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Assessing predictors of pulmonary sequel in COVID-19 patients through lung CT imaging; a two-month comprehensive evaluation

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Abstract

Introduction: The emergence of COVID-19 has resulted in an unprecedented global health crisis. While acute respiratory symptoms are well-documented, there is growing concern regarding the long-term pulmonary effects in survivors.

Objectives: This study aimed to evaluate the pulmonary sequel of COVID-19 patients referred to Imam Hossein Hospital, Tehran, Iran, in 2022.

Patients and Methods: This longitudinal study involved 180 patients who recovered from COVID-19 at Imam Hossein Hospital in 2022, selected based on confirmed diagnoses and resolution of acute symptoms. Data were collected through a demographic questionnaire and a clinical checklist. Participants were followed for two months, during which lung involvement was categorized as clear or non-clear, allowing for the evaluation of associations between demographic and clinical data with computed tomography (CT) outcomes.

Results: Results indicated a statistically significant correlation between clinical findings, including lung involvement exceeding 30%, intensive care unit (ICU) admission necessity, intubation status, and prolonged hospitalization duration in patients with clear or non-clear pulmonary status. Lung involvement greater than 30% and longer hospitalization duration were identified as independent predictors of adverse pulmonary outcomes, with odds ratios of 2.30 and 2.47, respectively.

Conclusion: The study highlights a significant relationship between clinical findings and pulmonary outcomes in COVID-19 patients, particularly emphasizing that lung involvement exceeding 30% and prolonged hospitalization are critical independent predictors of adverse respiratory complications.

Keywords: COVID-19, Lung CT imaging, Pulmonary sequel, Adverse respiratory outcomes

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Introduction

SARS-CoV-2 was first identified in December 2019 in Wuhan, China (1,2). The disease primarily spreads through respiratory droplets and symptoms typically manifest within 5 to 11.5 days after exposure, with common presentations including fever, dry cough, and shortness of breath (3). While many patients recover from the acute phase of the illness, a notable proportion experience long-term effects, commonly referred to as "long COVID," which can persist for weeks or months after initial recovery (4,5). These long-term symptoms can include respiratory issues, musculoskeletal pain, and neuropsychiatric disturbances, necessitating ongoing clinical evaluation and management strategies (5). Studies indicate that COVID-19 can lead to significant disorders such as kidney dysfunction, which in turn may exacerbate pulmonary complications; for instance, a meta-analysis found that acute kidney injury (AKI) occurred in approximately 16.2% of COVID-19 patients, with higher rates observed in those with severe disease, suggesting a direct link between kidney impairment and worse respiratory outcomes (6). Furthermore, biochemical analyses have shown that elevated serum creatinine and blood urea nitrogen levels as markers of kidney function are prevalent among patients experiencing severe COVID-19 symptoms, indicating that renal impairment could contribute to the severity of pulmonary sequelae (7).

Pulmonary sequelae in COVID-19 patients, assessed through lung computed tomography (CT) imaging, have emerged as a critical area of study due to the significant long-term effects observed in survivors of the virus. After

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Implication for health policy/practice/research/ medical education

The study's results highlight the critical relationship between clinical findings and pulmonary outcomes in COVID-19 patients, particularly emphasizing the significant correlations between lung involvement exceeding 30%, ICU admission necessity, intubation status, and prolonged hospitalization. These findings underscore the importance of vigilant monitoring of lung involvement as a key predictor of adverse respiratory complications, with independent risk factors identified as lung involvement greater than 30% and longer hospitalization duration. The implications of this study advocate for targeted interventions and enhanced clinical practices to improve recovery trajectories and mitigate long-term pulmonary sequel in COVID-19 survivors.

the acute phase of COVID-19, many patients experience persistent respiratory symptoms and abnormalities detectable via imaging techniques. Research has shown that lung involvement can manifest as ground-glass opacities, reticular patterns, and even pulmonary fibrosis, which may develop in a substantial proportion of patient's post-recovery (8,9). A study involving patients who had recovered from COVID-19 indicated that nearly half exhibited abnormal findings on chest CT scans months after their initial infection, highlighting the importance of longitudinal imaging assessment in these patients (10). These imaging findings correlate with clinical symptoms such as dyspnea and reduced exercise capacity, suggesting lung CT is invaluable for evaluating post-COVID pulmonary complications (11,12). Moreover, the identification of specific patterns of lung damage can aid in predicting long-term outcomes and guiding rehabilitation efforts for affected individuals. Thus, ongoing research into the pulmonary sequel of COVID-19 through advanced imaging techniques is vital for understanding and managing the lasting impacts of this disease on respiratory health.

Objectives

This study aimed to assess the long-term pulmonary sequelae in COVID-19 patients through a comprehensive evaluation of lung CT imaging over two months. By examining 180 patients who recovered from COVID-19 at Imam Hossein Hospital in Tehran, Iran, the research seeks to identify associations between demographic and clinical factors and the presence of lung involvement as determined by CT scan.

Materials and Methods

Study design and participants

This longitudinal study was conducted on 180 patients who have recovered from COVID-19 at Imam Hossein Hospital in 2022. Participants were selected based on confirmed COVID-19 diagnoses and subsequent partial recovery, defined as the resolution of acute symptoms and negative polymerase chain reaction (PCR) test.

Inclusion criteria

- Consent to participate in the study
- Age over 18 years
- Diagnosis of COVID-19 based on a CT scan during hospitalization or a positive PCR test
- Resolution of acute symptoms and negative PCR tests.

Exclusion criteria

- The presence of lesions in the chest wall such as pleural effusion or pneumothorax
- Participants' unwillingness to continue the study
- The patient's death for any reason before the completion of the two-month follow-up period

Data collection

Data were collected by a demographic characteristic's questionnaire through patients' interviews and a clinical checklist. The demographic questionnaire includes gender, age, smoking history, and pulmonary disease history, and the clinical checklist includes the lung involvement percentage at the initial chest CT scan, admission in ICU, intubation or extubation status, and hospitalization duration. Patients were followed for two months, and the chest CT-scan was taken, and the lung involvement was categorized as clear and non-clear. The association of demographic and clinical data was evaluated with the outcomes of lung CT-scan as clear and non-clear.

Statistical analysis

Statistical analysis for this longitudinal study was performed using appropriate statistical software, such as SPSS version 27. Descriptive statistics were utilized to summarize the demographic and clinical characteristics of the participants, including means, standard deviations, frequencies, and percentages. The chi-square test was employed to compare the frequency distributions of categorical variables. Meanwhile the independent T-test was utilized for continuous variables. A significance level of $P<0.05$ was established for all statistical tests. Additionally, logistic regression analysis was conducted to assess the association between demographic factors and clinical variables with the likelihood of having clear versus non-clear lung involvement at follow-up.

Results

The demographic and clinical characteristics of the patients in the study revealed a majority of females. A significant majority of the participants were non-smokers, while a notable portion reported smoking. Regarding lung involvement, a substantial number exhibited greater than thirty percent involvement, with a smaller group showing less involvement. Most patients did not require admission to the intensive care unit (ICU), nor did they undergo

intubation, indicating a relatively stable condition for most. Additionally, nearly all patients had no prior history of pulmonary disease. After a two-month follow-up, most patients showed non-clear lung involvement status. The average age of the participants was in the late forties, and the duration of hospitalization varied widely among individuals, reflecting diverse clinical courses (Table 1).

The analysis of patients' demographic and clinical characteristics in relation to their lung CT-scan status two months post-discharge reveals several notable trends. Notably, the frequency distribution of age, gender, and smoking among patients with clear versus non-clear pulmonary findings was not statistically significant. In contrast, significant differences were observed in the clinical characteristics, particularly among patients admitted to the ICU, where those with more than 30% lung involvement, and intubated patients exhibited a statistically significant correlation with non-clear lung findings. Additionally, the duration of hospital stay was also significantly longer for patients with non-clear lungs compared to those with clear lungs, suggesting a relationship between the severity of pulmonary involvement and recovery time (Table 2).

Results indicated a statistically significant correlation between clinical findings of lung involvement exceeding 30%, the necessity for ICU admission, intubation, and prolonged hospitalization duration, particularly in patients whose pulmonary status was classified as either clear or non-clear. The analysis revealed that lung involvement exceeding 30% was associated with significantly higher odds of non-clear lung status, with an odds ratio (OR) of 6.53 compared to patients with less than 30% involvement. Additionally, patients requiring admission to the ICU demonstrated an increased likelihood of non-clear lung status, reflected in an OR of 5.45 when contrasted with those admitted to general departments. Intubated patients also exhibited a heightened risk, with an OR of 4.78 relative to non-intubated patients. Furthermore, the duration of hospitalization was correlated with non-clear lung status, yielding an OR of 2.70 for patients experiencing longer stays (Table 3).

Upon adjusting for variables such as lung involvement, ICU admission, intubation, and hospitalization duration through multivariate logistic regression analysis, the results identified that only lung involvement exceeding 30% and prolonged hospitalization duration emerged as independent risk factors for non-clear lung status. Specifically, lung involvement greater than 30% was associated with an OR of 2.30, indicating a more than twofold increase in the likelihood of non-clear lung status. Similarly, longer hospitalization duration was linked to an OR of 2.47, emphasizing its role as a significant predictor of adverse pulmonary outcomes (Table 4).

Table 1. Demographic and clinical characteristics of included patients

Variable	Sub-variable	Frequency	Percent
Gender	Female	94	52.2
	Male	86	47.8
Smoking	No	126	70
	Yes	54	30
Lung involvement	≤ 30 %	60	33.33
	> 30 %	120	66.67
ICU admission	No	159	88.3
	Yes	21	11.7
Intubation	No	161	89.4
	Yes	19	10.6
Pulmonary disease history	No	173	96.1
	Yes	7	3.9
Lung involvement status after 2 months	Clear	60	33.33
	Non-clear	120	66.67

Variable	Mean	SD	Min	Max
Age (year)	49.69	15.2	20	77
Hospitalization duration (day)	4.28	4.12	1	27

SD; Standard deviation, Min; Maximum, Max; Maximum, ICU; Intensive care unite.

Discussion

The study's findings indicated that there was no significant correlation between demographic characteristics, including gender, age, and smoking status with pulmonary outcomes after a two-month follow-up period; however, revealed a significant correlation between clinical findings and pulmonary outcomes in COVID-19 patients, particularly highlighting that lung involvement exceeding 30%, ICU admission, intubated patients, and prolonged hospitalization were strongly associated with non-clear lung status. When we adjusted confounding variables, lung involvement greater than 30% and prolonged hospitalization duration emerged as independent risk factors for non-clear lung status, with respective ORs of 2.30 and 2.47, indicating a significant increase in the likelihood of adverse respiratory complications in these patients.

In a study conducted by Ali and Ghonimy in Egypt, which aimed to identify the predictive factors for pulmonary fibrosis in survivors of COVID-19, the findings aligned with our research by indicating that increased lung involvement and prolonged intubation duration were significant risk factors for the development of fibrosis post-infection. However, contrary to our study's results, which found no significant correlation between gender, older age, and cigarette smoking with pulmonary sequelae, Ali and Ghonimy identified these factors as notable risk contributors in their analysis (13). Vardavas et al inconsistent with our findings reported that smoking patients are 1.4 times more susceptible to experiencing severe COVID-19 symptoms and are 2.4 times more likely to require admission to the ICU, mechanical ventilation, or face mortality compared to non-smokers (14). Liu et al found that patients aged 44 years or younger exhibited a significantly higher lung clearance compared to those

Table 2. Patients' demographic and clinical data frequency distribution according to the lung CT-scan status two months after discharge

Variable		Pulmonary Status				*P* value
		Clear (n = 60)		Non-clear (n = 120)		
		N0.	%	N0.	%	
Gender	Female (n = 94)	30	31.9	64	68.1	0.673*
	Male (n = 86)	30	34.9	56	65.1	
Smoking	No (n = 126)	36	28.6	90	71.4	0.058*
	Yes (n = 54)	24	44.4	30	55.6	
Lung involvement	≥30 % (n = 120)	21	17.5	99	82.5	<0.001*
	<30 % (n = 60)	39	65	21	35	
ICU admission	No (n = 159)	58	36.5	101	63.5	0.014*
	Yes (n = 21)	2	9.5	19	90.5	
Intubation	No (n = 161)	58	36	103	64	0.026*
	Yes (n = 19)	2	10.5	17	89.5	
Pulmonary disease history	No (n = 174)	60	34.5	114	65.5	0.078*
	Yes (n = 6)	0	0	6	100	
Variable		**Mean**	**SD**	**Mean**	**SD**	***P* value**
Age (year)		47.80	17.34	50.64	13.98	0.238**
Hospitalization duration (day)		4.70	4.22	9.00	4.24	<0.001**

SD, Standard deviation; Min, Maximum; Max, Maximum; ICU, Intensive care unite.
*Chi-square; **Independent T-test.

Table 3. The association of clinical findings with pulmonary status using univariate Binary logistic regression (unadjusted)

Clinical findings	Pulmonary status (Non-clear/clear)			
	P value	OR	95% CI	
			Lower	Upper
Lung Involvement >30%	<0.001	6.53	3.24	13.17
ICU admission	0.026	5.45	1.22	24.26
Intubation	0.041	4.78	1.06	21.45
Hospitalization duration (day)	<0.001	2.70	1.89	3.84

OR, Odds ratio; CI, Confidence interval; ICU, Intensive care unite.

Table 4. The impact of clinical findings on pulmonary status using multivariate binary logistic regression

Clinical findings	Pulmonary status (Non-clear/clear)			
	P value	OR	95% CI	
			Lower	Upper
Lung Involvement >30%	0.048	2.30	1.008	5.281
ICU admission	0.525	0.19	0.001	31.278
Intubation	0.749	0.435	0.003	71.699
Hospitalization duration (day)	<0.001	2.47	1.722	3.544

OR, Odds ratio; CI, Confidence interval; ICU, Intensive care unite.

older than 44 years at the three-week follow-up, which is in contrast with our results; however, in line with our study, they stated that gender was not correlated with lung worse outcome (15). Other studies also demonstrated that older age and male gender are associated with poorer outcomes in COVID-19 patients; older individuals are at a heightened risk for severe disease, with age serving as a significant predictor of adverse health outcomes during infection (16,17). Similarly, male patients have been identified as having a greater likelihood of experiencing severe symptoms and complications compared to their female counterparts (17). These findings underscore the importance of demographic factors in assessing risk profiles and guiding clinical decision-making for COVID-19 management, emphasizing the need for targeted interventions for these vulnerable populations.

Our study results indicated that greater lung involvement is linked to poorer lung clearance outcomes after two months in COVID-19 patients, which aligns with the findings of Zhou et al, who asserted that disease severity is a reliable predictor of lung tissue damage. This relationship emphasizes the critical connection between disease progression and the extent of pulmonary impairment, as Zhou et al noted that escalating disease severity correlates with increased lung tissue destruction (18). Such insights reinforce the necessity for clinicians to

closely monitor disease severity in COVID-19 patients, as this can provide valuable information for anticipating long-term pulmonary complications and tailoring appropriate therapeutic interventions.

In our study, prolonged hospitalization emerged as an independent risk factor for worse pulmonary sequelae, a finding that aligns with the results reported by Yu et al, who noted that patients with extended hospital stays were more likely to develop lung fibrosis (16). This correlation suggests that the duration of hospitalization may significantly influence the recovery trajectory of COVID-19 patients, potentially leading to increased pulmonary complications such as fibrosis. The implications of these findings underscore the importance of effective management strategies during hospitalization to mitigate the risk of long-term respiratory issues, emphasizing the need for ongoing monitoring and intervention in patients with prolonged hospitalizations.

Overall, the findings of our study underscore the complex interplay between clinical characteristics and pulmonary outcomes in COVID-19 patients. While demographic factors such as gender, age, and smoking status did not show a significant correlation with pulmonary outcomes after two months, clinical indicators proved to be more telling. Specifically, lung involvement exceeding 30%, ICU admission, intubation, and prolonged hospitalization were strongly associated with non-clear lung status. These results emphasize the importance of focusing on clinical parameters rather than demographic characteristics when assessing the risk of adverse respiratory outcomes in COVID-19 patients. The identification of lung involvement greater than 30% and extended hospitalization as independent risk factors highlights the critical need for vigilant monitoring and management of these patients.

In conclusion, our study contributes to the growing body of evidence suggesting that clinical findings are pivotal in predicting pulmonary complications following COVID-19. The lack of significant association with demographic factors suggests that interventions should prioritize clinical management strategies aimed at reducing lung involvement and minimizing hospitalization duration to improve patient outcomes. Future research should continue to explore these relationships further, as understanding the dynamics between clinical characteristics and pulmonary health is essential for optimizing care for COVID-19 survivors.

Conclusion

In summary, the results of this study reveal critical insights into the relationship between clinical findings and pulmonary outcomes in COVID-19 patients. The significant correlations identified between lung involvement exceeding 30%, ICU admission, intubation, and prolonged hospitalization highlight the importance of these factors in predicting adverse respiratory complications. Notably, lung involvement greater than 30% and longer hospitalization duration emerged as independent risk factors for non-clear lung status, with odds ratios indicating a more than twofold increase in the likelihood of adverse outcomes. These findings underscore the necessity for vigilant monitoring and targeted interventions to improve recovery and mitigate long-term pulmonary sequel in COVID-19 survivors.

Limitations of the study

First, while substantial, the study's sample size of 180 patients may not fully represent the broader population of COVID-19 survivors, potentially limiting the generalizability of the findings. Second, the two-month follow-up may not capture the long-term pulmonary effects and complications that could emerge beyond this timeframe. Additionally, reliance on CT imaging to categorize lung involvement as clear or non-clear may introduce variability based on radiologist interpretation and subjective assessment. Furthermore, the study did not account for potential confounding factors such as pre-existing pulmonary conditions or other comorbidities that could influence lung outcomes, affecting the associations' robustness. Lastly, the study's setting at a single hospital may limit the diversity of the patient population, impacting the external validity of the results.

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Authors' contribution

Conceptualization: Amir Behnam Kharazmi and Zeinab Khazaei Poul.
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Writing–original draft: All authors.
Writing–reviewing and editing: All authors.

Conflicts of interest

The authors declare no conflict of interest.

Ethical issues

The research was conducted based on the principles outlined in the Declaration of Helsinki. This study resulted from the internal medicine residential thesis of Zeinab Khazaei Poul (Thesis #430023740), approved by the Shahid Beheshti University of Medical Sciences, Tehran, Iran (ethical approval no.: IR.SBMU.

MSP.REC.1401.498). Written informed consent was taken from all participants before any intervention. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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