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Original Article

Six-Week Follow-Up Chest CT Changes After Severe COVID-19 Pneumonia in Arak City, Iran

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Abstract
Background: Coronavirus disease 2019 (COVID-19) can lead to lung damage.
Methods: This study examines the clinical characteristics of 190 patients with severe COVID-19 admitted to a designated hospital in Arak, Iran, from initial diagnosis with chest CT to the recovery stage in the sixth week.
Results: Serial evaluation of CT imaging features over time of COVID-19 showed that peripheral GGO with or without consolidation, especially in the posterior or lower lung zones, were the most common features ($P<0.001$ - 0.002). During the first week of follow-up, patients demonstrated a higher prevalence of halo signs, peribronchvascular opacities, bronchial wall thickening, tree-in-bud appearance, and lobar in consolidations compared with pulmonary CT scans performed at the sixth week of onset. COVID-19 pneumonia showed the most severe pulmonary involvement approximately 10 days after symptom onset. After active treatment, in the second follow-up, these consolidations were complete resolution and regressed relatively faster than recovery from other types of lesions, as shown by chest CT imaging. In severe COVID-19, ground-glass opacities, consolidation, particularly in lower regions of the lungs, crazy-paving patterns, air bronchograms, and reverse halo signs are often found on the initial CT examinations (days 7 to 10). Most of these severe features gradually regressed in the absorption phase (on days 40 to 42 in early diagnosis and treatment).
Conclusion: CT imaging plays a crucial role in detecting pneumonia and has a high sensitivity in detecting COVID-19 pneumonia but cannot be used as gold-standard for COVID-19 diagnosis.
Keywords: COVID-19, Pneumonia, Computed tomography (CT)

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Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly became a global pandemic. COVID-19 is highly contagious and, in severe cases, can result in lung damage, acute respiratory distress syndrome (ARDS), severe hypoxemia, or organ failure (1-3). With established guidelines and criteria, diagnosis and treatment are now more structured. Chest computed tomography (CT) plays an important role in diagnosing COVID-19 and monitoring disease progression (3, 4).

Routine clinical follow-up of COVID-19 patients includes nucleic-acid tests for SARS-CoV-2 ribonucleic acid (RNA), which are repeated after discharge, with some patients testing positive again (5, 6). CT imaging manifestations serve as a frontline diagnostic test in some countries that yields a typical pattern in most laboratory-confirmed patients. The sensitivity of this noninvasive modality is approximately 97% in patients who test positive via COVID-19 RT-PCR (7). CT examinations remain widely available in developing countries, where laboratory test kits such as reverse transcription real-time fluorescence polymerase chain reaction (rRT-PCR) are often limited, even in developed nations (8). CT examination can assist in the diagnosis of more than 70% of patients with negative RT-PCR results. In such cases, a COVID-19 diagnosis can be confidently based on positive chest CT findings (7, 9).

COVID-19 pneumonia typically presents in chest CT scans with bilateral ground-glass opacities (GGO), multifocal patchy consolidations, and interstitial inflammation. Severe lung abnormalities were observed often 7 to 10 days after the initial onset of symptoms (2, 3).

In mild cases, over 50% of lung opacities resolve without lasting effects within three weeks post-discharge; however, long-term pulmonary changes remain largely unknown.

This study aimed to assess lung conditions in patients recovering from severe COVID-19 pneumonia through the six-week follow-up CT scans. Maintaining monitoring may help facilitate a better understanding of the effects of COVID-19 on the lungs and identify predisposing factors for residual pulmonary opacities(1, 2).

Methods

Patients and Data Collection

We reported changes in the six-week follow-up of chest CT imaging findings of 190 patients infected with SARS-CoV-2 who were admitted and treated at a tertiary referral university hospital in Arak City, Iran, from March 2020 to December 2020. All patients signed informed consent forms to participate in the study.

This study was ethically approved by the ethics committee of the Arak University of Medical Sciences (Reference number. IR.ARAKMU.REC.1400.340).

Inclusion criteria for hospitalized patients were as follows: (a) Confirmed COVID-19 with a positive rRT-PCR test; (b) Lung involvement in the initial chest CT scan; and (c) Agreement to undergo a six-week interval follow-up CT scan. Notably, all patients' admission, discharge criteria, and treatment followed the national protocol for COVID-19. The demographic, clinical, and paraclinical data (including radiological findings and progression information) were collected by physicians, nurses, or electronic medical records (Table 1). All patients were admitted, treated, and discharged following the national protocol for COVID-19 (2). Two experienced thoracic radiologists interpreted and peer-reviewed chest CT scans independently. Chest CT scan features were classified as follows: (a) Predominant pattern: substantial ground-glass opacity, fine subpleural reticulation or consolidation; (b) Dominant distribution pattern: peripheral, axial, or diffuse, including a mixed pattern (a combination of consolidation, ground glass opacity, and reticular opacity in the presence of architectural distortion); (c) Density of opacities (homogeneous opacification, a reticular coarse, linear pattern or a honeycomb pattern (2, 10, 11). (Figure 1, Table 1).

Additionally, pleural effusion and the number of involved lung lobes were recorded (2, 10, 11). All CT scans were performed using a 16-slice spiral CT scanner (Emotion 16 VC20B, Siemens Healthcare GmbH, Erlangen, Germany).

Statistical Analysis

Data analysis was performed using SPSS for Windows version 26 (Chicago, IL, USA). All *p*-values below 0.05 were considered statistically significant. Qualitative variables were reported as the frequency and percentages. The McNemar test was used to compare paired nominal data.

Table 1. CT Imaging manifestations of 190 patients with severe COVID-19 pneumonia between the initial and last follow-up

Variable	First week N (%)	Sixth week N (%)	*P* value
Ground glass opacities	183 (96.3)	125 (65.8)	<0.001
Consolidations	155 (81.6)	72 (37.9)	<0.001
Mix Ground glass and Consolidations	126 (66.3)	51 (26.8)	<0.001
Halo sign	26 (13.7)	8 (4.2)	<0.001
Reverse halo signs	5 (2.6)	4 (2.1)	1
Pulmonary nodules with a halo signs	35 (18.4)	32 (16.8)	0.76
Vascular enlargement in the lesion	12 (6.3)	6 (3.2)	0.18
Tree in bud appearance	32 (16.8)	12 (6.3)	0.001
Peribronchvascular opacities	81 (42.6)	47 (24.7)	<0.001
Lobar consolidations	51 (26.8)	28 (14.7)	<0.002
Centrilobular nodules	3 (1.6)	0	-
Bronchial wall thickening	118 (62.1)	89 (46.8)	<0.001
Subpleural bands	36 (18.9)	31 (16.3)	0.47
Target sign	2 (1.1)	0	-
Crazy paving appearance	188 (98.9)	190(100)	-

Notes: Statistical Tests Used: The Chi-square test was applied where sample sizes were sufficient, and Fisher's exact test was used for smaller sample sizes. Significance Level: A p-value threshold of <0.05 was considered statistically significant.

Results

Clinical Characteristics of Patients

Data on 190 COVID-19 patients (male: 117 (61.6%); female: 73 (38.4%); mean age:55.8 ± 18.6 years, range:20–98 years) were analyzed (Table 1).

Distribution

Among the 190 patients with COVID-19 pneumonia, 65% of the cases involved both lungs, while 35% involved only one lung. COVID-19 frequently affected the bilateral lower lobes (left lower lobe: 48 %; the right lower lobe: 52%). 104 cases (54.7 %) exhibited a predominant subpleural distribution (Fig. 1).

Imaging Manifestation

These male and female patients with severe COVID-19 completed the six-week follow-up.

Significant differences in imaging manifestation between the initial and last follow-up (from the first week to the sixth week) were observed ($P<0.001$ to 0.002, Table 1). Briefly, the proportion of patients with combined ground-glass opacities (GGO) and consolidation manifestation increased to 66.2% by day 7 post- disease onset, then gradually decreased to 26.8% by day 42.

Additionally, patients in the initial week of follow-up had a higher prevalence of halo signs, peribronchvascular opacities, bronchial wall thickening, tree-in-bud appearances, and lobar consolidations compared to the pulmonary CT scans at sixth-week post-onset (Table 1, Fig. 1). Throughout the six- week follow- up, a small number of target sign (n = 3) and centrilobular

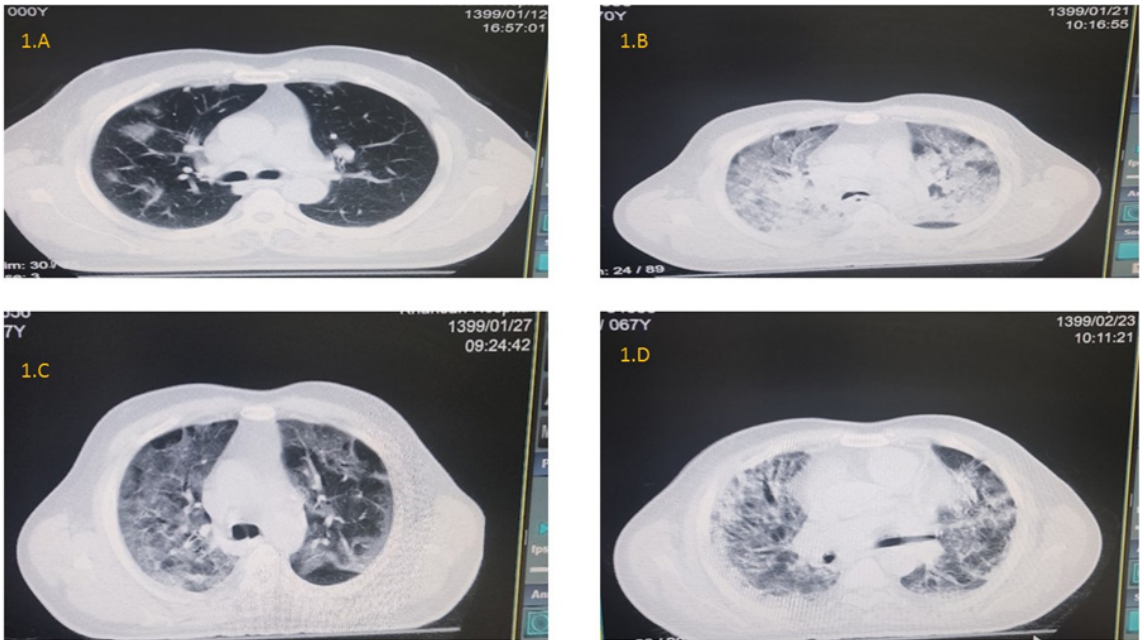

Figure 1. Infections (1.A- 1.D). 1.A Chest CT: Peripheral ground-glass opacities (GGO) in both lungs with predominance in the right lung. 1.B Chest CT: GGO (crazy-paving pattern) and centrilobular nodularity in both lungs. 1.C Chest CT: Predominance GGO in both lungs with desquamative interstitial pneumonia and patchy consolidation, a vascular prominence in the left lung, and distribution of spermatoceles. 1.D Chest CT: peripheralGGO with desquamative interstitial pneumonia, centrilobular nodularity in the right lung.

nodules (n = 2) were detected only in their first CT scans. Demographic data (age and sex) did not significantly correlate with residual CT findings.

Furthermore, no significant differences were detected in total subpleural bands, vascular enlargement within lesions, and reverse halo signs between the initial and final CT images ($P = 0.48$, 0.18, and 1, respectively), (Table 1).

Discussion

This study examined the clinical characteristics of 190 patients with severe COVID-19 who were admitted to a designated hospital in Arak, Iran, and followed from initial diagnosis via chest CT to the recovery stage at six weeks. These follow-up observations may assist in optimizing COVID-19 diagnosis and treatment. Over time, evaluation of COVID-19 CT imaging features showed that peripheral GGO, with or without consolidation, especially in the posterior or lower lung zones, was the most common finding (3, 4, 12-15).

Compared with pre-discharge CT features, combined GGO and consolidation, halo sign, peribroncho vascular opacities, bronchial wall thickening, tree-in-bud appearances, and lobar consolidations were significantly more likely to persist in early chest CT follow-ups, and these lesions were often bilateral. Other studies have similarly reported that peripheral GGO, with or without consolidation, interstitial thickening (crazy-paving pattern), parenchymal bands, and interlobular septal thickening were the common CT findings during mid-term follow-up (2). The lesions were often bilateral and multilobar (7). Notably, the proportion and density of the lung lesions significantly decreased after 6-weeks of follow-up. Several studies have indicated that COVID-19-associated lung lesions may be reversible or fully absorbed within 4 weeks (1,2,10). CT results in severe COVID-19 suggest a slower recovery due to the higher prevalence of mixed GGO/consolidation, fibrosis, air bronchograms and cavity compared with non-severe cases (3). Periodic chest CT scans in COVID-19 patients allow for more tailored therapies (3). Moreover, consistent with previous studies, pleural effusion and enlarged mediastinal lymph nodes remained rare (1,15).

After active treatment, the second follow-up revealed full absorption of consolidations, occurring relatively quickly compared to the recovery of other lesions, as demonstrated by chest CT imaging. As far as we know, diffuse GGOs correlate with mild edema of the alveolar septi and hyperplasia of the lobular interstitium, and consolidation may be related to edema, red blood cells, and cellulose deposition(1, 15).

Following recent follow-up studies, our findings suggest that different imaging manifestations at various stages correspond to the pathological mechanisms of viral pneumonia. Interval changes in imaging studies should be considered for proper staging of COVID-19 (8-10).

Since only hospitalized patients were included in the study, the midterm sequelae of COVID-19 in the community were not adequately reflected. Long-term imaging follow-up studies involving a larger r proportion of patients with severe COVID-19, spirometry measurements, and CT angiography could provide further insights into therapeutic strategies.

CT imaging can quickly and accurately identify suspected COVID-19 patients. It significantly aids in curbing transmission, especially when used for final diagnosis in patients with a clear epidemiological history but negative nucleic acid test results. Additional multicenter studies should be conducted to enhance diagnostic accuracy and control the spread of infection. However, the study's generalizability is limited by factors such as a regional focus, short follow-up duration, reliance on CT imaging, exclusion of mild/moderate cases, and the lack of treatment.

Future research should extend follow-up periods, include patients across severity levels, utilize multimodal diagnostics, analyze treatment impact, and incorporate multicenter studies for more comprehensive insights.

Conclusion

COVID-19 pneumonia exhibits severe pulmonary damage on CT imaging approximately 7-10 days after symptom onset. In severe cases, GGOs, consolidation-especially in the lower regions, crazy-paving pattern, air bronchograms, and the reverse halo signs are commonly observed in initial CT examinations (days 7 to 10). These severe features tend to diminish during absorption (days 40 to 42) with early diagnosis and treatment. CT imaging plays a crucial role in pneumonia detection, offering high sensitivity for identifying COVID-19 pneumonia, it cannot serve as the gold standard of COVID-19 diagnosis.

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Authors' Contribution

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Competing Interests

The authors declare that they do not have any conflict of interest.

Ethical Approval

This study was ethically approved by the ethics committee of the Arak University of Medical Sciences (Ethical code: IR.ARAKMU.REC.1400.340).

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