Updates in
Emergency Medicine

Research Article

# A Prospective Study of Lung Lesions in COVID-19 Survivors

**Behzad Aminzadeh[1], Morteza Talebi Doluee[2], Mona Maftouh[1], Mahnaz Amini[3], Farrokh Seilanian Toosi[1], Maryam Emadzadeh[4], Saeid Eslami[5], Ahmadreza Tavassoli[1*]**

1 Department of Radiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
2 Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
3 Lung Diseases Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
4 Department of Community Medicine, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
5 Department of Medical Informatics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.

* **Correspondence**: Ahmadreza Tavassoli, MD Department of Radiology, Mashhad University of Medical Sciences, Ghaem Hospital, Mashhad, Iran. Fax: +985138713638 , E-mail: tavassoli.art@gmail.com



**Citation:** Aminzadeh, B., Talebi Doluee, M., Maftouh, M., Amini, M., Seilanian Toosi, F., Emadzadeh, M., Eslami, S., & Tavassoli, A. A Prospective Study of Lung Lesions in COVID-19 Survivors. Updates in Emergency Medicine. Retrieved from https://uiemjournal.com/index.php/main/article/view/32

Received: December 12, 2022
Reviewed: December 25, 2022
Accepted: December 29, 2022
Published: December 30, 2022



**Abstract:**

**Background:** We investigated chest Computed tomography (CT) findings of patients with COVID-19 admitted to Intensive Care Unit (ICU) and wards two months after recovery.

**Objective:** We evaluated the relationship between 2-month follow-up CT findings with the lung involvement severity in their first CT scan upon admission and with the medications administered for them.

**Methods:** Forty-six COVID-19 patients were enrolled, including 23 admitted to the wards and 23 ICU admitted ones. A Chest CT scan was performed and the initial involvement score was recorded. Patients were recalled two months after recovery for follow-up CT. The prevalence of abnormalities in follow-up CT was compared between the two groups. Also, we evaluated the relationship between the first CT score and medications with follow-up CT involvement.

**Results:** Our results indicated that two-month follow-up CT abnormalities were found in 91.3% of ICU patients and in 47.8% of ward-admitted ones. The ground glass opacity(GGO) was the commonest (84.4%) abnormality of studied cases after two months, followed by reticulation(65.6%), and atelectasis(43.8%). The presence of abnormalities was related to age (P=0.002), initial total lung involvement scores (TLI) (P=0.007), and admission to ICU versus wards (P=0.001). ROC analysis showed that a TLI score equal to 11 had 65% sensitivity and 72% specificity to predict the presence of abnormalities in follow-up CT (P=0.007). We did not find any relationship between the administered medications and follow-up CT abnormalities, except for meropenem.

**Conclusions:** Two-month follow-up chest CT abnormalities are significantly more frequent in older patients, ICU-admitted survivors, and those with a higher TLI score in the initial chest CT scan.

**Keywords:** Aftercare, COVID-19, Lung Diseases, Spiral Computed Tomography

## Introduction

The new severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) can cause coronavirus disease 2019 (COVID-19) that led to a pandemic reported from nearly every country around the world (1, 2). World Health Organization (WHO) reported the pandemic of COVID-19 as an international public health issue (3). COVID-19 belongs to beta coronaviruses. They are enveloped single-stranded RNA viruses spread via the respiratory route (4). It has different clinical presentations and presents with or without symptoms. However, a number of symptoms including cough, fever, dyspnea, and sore throat are the most common (5). Up to now, the reference standard tool for the SARS-CoV-2 infection diagnosis is real-time reverse transcription-polymerase chain reaction (RT-PCR). Although Computed Tomography (CT) is not a screening tool to detect COVID-19, the role of CT in the diagnosis, triage, severity estimation, course of the disease and its prognosis has been confirmed. In RT-PCR negative patients, CT imaging could be a complementary modality for the detection of early pathological lung alterations, which could contribute to timely detection and immediate care for prevention of COVID-19 transmission. Moreover, CT is an outstanding tool to convincingly endorse or refute lung pathology in patients suspicious of COVID-19. Computed tomography features of COVID-19 include patterns like ground-glass opacities (GGO), consolidations, crazy paving, and mixed patterns with a predominance of GGO or other consolidation features (6-8). However, certain imaging characteristics may be more dominant in severe cases with COVID-19 admitted to the intensive care unit (ICU) compared to those hospitalized in the ward (9, 10).

On the other hand, long-term experienced evidence from COVID-19 survivors after their hospitalization is currently unknown. With respect to symptoms after hospital discharge, a previous study on 143 COVID-19 patients reported symptoms such as fatigue (53%), breathlessness (43%), and joint pain (27%) (11). A recent study on COVID-19 patients found that fatigue (72% in the ICU group and 60.3% in the ward group), psychological distress (46.9% in ICU group and 23.5% in the ward group) and breathl essness (65.6% in ICU group and 42.6% in the ward group) are frequently reported symptoms 4-8 weeks

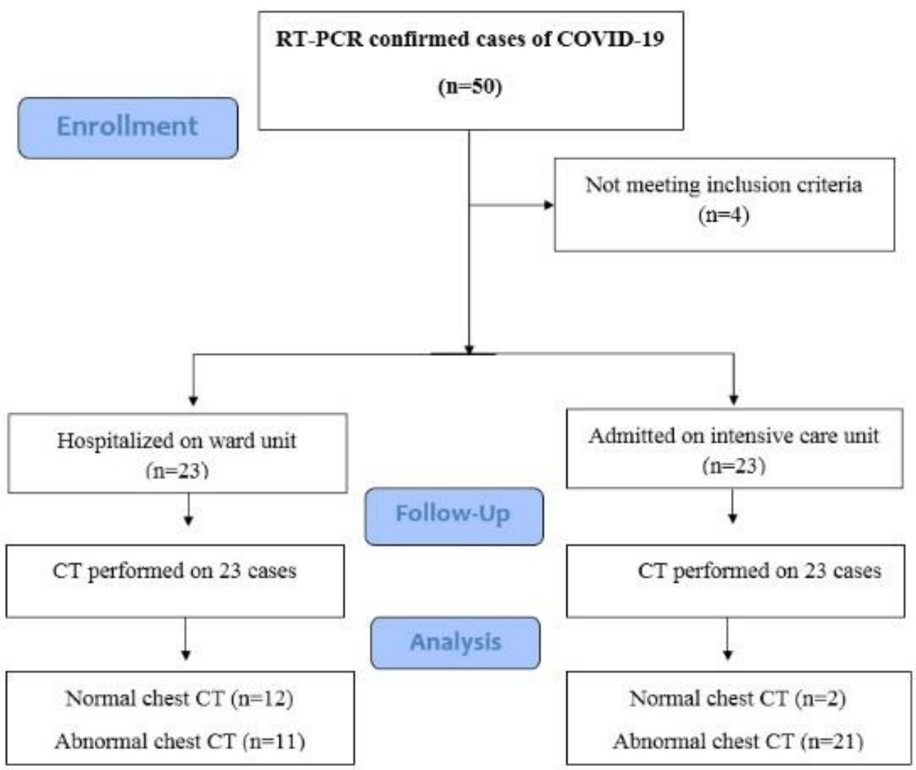


**Figure 1.** Flow chart of COVID-19 patients who underwent chest CT. COVID-19: Coronavirus disease 2019; CT: Computed Tomography; ICU: Intensive Care Unit; RT-PCR: reverse transcription-polymerase chain reaction.

after hospital discharges (12). A recent study investigated the pulmonary sequelae as well as risk factors for fibrotic-like lung lesions during a follow-up of six months among patients with severe COVID-19 pneumonia. Pulmonary fibrosis was found in 35% of surviving patients with severe COVID-19 pneumonia (13). Also, Chan et al in 2003 found that CT of the thorax in 24 patients with SARS after five weeks of follow-up showed alterations similar to pulmonary fibrosis that happened in 15 patients (62%). However, they reported that this fibrosis was patchy and not extensive in most cases without any significant impact on pulmonary function (14). As expressed by previous studies, rehabilitation services for addressing the effect of COVID-19 in cases who survive the infection are of high importance (12). We investigated the persistence of lung lesions in COVID-19 survivors by using chest CT two months after hospital discharge.

## Methods

### Study participants

The ethical protocol of this study was based on principles of the Declaration of Helsinki. Also, we had the approval of the local institutional review board and applied the written informed consent for all patients enrolled in the study.

In this cohort study, 50 COVID-19 patients with a diagnosis based on the WHO definition of COVID-19 confirmed by RT-PCR were included in the first year of pandemic onset. All patients recovered from COVID-19 infection. The patients were between 23 to 97 years old and consisted of 23 males and 23 females. Four patients with a pathologic appearance in their chest CT other than COVID-19 infection were excluded. The participants were enrolled in two groups: patients who had a history of hospitalization in the ICU and those who were only admitted to the ward. Each group contained 23 patients.

### Chest CT Evaluation

All the enrolled COVID-19-positive patients underwent follow-up chest CT two months after their discharge. We used available documents of initial chest CT in the mentioned hospital. A 16-row multidetector scanner (NeuViz 16 Classic CT, Neusoft Corporation, Shenyang, China) was used for obtaining these scans (20 kVp, 40 mA, reconstruction matrix of 512×512, 1.5 mm collimation, slice thickness of 1.0 mm, 1.35:1 pitch, sharp kernel (B80f), and high spatial resolution algorithm). The images were analyzed by two experienced senior chest radiologists. Image analysis focused on the lesion features such as the pattern and extent of involvement in different lobes as calculated by total lung involvement score and the number of involved lobes. In their interpretation of COVID-19 chest CT scans, our expert radiology team evaluated the location, presence, density and extent of lung parenchymal abnormalities. We reported the lobar extension of parenchymal abnormalities and their overall distribution as follows: Central (in inner two-thirds of lungs) and peripheral (in outer one-third of lungs) distribution. Findings were described based on the categorization of lung lesions according to Fleischner society glossary of terms (15). Patterns of lung involvement were assessed and scored using GGO, mixed consolidation and GGO, crazy paving, consolidation, reticulation, interlobular septal thickening, atelectasis, fibrotic band, and bronchiectasis. GGO and consolidation are described as density increment of the lung with and without visualization of vascular and bronchial structures via it, respectively. We used a semi-quantitative scoring system (i.e. TLI) for estimating the pulmonary involvement these abnormalities; therefore, each of the six lobes was scored from 0-4 points as follows: No involvement was scored 0; For 1 - 25% involvement, we used the score 1 (minimal); For 26-50% involvement, score 2 (mild); For 51-75% involvement, the score 3 (moderate); and for >76% involvement, the score 4 (severe). The TLI score was the sum of scores for each lobe from 0 (no involvement) to 24 (maximum) (16, 17). We assessed chest CT of 46 patients two times; first, upon hospital admission and second, two months after discharge. A flowchart of patients with COVID-19 who were subjected to chest CT is presented in Figure 1. Moreover, all prescribed medications related to COVID-19 treatment were noted. Then, the relationship between lung involvement score in the initial CT scan, changes in follow-up CT scan, as well as the relationship between medications and follow-up CT scan, was investigated.

### Statistical Analysis

SPSS 22 was applied for statistical analyses. Quantitative data were expressed as mean±standard deviation (minimum-maximum) and the categorical variables were indicated as frequency and percentage of specified data. Chi-square ($\chi 2$) test and Fisher exact test were applied for categorical variables. COVID-19 patients without any lung involvement in their follow-up chest CT were considered normal patients. The specificity and sensitivity of chest CT scans in prediction of persistent COVID-19 lung lesions were calculated according to normality and abnormality of follow-up CT. Also, Receiver Operating Characteristic (ROC) analysis was applied to calculate the clinical value of CT scores for finding the corresponding cut-off value. Logistic regressions were used to predict the factors that may cause abnormal follow-up CT scans. A P-value <0.05 was regarded as significant.

## Results

### Initial Chest CT results of studied COVID-19 patients

A total of 46 COVID-19 patients were included whose characteristics are presented in Table 1.

**Table 1.** Demographic features of studied COVID-19 patients

| | | Total | Ward Admission | ICU admission | P-value |
|---|---|---|---|---|---|
| **Age, mean±SD** | | 55.56±16.71 | 54.26±19.100 | 56.86±14.25 | 0.602* |
| **gender; Female/male, n(%)** | | 23 (50%)/ 23 (50%) | 11 (47.8%)/ 12 (52.2%) | 8 (34.8%) /15 (65.2%) | 0.55** |
| **Distribution of lesion involvement** | **Peripheral** | 28 (60.9%) | 19 (82.6%) | 9 (39.1%) | 0.008** |
| | **Central** | 2 (4.3%) | 0(0%) | 2 (8.6%) | |
| | **Diffuse** | 16 (34.8%) | 4 (17.4%) | 12 (52.1%) | |
| **Pattern of involvement** | **GGO** | 5 (10.9%) | 3 (13%) | 2 (8.6%) | 0.451** |
| | **Mixed GGO and consolidation with GGO predominance** | 13 (28.3%) | 6 (26%) | 7 (30.4%) | |
| | **Mixed GGO and consolidation with consolidation predominance** | 16 (34.8%) | 10 (43.5%) | 6 (26%) | |
| | **Consolidation** | 10 (21.7%) | 4 (17.4%) | 6 (26%) | |
| | **Crazy paving** | 2 (4.3%) | 0(0%) | 2 (8.6%) | |
| **Numbers of lobes** | **One** | 0(0%) | 0(0%) | 0(0%) | 0.032** |
| | **Two** | 0(0%) | 0(0%) | 0(0%) | |
| | **Three** | 1 (2.1%) | 1 (4.3%) | 0(0%) | |
| | **Four** | 5 (10.8%) | 5 (21.7%) | 0(0%) | |
| | **five** | 4 (8.6%) | 3 (13%) | 1 (4.3%) | |
| | **six** | 36 (78.2%) | 14 (60.8%) | 22 (95.6%) | |
| **Total lung involvement score, first CT on admission, mean±SD** | | 12.19±3.44 | 9.26±3.69 | 15.13±3.19 | 0.001*** |
| **Total lung involvement score, After two-month follow-up, mean±SD** | | 2.61±1.69 | 2.08±2.74 | 3.15±0.65 | 0.001*** |

P-value calculated by Mann-Whitney Test; **P-value calculated by chi-square test; ***P-value calculated by Mann-Whitney Test; CT: Computed tomography; ICU: Intensive Care Unit; GGO: Ground glass opacity

**Table 2.** Findings in 32 COVID-19 patients with abnormalities on two-month follow-up of chest CT

| Features | n (%) |
|---|---|
| **Ground glass opacities** | 27 (84.4) |
| **Reticulation** | 21 (65.6) |
| **Interlobular septa thickening** | 13 (40.6) |
| **Fibrotic band** | 14 (43.8) |
| **Atelectasis** | 14 (43.8) |
| **Bronchiectasis** | 3 (9.4) |

They underwent chest CT two times: first upon admission and second two months after hospital discharge and recovery. Patients were evaluated in two groups, namely those who were admitted to the ward and those admitted to ICU. No significant difference was detected between the age and gender of the studied groups (Table 1).

Chest CT results of the studied cases were documented (Table 1). Peripheral distribution was the most frequent (60.9%), followed by diffuse (34.8%) and central (4.3%) distribution. A significant difference was detected in the distribution of lesions between patients in the ward and ICU (P=0.008). Patients admitted to ICU had mainly diffuse distribution of lesions. Analyses showed that involvement patterns with respect to frequencies were mixed GGO and consolidation with consolidation predominance (34.8%), mixed GGO and consolidation with GGO predominance (28.3%), pure consolidation (21.7%), pure GGO (10.9%), and crazy paving (4.3%). No significant difference was observed between patients who were admitted to the ward and those who were hospitalized in ICU based on the pattern of lesions (P=0.451, Table 1).

Evaluating the number of involved lobes indicated that the frequencies were as follows: Six involved lobes (78.2%), four involved lobes (10.8%), five involved lobes (8.6%), and three involved lobes (2.1%). A significant difference was observed between the two studied groups regarding the number of involved lobes, and patients in ICU had significantly higher involved lobes than those in the ward (P=0.032, Table 1).

Statistical analyses of total lung involvement score (TLI) showed a significant difference between the two study groups and the mean of the TLI in ICU patients was significantly higher than TLI of cases admitted to wards (P=0.001, Table 1).

**Analysis of CT findings two months after hospital discharge**

The patients were divided into two groups with respect to finding any abnormality in their CT, which was normal and abnormal after two months of follow-up. Lung parenchymal abnormalities on chest CT were found in 32 cases, and 14 cases did not show any abnormalities. Abnormal CT features included ground glass opacity (84.4%), reticulation (65.6%), atelectasis (43.8%), the fibrotic band (43.8%), interlobular septal thickening (40.6%), and bronchiectasis (9.4%) (Table 2 and Figures 2). We scored the chest CT abnormalities quantitatively with TLI scoring system.

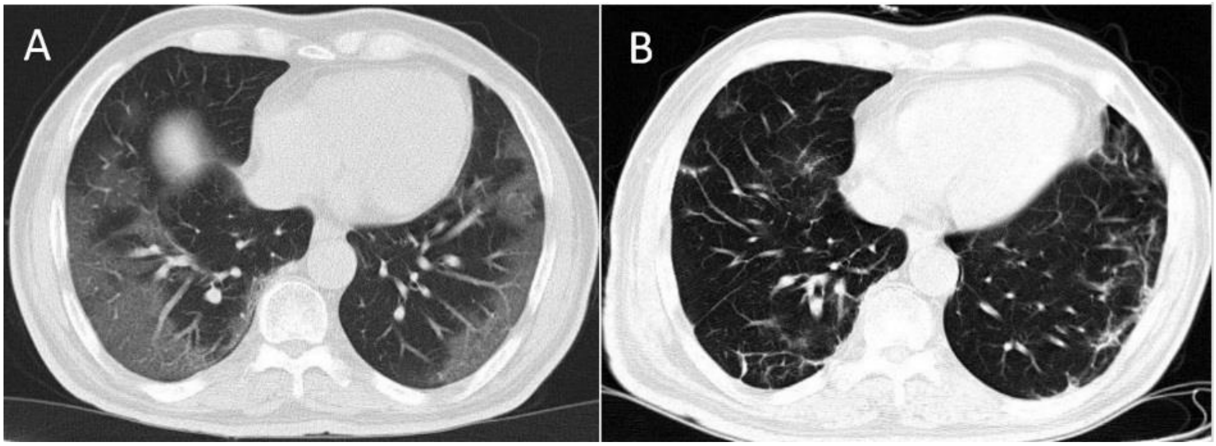


**Figure 2.** A: Initial chest CT scan of a 69-year-old patient admitted to ICU, which shows bilateral ground glass opacities. (The TLI score was 10.) B: Follow-up CT of the same patient shows atelectasis and fibrotic bands.

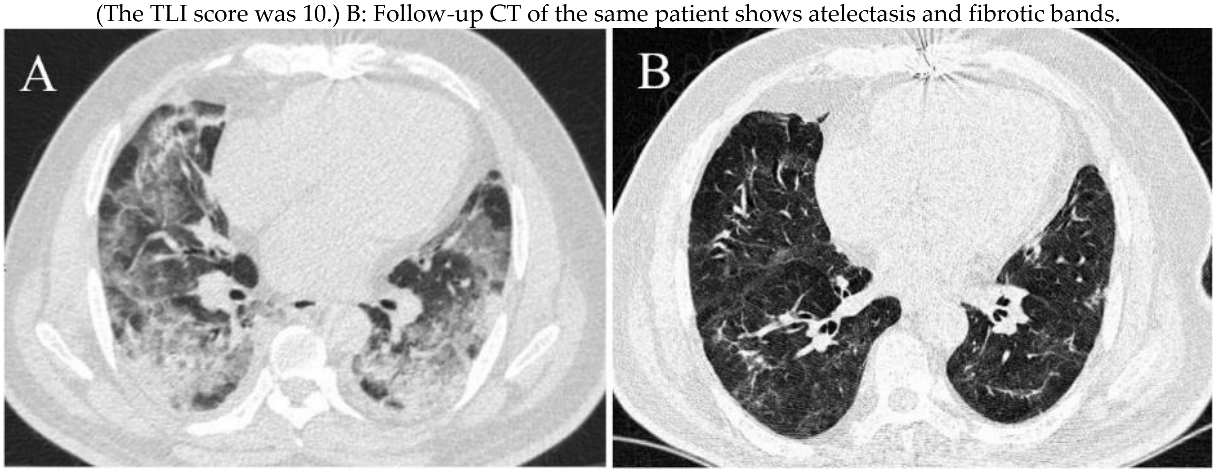


**Figure 3.** A:Initial chest CT scan of another ICU admitted patient who was 75 years old, which shows peripheral ground glass opacities and consolidations in both lower lobes. (The TLI score was 18.) B: Follow-up CT of the same patient shows ground glass opacities and fibrotic bands.

A comparison of studied patients with normal (14 cases) and abnormal (32 cases) follow-up chest CT is presented in Table 3. A significant difference was observed between the age of cases with normal and abnormal follow-up chest CT (P=0.002, Table 3), and patients who had abnormal CT were significantly older than patients in the normal group. There was no difference between the gender of patients with normal and abnormal follow-up CT (P=0.428). After two months, only 2 cases out of 23 (8.7%) in ICU had normal follow-up CT (Figure 1). A significant difference was found between the number of patients who had normal or abnormal follow-up CT in two groups of study (P=0.001). Moreover, investigation of TLI in the follow-up chest CT indicated a significant statistical difference between the patients admitted to ward versus ICU admitted patients. (P=0.001, Table 3).

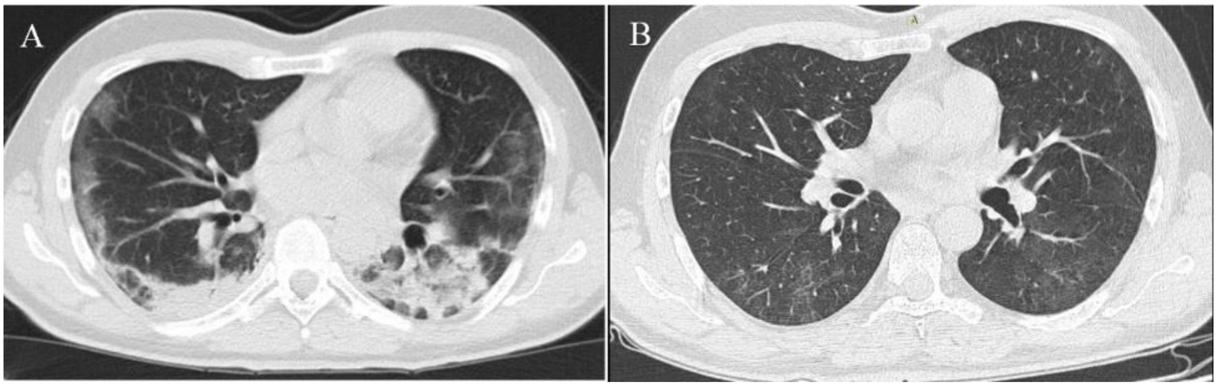


**Figure 4.** A: First chest CT scan performed for a 44-year-old ICU admitted patient shows bilateral peripheral mixed ground glass opacities and consolidations. (TLI score was equal to 11.) B: Follow-up CT of the same patient, which demonstrates ground glass opacities.

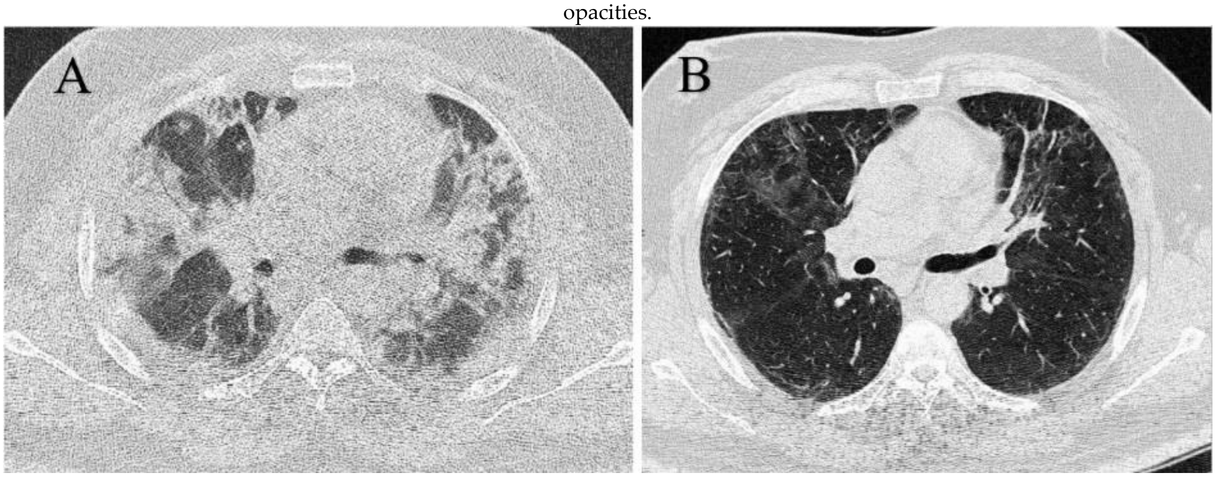


**Figure 5.** A: Initial chest CT scan performed for a 71-year-old ICU admitted patient shows bilateral peripheral consolidations. (TLI score was equal to 18.) B: Follow-up CT of the same patient, which demonstrates ground glass opacities, reticulations and fibrotic bands.

Furthermore, we evaluated the association between the persistence of lung lesions on follow-up CT scans and primary chest CT scan results. The differences between primary CT patterns in patients with normal and abnormal follow-up CT scans were not significant (Table 3). Nevertheless, we found a significant correlation between the TLI score of initial chest CT and presence of abnormalities in two-month follow-up CT. ( P=0.007). This means that a higher TLI score in the first CT is related to more abnormalities in follow-up CT (Table 3). Moreover, we performed ROC analysis between patients with normal and abnormal follow-up CT for finding the appropriate cut-off value for TLI score in the prognosis of COVID-19 patients, which may indicate the tendency to leave lung lesions. Our analysis showed that a TLI score equal to 11 in the first CT scan had 65% sensitivity and 72% specificity to predict the presence of abnormalities in the chest CT after two-month follow-up (P=0.007, Figure 3).

Also, we assessed all prescribed pharmacological agents between patients with normal and abnormal follow-up CT scan results (Table 3). Among 25 COVID-19 patients who consumed meropenem, only 4 cases (16%) had normal CT after two-month follow-up and the rest (84%) had abnormal CT (P=0.020). No significant differences were observed between other pharmacological medicines and CT groups (Table 3).

To indicate predictors of abnormal follow-up CT, we entered the variables (TLI score, age, meropenem and ward or ICU admission) as independent factors in logistic regression model. Admission in ICU [OR=12.4; CI(1.9, 78.3); P=0.007] and age (OR=1.08; CI(1.01, 1.14); P=0.01] were independent risk factors for abnormal CT.

## Discussion

This study investigated the post-discharge lesions among COVID-19 survivors. We followed the survivors of COVID-19 who were hospitalized in the ward and ICU after two months of hospital discharge.

Although a higher frequency of male relative to female COVID-19 patients has been described in Iran (18), there was no significant correlation between gender and hospitalization in ICU or ward in the current study. Also, no significant difference was observed in comparison of remaining lung lesions at follow-up CT between males and females.

According to recent reports, we found that COVID-19 patients with severe or critical conditions hospitalized in ICU were older than the other ordinary patients admitted to the ward (18). According to previous reports on COVID-19, age is considered one of the predisposing conditions for COVID-19 pneumonia in critical cases (19, 20). Besides, we found that older patients had considerably higher rates of abnormality in their chest CT after two months of hospital discharge.

**Table 3.** Comparison between studied groups with normal (14 cases) and abnormal (32 cases) follow-up chest CT scans

| Variable | | Normal follow-up CT<br>n=14 | Abnormal follow-up CT<br>n=32 | P-value |
|---|---|---|---|---|
| **Age (Mean± Standard deviation)** | | 44.92±15.85 | 61.87±15.11 | *0.002 |
| **TLI score in the initial CT scan** | | 9.36±4 | 13.44±4.1 | *0.007 |
| **Gender** | Female (%) | 7 (25.9) | 20 (74.1) | 0.428 |
| | Male (%) | 7 (36.8) | 12 (63.2) | |
| **Hospitalization** | Ward (%) | 12 (52.2) | 11 (47.8) | 0.001 |
| | ICU (%) | 2 (8.7) | 21 (91.3) | |
| **Findings in the first CT on admission** | GGO | 2 (40) | 3 (60) | 0.633 |
| | Mixed GGO and consolidation with GGO predominance | 4 (30.8) | 9 (69.2) | 0.975 |
| | Mixed GGO and consolidation with consolidation predominance | 6 (37.5) | 10 (62.5) | 0.447 |
| | Consolidation | 1 (10) | 9 (90) | 0.112 |
| | Crazy paving | 1 (50) | 1 (50) | 0.521 |
| **Medicines** | Azithromycin | 14 (35) | 26 (65) | **0.157 |
| | Vancomycin | 8 (26.7) | 22 (73.3) | *0.447 |
| | Lopinavir / Ritonavir (KALETRA) | 10 (29.4) | 24 (70.6) | *0.800 |
| | Meropenem | 4 (16) | 21 (84) | *0.020 |
| | Intravenous immunoglobulin | 0 | 2 (100) | **1.000 |
| | Ribavirin | 3 (30) | 7 (70) | *0.973 |
| | Corticosteroids | 6 (22.2) | 21 (77.8) | *0.149 |
| | Interferon | 3 (27.3) | 8 (72.7) | *0.794 |
| | Remdesivir | 0 | 3 (100) | **0.543 |
| | Favipiravir | 1 (16.7) | 5 (83.3) | **0.651 |
| | Oseltamivir | 9 (37.5) | 15 (62.5) | *0.277 |
| | Levofloxacin | 1 (25) | 3 (75) | **1.000 |
| | Hydroxychloroquine | 8 (28.6) | 20 (71.4) | *0.732 |
| | Ceftriaxone | 13 (33.3) | 26 (66.7) | **0.413 |

*P-value calculated by Mann-Whitney Test, **P-value calculated by Fisher's Exact Test. others P-value calculated by Chi-square Test. CT: Computed tomography; GGO: Ground glass opacity; ICU: Intensive Care Unit; TLI: Total Lung Involvement.

Patients with severe symptoms and higher TLI scores were of advanced ages, namely older than 55 years. Similar to our research, a recent study found that age higher than 50 years, duration of hospitalization and total score at initial CT are independent predictors for fibrotic-like alterations in six-month follow-up among survivors of COVID-19 pneumonia (13).

Similar to previous studies, almost all of our COVID-19 cases admitted to ward or ICU had lung parenchymal abnormalities at initial CT scan (21-24). Our study results from initial chest CT revealed that the most frequent lung involvement pattern was mixed GGO and consolidation with the predominance of consolidation in 34.8% of COVID-19 cases. Thereafter, the order of patterns was mixed GGO and consolidation with the predominance of GGO (28.3%), consolidation (21.7%), GGO (10.9%), and crazy paving (4.3%). As previous studies have shown, the frequency and distribution of lung abnormalities were mostly GGOs with posterior and peripheral predilection (21, 23, 24). Moreover, like previous research, bilateral lung involvements were shown in all our COVID-19 cases (25). It is likely that the occurrence of patterns like crazy paving, consolidations, and air bronchogram superimposed on ground glass opacities on initial chest CT enhanced the possibility of patient deterioration and ICU admission (10). In this study, we found no significant difference in involvement patterns between patients in the ward and ICU.

In our study, chest CT abnormalities were found in 32 out of 46 COVID-19 survivors two months after discharge. The analysis revealed that abnormalities in chest CT were detected in 91.3% of patients admitted to ICU compared to 47.8% of patients in wards. Thus, the patients who were admitted to ICU had 12 times higher tendency to develop persistent lung lesions in the follow-up scans than the patients admitted to wards. We found that there is no significant association between different CT patterns in the initial CT scan and the follow-up CT abnormalities, but the severity of lung involvement in the initial CT may influence the chest CT abnormalities in follow-up.

Although a number of studies have declared that most hospitalized patients recover from their symptoms after 10 to 20 days of hospital discharge (26, 27), some investigations have recommended that COVID-19 patients need post-acute care due to their residual symptoms (11-13). Therefore, it would be helpful to use TLI score in the initial CT scan to find out the patients who are in need of close follow-up.

Herein, we found that TLI scores on both initial and follow-up chest CT scans were significantly different between patients admitted to the ward and those hospitalized in ICU and that ICU-admitted patients had higher TLI scores. Our results under ROC analysis showed that TLI score equal to 11 has 65% sensitivity and 72% specificity to predict CT abnormalities after two months of follow-up. Similar to our results, recent investigations on the prognosis of COVID-19 pneumonia by radiological markers of prognosis found that TLI scores were markedly higher in severely ill patients than in other patients (17, 22, 28).

We found that the GGO pattern was the most common abnormality (84.4%) of studied cases after two months of follow-up. After that, reticulation (65.6%), atelectasis (43.8%), fibrotic band (43.8%), interlobular septal thickening (40.6%) and bronchiectasis (9.4%) had the highest frequencies, respectively. Similar to our results, Han et al investigation (13) on 6-month follow-up of chest CT results in survivors of COVID-19 pneumonia revealed that the predominant persistent pulmonary lesions were fibrotic-like changes in 35%, complete radiologic resolution in 38% and residual GGO and interstitial thickening in 27% of patients. Moreover, compared to initial CT, the six-month follow-up scans showed a markedly higher frequency of masses or nodules , interlobar pleural traction, pulmonary atelectasis, and bronchiectasis, whereas pleural effusion was completely resorbed (13). CT investigation of thorax on SARS pneumonia indicated that pulmonary fibrosis occurred in 62% of cases after five weeks of hospital discharge and that the patients were older with more severe disease during the acute phase (23). Moreover, they found that the fibrosis was patchy and not extensive in most cases without significant effect on lung function in SARS cases.

There are different pharmacological agents for COVID-19 infection management. Meanwhile, there have been several therapeutic factors since the early progression of this pandemic (29). In the present research, we evaluated the relationship between different pharmacological agents and the second chest CT after two-month follow-up. However, these approved drugs from different pharmacological and chemical classes reflect various mechanisms of action and their possible therapeutic benefits. We found that most patients (84%) who used meropenem had abnormal follow-up CT, which may be related to the consumption of meropenem in patients with severe pulmonary COVID-19 infections in ICU admitted patients. Nevertheless, there were no significant differences in other pharmacological agents between cases with normal and abnormal follow-up chest CT.

Despite the large number of patients admitted to COVID-19 setting, only 50 patients agreed to perform follow-up chest CT scans. The small sample size and the absence of further follow-up CT scans after two months were the main limitations of this study. Therefore, further studies in a prospective setting with higher number of patients and a long-term follow-up are warranted to perform a more accurate prediction of persistent lung lesions in COVID-19 patients. Given that most patients were admitted at the beginning of the pandemic, only the medications used at that time were reviewed in this research. Therefore, further research on medications used in the treatment of COVID-19 and their effect on persistent lung lesions is recommended. Other limitations of this study were that we only used CT scans to follow-up patient recovery; while it might not be addressive of all aspects of lung function and general quality of health in survived COVID-19 patients. Also, we were not able to record comorbidities that might have affected the progression or recovery process of the disease.

## Conclusion

Two-month follow-up chest CT scan showed the presence of residual pulmonary findings in approximately seventy percent of patients surviving COVID-19, especially in those admitted to ICU (91%) than those who were admitted to the ward (48%). These findings were observed mainly in patients with higher primary lung involvement scores as well as in older patients.

We found no significant correlation between follow-up CT abnormalities and routine medications used during admission except for meropenem, which was used for critical patients in ICU. ROC analysis showed that total lung involvement scores equal to 11 had 65% sensitivity and 72% specificity to predict the abnormality of CT after two months of follow-up. We concluded that severe chest CT scores could help predict persistent adverse effects on COVID-19 patients' pulmonary parenchyma.

### Declarations:

**Funding:**

The study was supported by the Vice-Chancellor of Research, Mashhad University of Medical Sciences, Mashhad, Iran under thesis research number 990061.

**Conflicts of interest:**

None.

**Authors' contributions:**

Conceptualization and methodology:
Data curation and analysis:
Writing - original draft preparation:
Writing - review and editing:

**Acknowledgments**

We would like to express our gratitude to the Clinical Research Development Unit of Ghaem Hospital.

**Ethical considerations**

The ethical protocol of this study was based on principles of the Declaration of Helsinki (IR.MUMS.REC.1399.063). (webpage of ethical approval code is: https://ethics.research.ac.ir/EthicsProposalView.php?id=127653 )

**REFERENCES**


1. Lewnard JA, Liu VX, Jackson ML, Schmidt MA, Jewell BL, Flores JP, et al. Incidence, clinical outcomes, and transmission dynamics of severe coronavirus disease 2019 in California and Washington: prospective cohort study. bmj. 2020;369.

2. Moradzadeh R. The challenges and considerations of community-based preparedness at the onset of COVID-19 outbreak in Iran, 2020. Epidemiology & Infection. 2020;148.

3. Sohrabi C, Alsafi Z, O'neill N, Khan M, Kerwan A, Al-Jabir A, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). International journal of surgery. 2020;76:71-6.

4. Chen Y, Li L. SARS-CoV-2: virus dynamics and host response. The Lancet Infectious Diseases. 2020;20(5):515-6.

5. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020;395(10223):497-506.

6. Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology. 2020;295(1):202-7.

7. Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology. 2020:200463.

8. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. European radiology. 2020;30(8):4381-9.

9. Tabatabaei SMH, Talari H, Moghaddas F, Rajebi H. CT features and short-term prognosis of COVID-19 pneumonia: a single-center study from Kashan, Iran. Radiology: Cardiothoracic Imaging. 2020;2(2):e200130.

10. Parry AH, Wani AH, Shah NN, Yaseen M, Jehangir M. Chest CT features of coronavirus disease-19 (COVID-19) pneumonia: which findings on initial CT can predict an adverse short-term outcome? BJR| Open. 2020;2:20200016.

11. Carfì A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. Jama. 2020;324(6):603-5.

12. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. Journal of medical virology. 2021;93(2):1013-22.

13. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, et al. Six-month follow-up chest CT findings after severe COVID-19 pneumonia. Radiology. 2021;299(1):E177-E86.

14. Chan K, Zheng J, Mok Y, Li Y, LIU YN, Chu C, et al. SARS: prognosis, outcome and sequelae. Respirology. 2003;8:S36-S40.

15. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008;246(3):697-722.

16. Chang Y-C, Yu C-J, Chang S-C, Galvin JR, Liu H-M, Hsiao C-H, et al. Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome: evaluation with thin-section CT. Radiology. 2005;236(3):1067-75.

17. Aminzadeh B, Layegh P, Foroughian M, Tavassoli A, Emadzadeh M, Teimouri A, et al. Evaluation of the Prognostic Value of Chest Computed Tomography Scan in COVID-19 Patients. Iranian Journal of Radiology. 2021;18(2).

18. Nikpouraghdam M, Farahani AJ, Alishiri G, Heydari S, Ebrahimnia M, Samadinia H, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single

center study. Journal of Clinical Virology. 2020;127:104378.

19. Yang X, Yu Y, Xu J, Shu H, Liu H, Wu Y, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020;8(5):475-81.

20. Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Investigative radiology. 2020.

21. Huang G, Gong T, Wang G, Wang J, Guo X, Cai E, et al. Timely diagnosis and treatment shortens the time to resolution of coronavirus disease (COVID-19) pneumonia and lowers the highest and last CT scores from sequential chest CT. American Journal of Roentgenology. 2020;215(2):367-73.

22. Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, et al. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). European radiology. 2020;30(8):4407-16.

23. Li Y, Xia L. Coronavirus disease 2019 (COVID-19): role of chest CT in diagnosis and management. American Journal of Roentgenology. 2020;214(6):1280-6.

24. Zhu Y, Gao Z-H, Liu Y-L, Xu D-Y, Guan T-M, Li Z-P, et al. Clinical and CT imaging features of 2019 novel coronavirus disease (COVID-19). The Journal of infection. 2020;81(1):147.

25. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. American Journal of Roentgenology. 2020;215(1):87-93.

26. Wyrwich KW, Yu H, Sato R, Powers JH. Observational longitudinal study of symptom burden and time for recovery from community-acquired pneumonia reported by older adults surveyed nationwide using the CAP Burden of Illness Questionnaire. Patient related outcome measures. 2015;6:215.

27. Wootton DG, Dickinson L, Pertinez H, Eneje O, Keogan L, Macfarlane L, et al. A longitudinal modelling study estimates acute symptoms of community acquired pneumonia recover to baseline by 10 days. European Respiratory Journal. 2017;49(6).

28. Yang R, Li X, Liu H, Zhen Y, Zhang X, Xiong Q, et al. Chest CT severity score: an imaging tool for assessing severe COVID-19. Radiology: Cardiothoracic Imaging. 2020;2(2):e200047.

29. Heustess AM, Allard MA, Thompson DK, Fasinu PS. Clinical Management of COVID-19: A Review of Pharmacological Treatment Options. Pharmaceuticals. 2021;14(6):520.