWD) was determined in m, and the predicted distance was calculated according to the equation published for the Brazilian population.[20]

Spirometry was performed in a large, ventilated room (by WV), with all necessary precautions to ensure the safety of the patient and health professionals, according to the American Thoracic Society/European Respiratory Society (ATS/ERS) recommendations.[21] The portable Easy One Word® spirometer was used, and Brazilian reference values were adopted.[22] Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and FEV1/FVC ratio were evaluated. Ventilatory disorders were classified as obstructive ventilatory disorder (OVD): FEV1/FVC ratio <0.7 or below the lower limit of normality (LLN); obstructive ventilatory disorder with reduced FVC (FVC < LLN); probable restrictive ventilatory disorder (RVD): FVC < LLN and FEV1/FVC ratio >0.7; and normal spirometry.

Data and statistical analyses

Test results and collected data were recorded and stored in the Research Electronic Data Capture online platform (REDCap; https://www.project-redcap.org/).[23] Data were analysed using Jamovi software, version 2.2 (The Jamovi project [2021], https://www.jamovi.org) and R software, version 4.0 (https://cran.r-project.org).

Categorical data are presented as absolute and percentage values. Quantitative

data are presented as mean ± SD and median (depending on normality of distribution). The normality of data distribution was assessed with Shapiro–Wilk test, and a sample size of 134 participants was considered suitable considering an alpha error = 0.05, beta error = 0.8, and r = 0.40. A P value <0.05 was considered statistically significant.

Patients were grouped according to hospital admission SpO_2 (<88%, 88–92% or ≥93%); use of mechanical ventilation (yes or no); admission to the intensive care unit (ICU) during hospital stay (yes or no); severity of lung involvement at admission according to CT (<25%, 25–50% or >50%); CT results at 3–6 months following discharge (normal or abnormal); modified Medical Research Council (mMRC) dyspnea scale classification after discharge (mMRC 0–1 or mMRC ≥2); and FVC (<LLN or >LLN). Between-group differences in categorical variables were compared using χ^2-test, whereas Student's unpaired t-test and Mann–Whitney U-test were used to compare parametric and non-parametric continuous variables, respectively. Bivariate correlations between variables were examined using Pearson's correlation coefficient for normally distributed data and Spearman's rank correlation coefficient for non-normal or categorical data. Given that age, sex, presence of comorbidities (hypertension, respiratory disease, diabetes, and obesity), ICU hospitalization, use of mechanical ventilation, SpO_2 on admission, mMRC dyspnea scale after discharge, abnormal CT at 3–6 months following discharge, FVC < LLN and 6MWD were considered to be the major parameters, only these parameters were evaluated in correlation analysis.

The independent predictors of selected parameters were evaluated by stepwise regression analysis. Multiple logistic regression with stepwise selection of the dependent variables to be included in the models was performed to identify independent associations between SpO_2 and CT at 3–6 months. Given the high collinearity among the parameters, only SpO_2 and age variables were included at a time in the regression model.

Analysis of variance (ANOVA) was used to compare 6MWD between patients grouped by SpO_2 (<88%, 88–92%, or ≥93%). Variables were considered for ANOVA after analysis with histograms, normality plots, and residual scatter plots that tested for linearity, normality, and variance. Tukey's post-hoc test was used to identify which SpO_2 category was more closely associated with shorter distances in the 6MWT.

Results

A total of 469 patients with COVID-19 viral pneumonia were admitted to the Hospital de Clínicas, State University of Campinas between 1 May and 31 October 2020. Of these patients, 134 were included in the present study (Figure 1), 60.4% of whom (81 patients) were male. The mean age of the study population was 55.7 years, mean body mass index (BMI) was 31.1 kg/m^2, and patients were mostly white (95/120 [79%]). Ninety-three percent (125/134) of the patients had comorbidities, the main ones being hypertension (46%), obesity (40%), and type 2 diabetes mellitus (29%), and (35.6%) were former smokers. Medications were used by 75% of the patients, and the most used was the angiotensin receptor blockers class (35/134 patients [26%]). Demographic and clinical data are summarised in Table 1.

Patients were admitted 8.8 ± 4.1 days after symptom onset; 33/118 (28%) were admitted to the ICU. The main symptoms reported were dyspnea in 96 cases (72%), cough in 88 (66%), fever in 73 (54%), and myalgia in 51 (38%). At admission, 33/90 (37%) presented with tachycardia, 80/98 (82%)

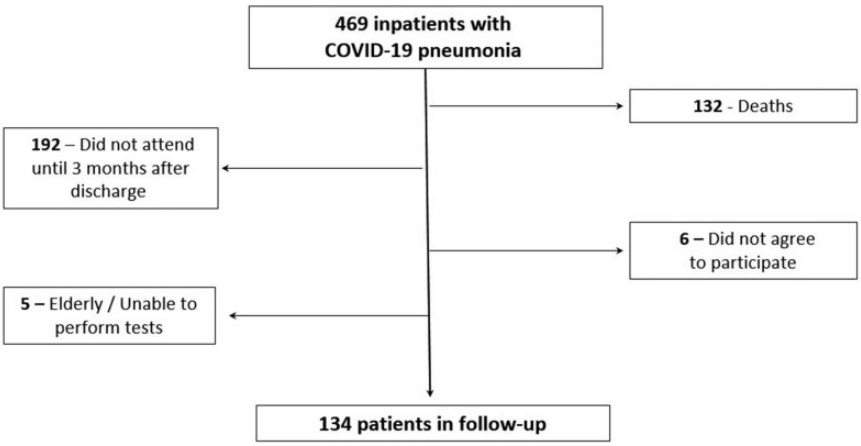

Figure 1. Flow diagram showing patient selection for inclusion in the cohort study.

Table 1. Clinical and demographic characteristics of patients who were hospitalized with coronavirus disease 2019 pneumonia.

Variable	Study population ($n = 134$)
Sex	
Male	81 (60.4)
Age, years	55.7 ± 13.3
Ethnicity*	
White	95 (79)
Afro-descendants	25 (21)
Not available	14 (10)
Comorbidities	125 (93)
Hypertension	62 (46)
Obesity	53 (40)
Diabetes mellitus	39 (29)
Respiratory disease	
Asthma	9 (7)
COPD	3 (2)
PH	1 (1)
Smoking ($n = 104$)*	
Active	0 (0)
Former	37 (35.6)
Never smoked	67 (64.4)
Body mass index	31.1 ± 6.5
Medications in use	101 (75)
ARB	35 (26)
ACEI	13 (10)
Insulin	9 (7)

Data presented as *n* (%) prevalence or mean ± SD.
ARB, angiotensin receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; COPD, chronic obstructive pulmonary disease; PH, pulmonary hypertension.
*Full data was not available on medical records.

with tachypnea, and 25/114 (22%) with $SpO_2 < 88\%$. The mean length of hospital stay was 15.2 ± 15.8 days, and ICU stay was 17 ± 16.4 days. Thirty percent of patients (33/109 who received oxygen) remained on mechanical ventilation at some point during hospitalization, for a mean duration of 15.4 ± 11.0 days, 20 of whom (61%) were ventilated in prone position (Table 2).

On admission, 132 CT scans were performed, of which, 124 (94%) were typical in appearance. Ground-glass findings were observed in 124 of the typical CTs (100%), consolidations in 92 (74%), and crazy paving in 48 (39%). Bilateral alterations were present in 118 (95%), peripheral distribution in 69 (56%), and 89 (72%) had 25% or greater involvement of the lung parenchyma. The mean time between hospital admission and follow-up CT was 127 ± 33.9 days. At follow-up, 92 CT scans were performed between 3 and 6 months following hospital discharge, with 29 (32%) of the scans already free of changes attributable to COVID-19 pneumonia. The radiological findings are summarised in Table 3.

In the follow-up clinical evaluation, 61 patients had dyspnea, of whom, 26 patients

Table 2. Hospital admission characteristics and hospital care in patients who were hospitalized with coronavirus disease 2019 pneumonia.

Variable	Study population
Destination on admission ($n = 118$)*	
ICU	33 (28)
Ward	85 (72)
Hospitalization from symptom onset (days)	8.8 ± 4.1
Initial symptom	
Dyspnea	96 (72)
Cough	88 (66)
Fever	73 (54)
Myalgia	51 (38)
Vital signs on admission	
HR ($n = 90$)*	
≤99 bpm	57 (63)
> 100 bpm	33 (37)
RR ($n = 98$)*	
≤20 rpm	18 (18)
21–30 rpm	63 (64)
>30 rpm	17 (17)
Peripheral oxygen saturation ($n = 114$)*	
<88%	25 (22)
88–92%	59 (52)
≥93%	30 (26)
ICU hospitalization ($n = 117$)*	53 (45)
Days in ICU	17.1 ± 16.4
Days hospitalized ($n = 117$)	15.2 ± 15.8
Oxygen supply ($n = 109$)*	
Catheter <2 L/min	20 (18)
Catheter 3–5 L/min	35 (32)
Non-rebreathing mask	21 (19)
Mechanical ventilation	33 (30)
Days on MV ($n = 33$)	15.4 ± 11.0
Pronation ($n = 115$)*	
No	47 (41)
Yes, 'awake prone'	48 (42)
Yes, on MV	20 (17)
Treatment ($n = 115$)*	
Prophylactic enoxaparin	85 (74)
Corticosteroids	101 (88)

Data presented as *n* (%) prevalence or mean ± SD.
ICU, intensive care unit; HR, heart rate; RR, respiratory rate; MV, mechanical ventilation.
*Full data was not available on medical records.

(43%) had an mMRC dyspnea classification ≥2. Pulmonary function tests were performed at a mean of 139 ± 26.8 days after discharge from hospital. Of the 101 follow-up spirometries performed, 52 patients (51%) had possible restrictive lung disorder, and 40 (40%) were within the normal range. In the 6MWT, the mean walking distance was 447 m. Results are summarised in Table 4.

In logistic regression analysis, hospital admission SpO_2 levels <88% and 88–92% were found to be predictors of the persistence of CT abnormalities at follow-up between 3 and 6 months after discharge, regardless of age (odds ratio [OR] 6.20; 95% confidence interval [CI] 1.37, 28.16) and (OR 4.03; 95% CI 1.19, 13.63), respectively (Table 5). Model 1, containing only categorized SpO_2 levels was significant ($X^2 = 9.09$; $P < 0.05$; Nagelkerke's $R^2 = 0.148$), and model 2, containing categorized SpO_2 levels and age, was superior to model 1 in predicting persistence of tomographic changes at 3–6 months after discharge ($X^2 = 16.85$; $P < 0.001$; Nagelkerke's $R^2 = 0.263$).

Regarding the 6MWD, ANOVA and Tukey's post hoc analysis showed that patients with $SpO_2 < 88\%$ on admission walked shorter distances in the 6MWT (379 ± 120.2 m) than those who were admitted with SpO_2 between 88 and 92% (471 ± 103.2 m; $P = 0.028$).

Patients who used mechanical ventilation had a lower median 6MWD compared with those who did not use mechanical ventilation (419 m versus 471 m, $P < 0.05$; Mann–Whitney *U*-test), and lower % of predicted distance (76.9% versus 86.1%, Iwama et al.[20] reference values; $P < 0.05$; Mann–Whitney *U*-test). In addition, patients with abnormal CT at 3–6 months following discharge presented with lower median 6MWD

Table 3. Computed tomography (CT) aspects of hospitalization and follow-up (3–6 months) after discharge in patients who were hospitalized with coronavirus disease 2019 pneumonia.

Variable	Study population	
Chest CT	Admission CT ($n = 132$)	Follow-up CT ($n = 92$)
Typical appearance	124/132 (94)	58/92 (63)
Ground glass opacities	124 (100)	58 (100)
Consolidations	92 (74)	3 (5)
Crazy paving	48 (39)	1 (2)
Inverted halo	3 (2)	13 (22)
Peripheral distribution	69 (56)	45 (78)
Bilateral distribution	118 (95)	52 (90)
Multifocal distribution	62 (50)	8 (14)
Lung involvement <25%	35 (28)	52 (90)
Lung involvement 25–50%	52 (42)	6 (10)
Lung involvement >50%	37 (30)	0 (0)
Indeterminate appearance	4/132 (3)	1/92 (1)
Atypical appearance	2/132 (2)	4/92 (4)
Negative for pneumonia	2/132 (2)	29/92 (32)
Pulmonary thromboembolism	10/41 (24)	–

Data presented as *n* (%) prevalence.

than those with normal CT (442.3 m versus 497.6 m; $P < 0.05$).

There was a positive and moderate correlation between the severity of initial CT involvement and longer ICU stay (<25% [10.5 ± 7.99 days], 25–50% [9.24 ± 6.47 days], and >50% [23.6 ± 19.6 days]; $r = 0.42$, $P = 0.002$; Spearman's rank correlation coefficient). In addition, the number of days using mechanical ventilation, days in the ICU, and mMRC dyspnea scale score after discharge were each found to moderately inversely correlate with the 6MWD ($\rho = -0.434$; $P < 0.05$; $\rho = -0.489$; $P < 0.05$; and $\rho = -0.476$; $P < 0.001$, respectively; Spearman's rank correlation coefficient).

The severity of CT involvement at admission was not found to be associated with the persistence of abnormal CT scans at 3–6 months following discharge ($P = 0.87$; χ^2-test) or with FVC < LLN on spirometry ($P = 0.15$; χ^2-test). In terms of lung function, there was no association between desaturation on admission and FVC < LLN during follow-up ($P = 0.219$), or between abnormal CT at 3–6 months following discharge and possible restrictive ventilatory disorder ($P = 0.215$).

Additional data analyses are presented in Supplementary Figure 1 and 2 (admission SpO_2 levels versus follow-up CT and follow-up CT according to patient sex, respectively), Supplementary Graphs 1–5 (6MWD analyses), and Supplementary Table 1 (association between 6MWD and FVC < LLN).

Discussion

The medium and long-term consequences related to hospitalization for severe COVID-19 are not yet fully known, and risk factors associated with persistent pulmonary structural and functional changes are only recently being described. Patients who are more critically

Table 4. Follow-up lung functional tests (3–6 months) after discharge in patients who were hospitalized with coronavirus disease 2019 pneumonia.

Variable		Study population ($n = 134$)
Dyspnea after discharge		61 (46)
mMRC scale score 0–1		35 (57)
mMRC scale score ≥2		26 (43)
Spirometry ($n = 101$)		
OVD with reduced FVC		5 (5)
OVD		4 (4)
Possible RVD		52 (51)
Normal		40 (40)
FVC (L)		3.1 ± 0.9
FVC (%)		79.5 ± 15.8
FEV1 (L)		2.5 ± 0.8
FEV1 (%)		80.7 ± 17.9
FEV1/FVC		80.4 ± 7.8
6MWT ($n = 90$)	Rest	6th minute
SpO_2 (%)	97.3 ± 1.5	95.4 ± 3.4
RR (rpm)	17.0 ± 3.5	22.7 ± 4.6
Borg	0.7 ± 1.3	2.9 ± 2.7
Delta SpO_2 (%)		–2.0 ± 3.0
Walked distance (m)		447 ± 114.2
% of predicted distance (Iwama et al.[20])		80.4 ± 20.0
Delta HR		25.8 ± 15.5

Data presented as *n* (%) prevalence or mean ± SD.
OVD, obstructive ventilatory disorder; RVD, possible restrictive ventilatory disorder; FVC, forced vital capacity; FEV1, forced expiratory volume in one second; 6MWT, 6-minute walking test; HR, heart rate; RR, respiratory rate; mMRC, modified Medical Research Council.

Table 5. Logistic regression analysis.

Predictor	Estimate	SE	Z	Statistical significance	OR	95% CI Lower	95% CI Upper
Intercept	–3.711	1.401	–2.65	$P = 0.008$	0.024	0.001	0.381
SpO_2 on admission							
<88% – ≥93%	1.826	0.772	2.37	$P = 0.018$	**6.208**	1.368	28.165
88–92% – ≥93%	1.393	0.622	2.24	$P = 0.025$	**4.028**	1.191	13.628
Age	0.060	0.023	2.59	$P = 0.010$	1.062	1.014	1.112

Estimates represent the log odds of 'CT at 3–6 months = abnormal' versus 'CT at 3–6 months = normal'.
SpO_2, saturation of peripheral oxygen; OR, odds ratio; CI, confidence interval.

ill seem to be more likely to have residual symptoms, and physiological, radiological, and respiratory functional changes,[14,15] similar to findings previously described in the follow-up of patients hospitalized with severe acute respiratory syndrome (SARS).[24]

The demographic and clinical characteristics of the current patients – mostly men in

their 50s, with comorbidities and a mean BMI of 31 kg/m^2 – were compatible with a large population-based observational study conducted in the Brazilian population during the same period.[25]

At hospital admission, most of the current patients exhibited severe CT involvement, with 42% showing impairment between 25 and 50%, and 30% of patients exhibiting greater than 50% involvement, similar to admission CT findings presented by another Brazilian prospective study.[26] Nevertheless, at follow-up CT after discharge, 32% of patients already had normal CT, regardless of the severity of initial tomographic involvement. This rate of resolution of CT involvement was similar to findings of two other prospective cohort studies that performed CT within 6 months of hospitalization and showed normal CTs in 30–38% of the scans.[9,27] In the current study, abnormal follow-up CT and dyspnea after discharge were found to be correlated with shorter 6MWD, which may reveal a medium-term lower exercise capacity and daily activities performance impairment. The further clinical impact of these findings require clarification with long-term follow-up studies.

Corroborating the finding of complete radiological recovery in almost one-third of the patients, approximately 40% of the spirometries performed in the study were found to be normal. These results are similar to those found in previously published studies with 6- and 12-month follow-ups, in which the patients had good functional and physical capacity recovery in the long term.[14,15] In the 6MWT, the mean walking distance was 447 m, which corresponded to 80.4% of the mean predicted value for the Brazilian population, and was similar to the mean distances reported by other studies, of between 400 m and 585 m by the 6th month.[14,15,26–30]

A very crucial finding was the evidence that low SpO_2 on admission was correlated with the persistence of CT changes at follow-up, as well as functional abnormalities. Patients who were admitted with SpO_2 <88% were 6.2 times more likely to persist with tomographic changes at 3–6 months after hospital discharge compared with patients who arrived with SpO_2 ≥93%. Furthermore, regardless of age, SpO_2 between 88 and 92% was also a significant predictor of persistent tomographic changes: patients who arrived with SpO_2 between 88 and 92% were 4.03 times more likely to persist with CT abnormalities at 3–6 months following discharge. This finding underscores the already established importance of the noninvasive measurement of oxygenation in other acute respiratory failure settings. This point has become even more relevant after observing the silent hypoxia that occurs in patients with COVID-19,[31] which can often delay the diagnosis and consequently the management of acute respiratory failure.

Several possible explanations have been considered for the occurrence of silent hypoxia in patients with COVID-19, including reduced patient perception due to the absence of dyspnea associated with a hypoxic condition with normal $PaCO_2$.[31–33] In addition, the virus may exert a direct action on the nervous system and brain, causing changes in the mechanisms responsible for regulating respiration.[33] There is also some evidence that the virus acts on blood vessels and endothelial cells, causing loss of hypoxic vasoconstriction,[34] which would lead to hyperperfusion of compromised lung regions.[35]

Pneumonia is the leading cause of hypoxia in patients with the disease. Importantly, unlike bacterial pneumonia, in SARS-CoV2-induced pneumonia, there is a tendency towards alveolar collapse (atelectasis and micro atelectasis), which causes hypoxia.[36] The sequence of events that culminates in the alveolar collapse seen in COVID-19 appears to begin with damage to alveolar cells (type II pneumocyte), which leads to surfactant dysfunction and alveolar instability, predisposing to collapse and atelectasis.

The collapsed air spaces are then 'epithelialized', resulting in the septal formation and loss of alveolar function.[37]

Hypoxia-inducible factor (HIF-1) plays a key role in the onset and perpetuation of hypoxic conditions. HIF-1 is a transcriptional factor that regulates oxygen homeostasis intracellularly and is activated under low oxygen conditions. Activation of HIF-1 results in some adaptive events to the hypoxic situation (increased ventilation, switch from aerobic to anaerobic processes, and increased vascularization).[38] However, its activation may lead to further damage to endothelial cells and epithelial cells, leading to increased inflammation through the recruitment of cytokines, chemokines, and inflammatory mediators. Interestingly, one of the subunits (HIF1-α) has a potent effect on angiotensin-converting enzyme-2 (*ACE-2*) gene expression. Thus, hypoxia appears to increase *ACE-2* receptor gene expression in the early stages, which may worsen infection in COVID-19 and increase damage to lung cells, although, in the later stages of the disease, a reduction in *ACE-2* expression is observed.[39] Hypoxia also drives the immune reactions of cells involved in the inflammatory storm (eosinophils, basophils, mast cells) seen in patients with COVID-19.[40]

Hypoxia is a harmful condition for cellular homeostasis, and in the case of COVID-19, there may be longer periods of exposure to tissue hypoxia due to some mechanisms that probably result directly from viral action, as described above. These findings clarify the important role of hypoxia in the persistence of lung structural findings, as seen on the present imaging exams.

Although there are differences and particularities in the functioning and sensitivity of oximetry in specific population groups,[41] due to the extreme simplicity of this measurement, the current findings acquire great clinical relevance.

The true meaning of the radiological persistence of residual pulmonary changes after COVID-19 remains uncertain, since most patients recover over time, with a few cases remaining with abnormalities after 12 months.[14] However, the occurrence of pulmonary fibrosis secondary to COVID-19 has been already described in the medical literature, including the possible role of antifibrotic agents as a treatment option and even lung transplantation.[42,43]

In addition to being a risk predictor for radiological changes at follow-up in the present study, severe oxygen desaturation on admission (<88%) was associated with shorter distances in the 6MWT. Likewise, patients who received mechanical ventilation during hospitalization walked shorter follow-up distances. Another interesting association was that patients with abnormal CT at 3–6 months following discharge presented with shorter 6MWD compared with those with no radiologic abnormalities. Correlations between walking distance in the 6MWT and disease severity have also been reported in previously published studies.[8,26–28,30] The clinical impact of this outcome remains unclear and requires additional research and follow-up.

In the present association analyses, the severity of initial CT involvement did not help to predict who remained with radiological changes, nor who had reduced FVC or walked shorter distances on the 6MWT. Radiological involvement at hospital admission had a moderate positive correlation with a longer ICU stay. Few studies have searched for this correlation between admission CT involvement and functional assessment after discharge. In the prospective Chinese cohort study by Wu et al,[14] an association was found between peak CT involvement during hospitalization and persistence of abnormal CT, but no association with DLCO < 80% of predicted. Another study, which followed patients for 12 months, found no association between initial CT severity and the persistence of radiological changes after 1 year ($P = 0.301$).[44] This dissociation may suggest

the limited role of CT alone to stratify and predict the risk of lung functional and structural sequelae.

The results of the present study may be limited by several factors, including the difficulty in maintaining patient compliance with outpatient consultations and tests. The great social and emotional impact caused by COVID-19, coupled with the progressive and sometimes rapid improvement of symptoms and functionality of these individuals after hospital discharge, are factors that might explain this noncompliance. Although 13 patients had a history of respiratory disease, none of them had previous hypoxemia, which may have affected the results of the statistical analysis. Moreover, the single-center study setting, and the inclusion of patients hospitalized with COVID-19 pneumonia, selecting participants with a more severe clinical status, may prevent the generalization of the present results to patients with distinct disease severity.

In conclusion, the present findings emphasized the importance of evaluating initial hypoxemia, not only for diagnosing acute respiratory failure, but also for predicting the persistence of functional and radiological changes after discharge. The long-term clinical and functional significance of these abnormalities remains uncertain and requires further investigation.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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Supplemental material

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