ISSN: 2754-4761

Journal of Pulmonology Research & Reports

SCIENTIFIC Research and Community

Research Article

Open Access

Long-Term Pulmonary Sequelae in COVID-19 Survivors: A 3-Year Prospective Cohort Study

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ABSTRACT

Background: Individuals recovering from the initial COVID-19 infection experienced persistent symptoms and radiological lesions. This study is a long-term follow-up of COVID-19 survivors to assess the progression and persistence of pulmonary sequelae. This will provide critical insights into the natural history of post-COVID-19 syndrome.

Objectives: To evaluate the long-term radiological changes in COVID-19 survivors over three years and to identify risk factors associated with it.

Methodology: This is a prospective, longitudinal cohort study designed to follow a group of COVID-19 survivors over three years. Clinical data during the initial infection such as admission to the ICU, Oxygen requirement, Ventilator assistance, and length of hospital stay were collected from case records. High-resolution computed tomography (HRCT) scans were taken at one-year intervals and CT severity scores were recorded to study the interval changes. Appropriate statistical analysis was done to establish significance.

Results: In this study, 40 patients with residual lung lesions on HRCT in the first follow-up visit were enrolled, out of which 6 were excluded from the final analysis. Out of the 34, 55.9% were males and 44.1% were females. The mean age of the study population was 58.26. 41.1% were treated in ICU and 58.9% in the wards. Invasive ventilation was used in 23.5%, NIV in 35.29%, and oxygen alone in 41.1%. The average length of stay was 18 days. CT severity score at presentation was mild in 44.1%, moderate in 29.4%, and severe in 26.47% of patients. During the 3-year follow up CT score improved in 76.47%, remained static in 17.64%, and progressed in 5.88% of patients (p-value <0.001). The age of the patient correlated with the initial CT score and the outcome, follow-up CT severity scores improved better in young cohorts when compared to elderly patients. However, ICU admission, use of mechanical ventilation, and length of stay were not correlated with the subsequent CT severity score.

Conclusion: This study is expected to provide valuable insights into the long-term health consequences of COVID-19 and identify key factors that contribute to the persistence of symptoms and lung sequelae in survivors.

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Received: June 12, 2025; **Accepted:** June 19, 2025; **Published:** June 26, 2025

Keywords: COVID-19, Post COVID Lung, Lung Fibrosis, Follow Up

Introduction

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a profound global impact, affecting millions of individuals and healthcare systems worldwide. There is growing concern regarding the long-term health consequences faced by COVID-19 survivors [1]. Emerging evidence suggests that a significant proportion of individuals who recover from the acute infection experienced persistent symptoms and developed new-onset complications that may extend well beyond the resolution of the initial illness [2].

This study aims to conduct a comprehensive, long-term follow-up of COVID-19 survivors to assess the progression and persistence of pulmonary sequelae. By enrolling a cohort of individuals who have recovered from COVID-19, we will systematically monitor clinical, and radiological outcomes over three years. This study will provide critical insights into the natural history of post-COVID-19 syndrome, identify risk factors for long-term complications, and guide future management strategies for this vulnerable population.

Primary Objective

To evaluate the long-term radiological changes in COVID-19 survivors over a three-year follow-up period.

Secondary Objectives

To identify risk factors (age, severity of acute illness, length of hospital stays) associated with the development of long-term complications in COVID-19 survivors.

Study Design

This is a prospective, longitudinal cohort study designed to follow up a group of COVID-19 survivors over three years. Participants will be assessed at multiple time points to track changes in HRCT Thorax.

Inclusion Criteria

1. Adults (age 18 and above) who have recovered from COVID-19, confirmed by a positive RT-PCR test.
2. Willingness to participate in a 3-year follow-up study.
3. Ability to provide informed consent.

Exclusion Criteria

1. Individuals with pre-existing severe respiratory conditions (e.g., severe COPD, pulmonary fibrosis, bronchiectasis) before COVID-19 infection.
2. Inability to comply with follow-up assessments.

Sample Size

The sample size will be determined based on the expected prevalence of long-term sequelae in COVID-19 survivors, allowing for sufficient statistical power to detect significant changes over time. Being a single-center study, all patients having post-COVID pulmonary sequelae were enrolled.

Data Collection

Clinical data during the initial infection such as admission to the ICU, Oxygen requirement, Ventilator assistance, and length of hospital stay were collected from case records. High-resolution computed tomography (HRCT) scans were taken at one-year intervals and CT severity scores were recorded to study the interval changes. CT severity score was classified as mild (<8), moderate (9-15), and severe (>16).

Data Analysis

Descriptive Statistics is used to summarize baseline characteristics and symptom prevalence. Mixed-effects model will be used to analyze changes in outcomes over time. Paired t-test is used to identify risk factors associated with the development of long-term complications.

Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee. Informed consent was obtained from all participants before enrollment.

Results

Out of the 149 patients who attended the follow-up clinic of post-COVID survivors, 40 (26.84%) had residual lung lesions on HRCT. In this study 40 patients with residual lung lesions were enrolled, out of which 6 were excluded (1 due to subsequent tuberculosis,1 due to congestive heart failure, and 4 who failed to take follow-up HRCT scans), Out of the 34 under evaluation, 19 (55.9%) were males and 15 (44.1%) were females. The mean age of the study population was 58.26 with a median of 56. Fourteen patients (41.1%) were treated in ICU and 20 (58.9%) in the wards. Invasive ventilation was used in 8 (23.5%), NIV in 12 (35.29%), and oxygen alone in 14 (41.1%). The average length of stay was 18 days with 4 patients staying beyond 30 days (Range 6-90 days) (Table 1). CT severity score at presentation was mild in 15 (44.1%), moderate in 10 (29.4%), and severe in 9 (26.47%) patients (Table 2, Table 3). During the 3-year follow-up, CT scores improved in 26 (76.47%), remained static in 6 (16.64%), and progressed in 2 (5.88%) patients (Figure 1, Figure 2, and Figure 3). The age of the patients correlated well with the initial CT and the follow-up CT score (Table 4). ICU admission, use of mechanical ventilation, and length of stay correlated with the initial CT severity score but had no impact on the follow-up scores.

Table 1: Clinical and Radiological Characteristics of the Post-COVID-19 Patients Reviewed During the First Follow-Up After Hospital Discharge

Clinical and radiological features	n (34)
Gender (%)	
Male	55.9
Female	44.1
Age (years)	
Mean	56.26
Range	(34–81)
Standard deviation	9
Invasive mechanical ventilation (%)	23.5
Non-invasive ventilation	35 29
Oxygen alone	44.1
Average Length of stay	18 days (Range 6-90 days)
Radiological feature- CT Severity Score (%)	
Mild (<8)	44.1
Moderate (9-15)	29.4
Severe (>16)	26.1

Of the 34 participants, 21(61.76%) were 60 years or below and 13 (38.24%) were above 60 years. As per initial CT severity, both groups noted moderate and severe involvement in equal numbers. Mild involvement was seen in 11 of the younger group compared to 5 in the elderly. When interval changes were studied, the younger group showed good improvement whereas static and progressive changes were not influenced by age.

Table 2: Initial CT Severity Score and Change During Follow-Up in Relation to Age Group

CT Severity Score (Initial & Follow-up)	40-60 years (n=21)	>60 years (n= 13)	p-value
Mild	11	5	0.024
Moderate	5	4	
Severe	5	4	
Improved	17	9	0.001
Static	2	4	
Progressive	1	1	

Table 3: CT Severity Score in Patients Admitted to ICU and those who are Mechanically Ventilated

CT Score	ICU admission (n=14)	Invasive Ventilation (n=8)
Mild	1 (7.14%)	0
Moderate	4 (28.56%)	0
Severe	9 (64.28%)	8 (100%)
Improved	13 (92.84%)	7 (87.5%)
Static	0	0
Progressive	1 (7,14%)	1 (12.5%)

Table 4: Initial CT Score and Follow-Up Score in Relation to Length of Stay

LOS	<14	15-30	>30
Mild	17	2	0
Mod	5	3	0
Severe	0	3	4
Improved	16	7	4
Static	5	0	0
Progressive	1	1	0

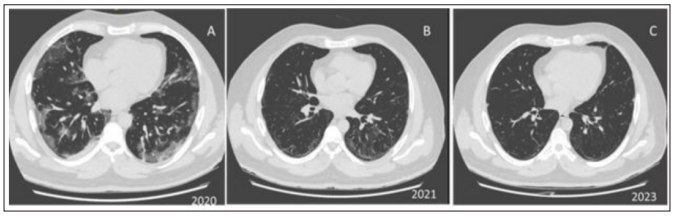

Figure 1: (A) HRCT Thorax Axial Cut, (B) Showed Multiple areas of Ground Glass Shadows and Reticular Shadows. HRCT after One Year, (C) Showed Resolution of Ground Glass Opacities and Persistence of Reticulations which Resolved Completely on the Third Follow Up

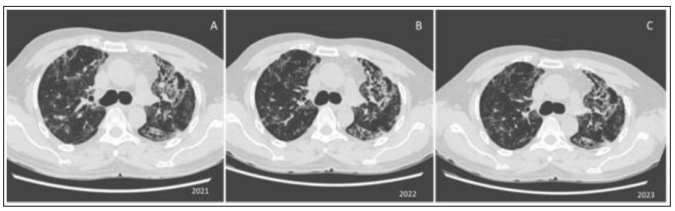

Figure 2: (A) HRCT Axial Cut in 2021 Showed Severe Interstitial Involvement in the Form of Ground Glass Shadows, Consolidation, and Reticulations (B) After 1 Year no Significant Change in Shadows (C) and in 2023 Shadows Persist

Discussion

A significant proportion of COVID-19 survivors especially those with moderate/severe clinical disease develop persistent clinical and radiological abnormality over a considerable period. Such patients require clinical and radiological follow-up. There are virtually no references or clinical guidelines on the long-term follow-up of these post-COVID-19 patients [3]. We followed up a cohort of COVID-19 survivors with interval HRCT for 3 years, essentially looking at the changes over time. We looked for 3 outcomes- Improved, static, and progressive- based on initial and follow-up CT severity scores. The initial HRCT scores were correlated with clinical data, such as age, site of treatment, use of respiratory support, and length of stay. These clinical data were correlated with the final CT outcome at 3 years.

In our study, we observed that CT severity score at presentation was mild in 44.1%, moderate in 29.4%, and severe in 26.47% of patients. This is obvious because most of the patients with severe involvement succumbed to death. When we followed up these patients with HRCT every year for 3 years, we found that 26 patients had improvement in CT score, 6 patients had static lesions and 2 had progressive fibrosis. The fixed effect model indicates that both the initial CT score and age are significant predictors of the CT score after 3 years. The initial severity of the lung damage and the patient's age at baseline are associated with the extent of improvement or progression in the CT score over time. The coefficient for the initial CT score is 0.658 which is statistically significant ($p<0.001$). The coefficient for age is 0.129, which is statistically significant ($p=0.024$). On applying the Paired t-test, the change in CT scores over 3 years is statistically significant ($p<0.001$). This showed a significant difference between the initial CT scores and the scores after 3 years, suggesting that the lung condition of COVID-19 survivors has notably changed over this period.

It is reported that 20%–60% of COVID-19 survivors will show fibrotic changes on imaging tests [4,5]. The study by Huang C, et al described the clinical follow-up of a cohort of 1733 adult patients (48% women, 52% men; median age 57·0 years, IQR 47·0–65·0) with COVID-19 who were discharged from the hospital [6]. Six months after illness onset, 76% of the patients reported at least one symptom that persisted, with fatigue or muscle weakness being the most frequently reported symptom in 63%. More than 50% of patients presented with residual chest imaging abnormalities. Disease severity during the acute phase was independently associated with the extent of lung involvement. Lesion volume decreased gradually from the peak period to discharge and through follow-up, with a notable decrease observed after discharge. Absorption of lesions continued 6 months after discharge [7]. Our findings are also in agreement with the observation of this study.

In another observational study on Post-COVID survivors, Zubairi et al, reported that 32.0% of their patients recovered completely, 36.0% improved, while 32.0% had static or progressive disease [8]. But this was a three-month follow-up study and we believe that most of the patients will recover in 2-3 years as seen in our study. Hino T, et al, after 18-24 months follow up reported that out of 132 post-COVID patients, 42 (32%) developed residual lung damage [9]. Stewart et al, after observing a large cohort of 3700 patients reported that residual lung abnormalities were estimated in up to 11% of people discharged after COVID-19-related hospitalization [10]. The findings of this study agree with the statement that unlike other interstitial lung diseases such as Usual Interstitial Pneumonia, most post-COVID pulmonary fibrosis will recover to a satisfactory level in 2-3 years [11].

Conclusion

Our study found long-term effects, in the form of fibrotic alterations, emphasizing the varied character of post-COVID-19 lung sequelae. The majority of the patients had resolution of shadows with persistence of minimal lesions. However, few patients had either static lesions or progressive fibrosis which require long-term follow-up and treatment. This study is expected to provide valuable insights into the long-term health consequences of COVID-19 and identify key factors that contribute to the persistence of symptoms. Understanding the extended consequences of lung health is critical for improving clinical care in post-COVID lung sequelae.

Limitations

Since the study population was less in number, the observations may have to be confirmed by larger studies.

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