ORIGINAL ARTICLE

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COVID-19 Pneumonia: Variation of Chest Computed Tomographic Findings at Different Phases of Disease

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Abstract

Objective: We determined the temporal changes on thoracic computed tomography (CT) in patients with Coronavirus disease-2019 (COVID-19) pneumonia, during the disease.

Methods: Our sample included 55 patients (29 men, 26 women) who were admitted to our hospital between March 10 and May 10 2020 with COVID-19, diagnosed by reverse-transcription polymerase chain reaction, who underwent at least two CT examinations in our hospital. From the onset of the symptoms, the disease process was divided into six stages, and CT patterns at each stage were analyzed. Additionally, we calculated the CT score by using a semiquantitative method to measure the involvement in all five lung lobes.

Results: The most common CT patterns in all stages were ground-glass opacification, crazy-paving pattern, and consolidation. The total CT scores were highest between the 10th and 21st days. This pattern continued similarly for a while later. Residual signs of disease were found in 92% of the patients who underwent CT after the 28th day.

Conclusion: CT findings in COVID-19 pneumonia progress in a certain time-dependent pattern. CT findings of the disease is most severe between the 10th and 21st days. Residual disease findings are observed even after 28 days in most patients.

Keywords: COVID-19, computed tomography, ground-glass opacity

INTRODUCTION

In December 2019, cases of pneumonia caused by a new coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appeared in Wuhan, China. The resulting disease, Coronavirus disease-2019 (COVID-19) quickly spread worldwide within 3 to 4 months (1). By December 29, 2021, COVID-19 had been diagnosed in 281,808,270 patients worldwide, and 5,411,759 patients had died (2).

Computed tomography (CT) plays an important role in the diagnosis and management of COVID-19 pneumonia (3). CT findings continue to be analyzed. A better understanding of the changes in CT findings during the disease will facilitate the diagnosis of the disease, help determine the stage of the disease at the time of the CT examination and help identify complications that may develop. Serial CT scans of the thorax help clinicians better understand the development and progression of the disease. Our aim was to evaluate the temporal changes in thoracic CT findings during the disease.

METHODS

Patients

This study was approved by the Ethics Committee of University of Health Seciences Turkey, Prof. Dr. Cemil Tascioglu City Hospital (protocol number: 192) and the Republic of Turkey Ministry of

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Health, COVID-19 Scientific Research Committee. All patients gave informed consent. In 78 patients who were admitted to our hospital between March 10 and May 10 2020, COVID-19 was confirmed in the first or control reverse-transcription polymerase chain reaction, and at least two CT scans were performed in our hospital during the diagnosis and follow-up processes; the scans were retrospectively evaluated. Inclusion criteria were (1) known date of onset of the patient's symptoms and (2) two or more thoracic CT evaluations performed in our hospital as of the date of admission. An age of younger than 18 was an exclusion criterion. Of the 78 patients, 23 were excluded from the study because their symptom onset dates were unknown. Data from 55 patients were included in the final analysis.

Computed Tomographic Imaging

Patients underwent at least two CT examinations in our picture archiving and communication system. All CT scans were performed without intravenous contrast material with the patients in the supine position during end inspiration. A Philips Ingenuity Core (Philips Medical Systems, Amsterdam, The Netherlands) was used for all chest CT examinations. The tube voltage was set at 120 kV with automatic tube current modulation. Thin-section CT slices were reconstructed by a lung algorithm with a slice thickness of 1.5 mm.

Image Evaluation

CT images were evaluated by two radiologists with 6 and 15 years of experience, respectively. Final decisions were reached by consensus. For the cases in which the radiologists disagreed, a third thoracic radiologist with 20 years of experience made a final decision. Ground-glass opacification (GGO), consolidation, the tree-in-bud sign, a crazy-paving pattern, and septal thickening were defined as elsewhere (4). GGO, honeycombing, consolidation, linear opacities, air bronchogram, bronchiectasis, pleural effusion, and mediastinal lymphadenopathy were among the findings recorded on thin-section CT. The extent of disease evident on thin-section CT was also evaluated. The distribution of abnormalities was also recorded. Lesions are involving mainly the peripheral one-third of the lung as peripheral, and lesions involving mainly the central two-third of the lung as central.

We quantified the CT images by using a previously published method (5-7) of scoring (0-5) for each lobe; the total possible score ranged from 0 to 25 (Table 1).

We categorized the CT scans according to the period between the onset of initial symptoms and the date when they were performed: Stages 1 (0-4 days, in 43 patients), 2 (5-9 days, in 31 patients), 3 (10-14 days, in 18 patients), 4 (15-21 days, in 8 patients), 5 (22-28 days, in 7 patients), and 6 (>28 days, in 25 patients) (6,7).

Statistical Analysis

To perform statistical analysis, we used NCSS 10 software (NCSS, LLC, East Kaysville, UT, USA). Normal distribution was checked with the Shapiro-Wilk test, histograms, Q-Q plots, and box plot graphics. The data were calculated as means and standard deviations, medians, minimums and maximums, frequencies, and percentages. We used Kruskal-Wallis One-Way analysis of variance to compare the total CT scan scores in each stage, and we used Dunn's test for multiple comparisons. Intragroup variables were evaluated with Friedman's repeated measures analysis of variance, and multiple comparisons were made with the Bonferroni-corrected Wilcoxon test (limit of significance was set as $p<0.0167$). Intragroup paired comparisons were evaluated with the Wilcoxon test. Fisher's Exact probability test was used to compare nominal variables. A p value of less than 0.05 indicated bidirectional statistical significance.

RESULTS

Data from 55 patients (26 women and 29 men) were included in the analysis; the patients' mean age was 44.6±11.5 years. Each patient had a median of 2.62±0.9 chest CT scans (Table 2). In total, 132 CT scans were evaluated.

The most prevalent symptoms at presentation were dry cough [in 40 patients (73%)] and fever [in 28 (51%)]. The distribution of lesions and changes in CT patterns at the six different disease stages were evaluated. At all stages, most of the lesions were peripheral and subpleural in location and in most patients, involvement was bilateral. The most common CT findings in all stages were GGO, consolidation, and crazy-paving patterns (Table 3).

Four of the 55 patients showed no pneumonia in the initial CT scan (Figure 1). Of the 43 patients in whom CT scans were performed in stage 1, 13 (30.2%) showed a unilateral

Table 1. Scoring system

Score	Definition
0	None
1	<5% of lobe
2	5%-25% of lobe
3	26%-49% of lobe
4	50%-75% of lobe
5	>75% of lobe

involvement, and 9 (20.9%) showed a single lobe involvement (Table 3). The most common abnormalities in stage 1 were GGO, in 39 patients (91%); crazy-paving pattern, in 12 (28%); and consolidation, in 11 (26%). The incidence of crazy-paving pattern differed between stages ($p<0.001$) and was observed mostly in stages 2 and 3 (Figure 1). The frequency of consolidation also differed between the stages ($p<0.001$); it was observed least in stage 6 and most in stages 3 and 4 (Figure 2). The frequency of linear opacification differed between stages as well ($p=0.04$) and was observed mostly in stages 4, 5, and 6. Of the 25 patients who underwent CT examinations in stage 6, 22 (88%) exhibited GGO, 8 (32%) exhibited linear opacities, and only 2 (8%) exhibited no radiological abnormality (Figure 3).

Table 2. Characteristics of the patient cohort

	All patients (n=55)
Age (y)	46.64±12.50 (21-81)
Gender	
Male	29 (52.7%)
Female	26 (47.3%)
Initial symptoms	
Throat pain	3 (5.5%)
Cough	40 (72.7%)
Fever	28 (50.9%)
Headache	10 (18.2%)
Myalgia	15 (27.3%)
Fatigue	13 (23.6%)
Numbers of scans	2.62±0.9 (2-5)
The frequency of CT scans	
2 scans	39
3 scans	12
4 scans	2
5 scans	2
Total number of the CT scans	132
Examination day	14.06±16.19 (0-91)
Clinical outcomes	
Discharged	50
Died	5

CT: Computed tomography

Total CT scores differed between stages ($p<0.001$; Table 4). The total CT scores were highest in stages 3 (9.0±3.4) and 4 (10.5±6.2). The score of stage 1 was lower than those of stages 2, 3, and 4 ($p<0.001$). When we evaluated 43 patients in whom first CT scans were performed in stage 1, again total CT scores were highest in stages 3 and 4. Evaluation of the score differences between lobes revealed that the right middle lobe scores were lower than the other lobe scores. Right lower lobe scores were higher than the right upper and middle lobe scores ($p=0.011$ and $p<0.001$, respectively) and left lower lobe scores were higher than left upper lobe scores ($p<0.001$).

DISCUSSION

In our study, we evaluated the changes in CT patterns in pneumonia caused by COVID-19 from the onset of symptoms throughout the disease process.

In the early stage of the disease (0-4 days), GGO was the main radiological abnormality; crazy-paving patterns and

Table 3. Distribution and frequency of the pulmonary lesions on CT at different stages

	Stage 1 (n=43)	Stage 2 (n=31)	Stage 3 (n=18)	Stage 4 (n=8)	Stage 5 (n=7)	Stage 6 (n=25)
Distribution of pulmonary lesions						
No lesion	4 (9.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
Peripheral	34 (79.1%)	27 (87.1%)	16 (88.9%)	6 (75.0%)	7 (100%)	23 (92.0%)
Central	3 (7.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Diffuse	2 (4.7%)	4(12.9%)	2 (11.1%)	2 (25.0%)	0 (0.0%)	0 (0.0%)
Involvement of the lung						
No involvement	4 (9.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (8.0%)
Unilateral	13 (30.2%)	4 (12.9%)	1 (5.6%)	0 (0.0%)	2 (28.6%)	2 (8.0%)
Bilateral	26 (60.5%)	27 (87.1%)	17 (94.4%)	8 (100%)	5 (71.4%)	20 (84%)
GGO	39 (90.7%)	31 (100.0%)	18(100.0%)	7 (87.5%)	7 (100%)	22 (88.0%)
Crazy-paving pattern	12(27.9%)	19 (61.3%)	11 (61.1%)	2 (25.0%)	2 (28.6%)	1 (4.0%)
Consolidation	11 (25.6%)	19 (61.3%)	15 (83.3%)	7 (87.5%)	2 (28.6%)	0 (0.0%)
Linear opacities	3 (7.0%)	4 (12.9%)	5 (27.8%)	3 (37.5%)	3 (42.9%)	8 (32.0%)

CT: Computed tomography, GGO: Ground-glass opacification

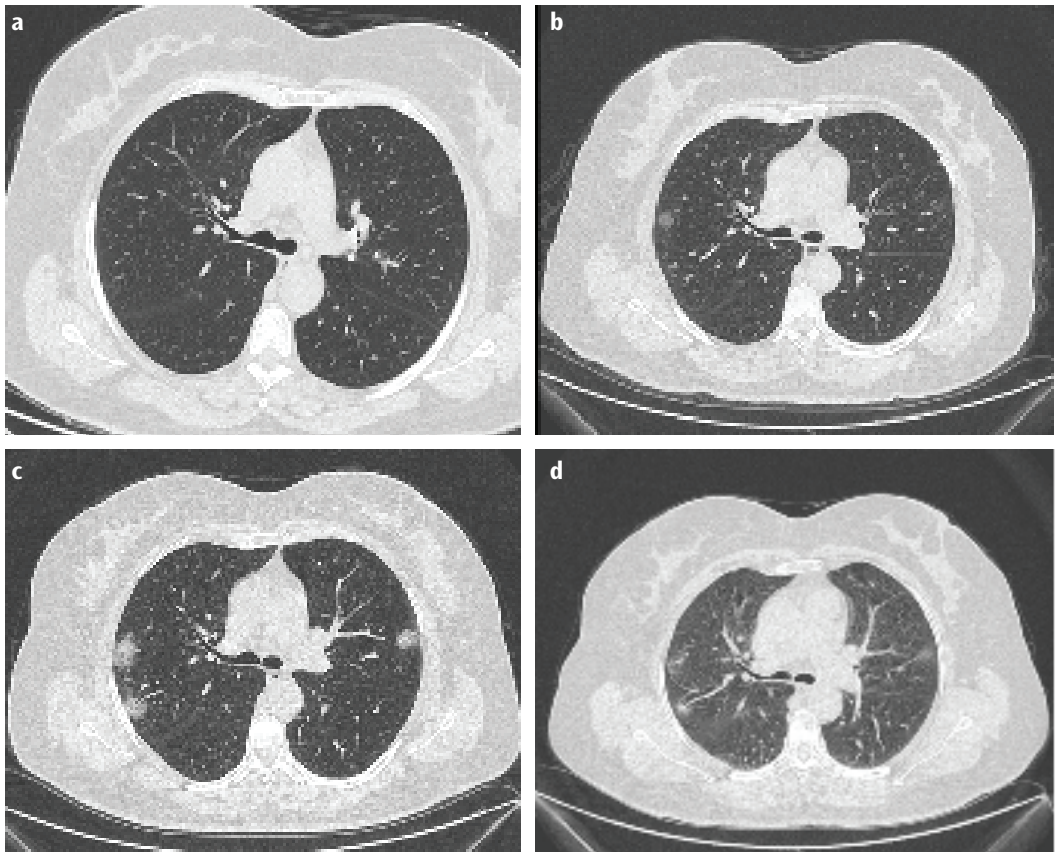

Figure 1 a-d. CT scans in a 48-year-old woman with coronavirus 2019 pneumonia. Axial CT image (a) obtained 3 days after the onset of initial symptoms (stage-1) shows no abnormal findings . Axial CT image (b) obtained 7 days after the onset of initial symptoms (stage-2) shows a round and patchy GGO around the subpleural area of right upper lobe. Axial CT image (c) obtained 12 days after the onset of initial symptoms (stage-3) shows crazy-paving pattern appear within the GGOs with increased extent, GGO and crazy-paving pattern also appeared in the left upper lobe. Axial CT image (d) obtained 34 days after the onset of initial symptoms (stage-6) shows small residual GGOs in both upper lobes
CT: Computed tomography, GGO: Ground-glass opacification

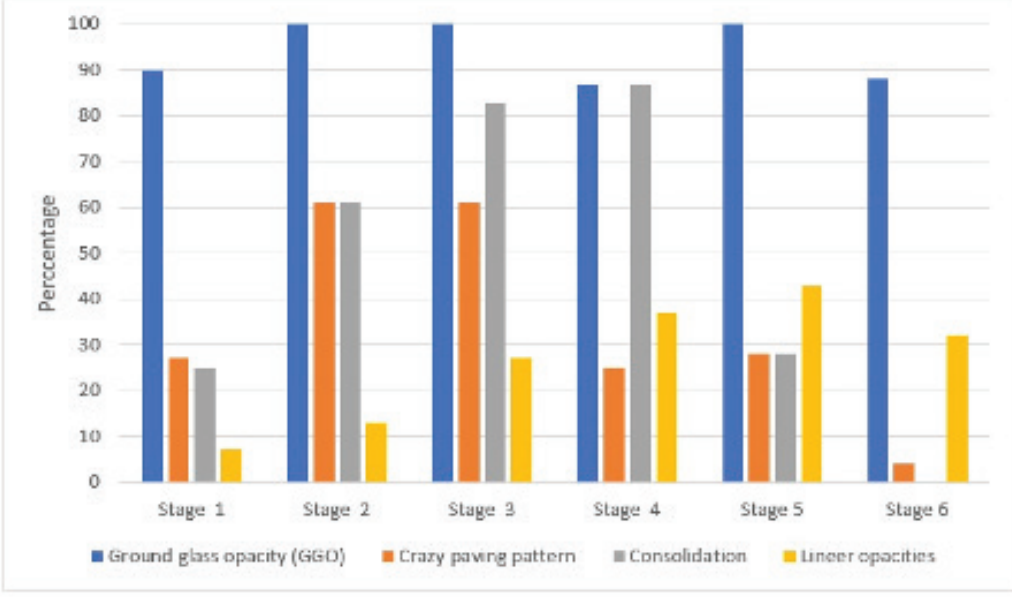

Figure 2. The frequency of major CT findings at different stages
CT: Computed tomography

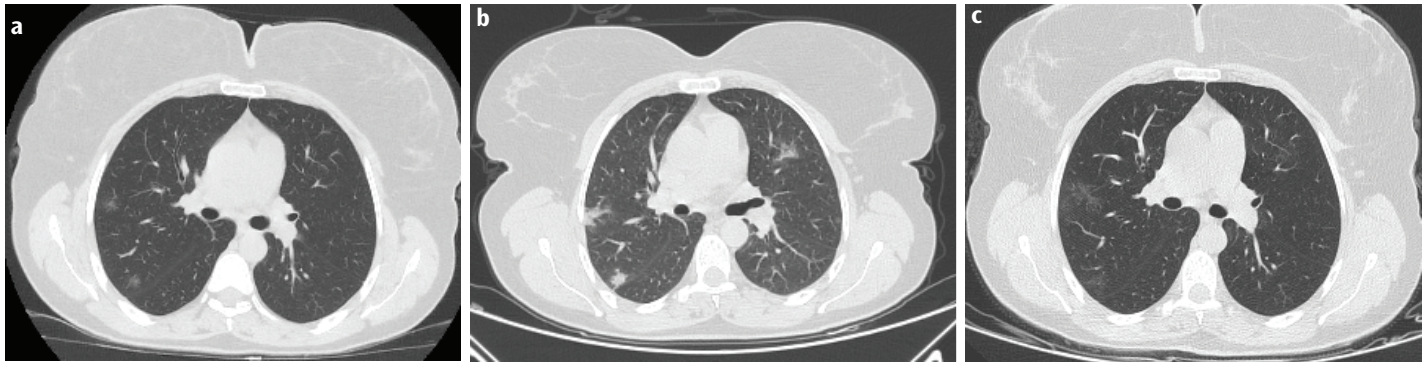

Figure 3 a-c. CT scans in a 49-year-old woman with coronavirus 2019 pneumonia. Axial CT image (a) obtained 3 days after the onset of initial symptoms (stage-1) shows round and patchy GGOs distributed around the subpleural area of right upper and middle lobes . Axial CT image (b) obtained 7 days after the onset of initial symptoms (stage-2) shows increased density on right lobe lesions which mainly became consolidations and a patchy ground-glass opacity is newly developed in left upper lobe. Axial CT image (c) obtained 30 days after the onset of initial symptoms (stage-6)) shows patchy residual GGOs in both upper lobes and right middle lobe
CT: Computed tomography, GGO: Ground-glass opacification

Table 4. The CT score of the pulmonary involvement in six stages

	Stage 1 (n=43)	Stage 2 (n=31)	Stage 3 (n=18)	Stage 4 (n=8)	Stage 5 (n=7)	Stage 6 (n=25)
Total CT score of the pulmonary involvement	3.7±2.9 (0-12)	6.8±2.5 (1-11)	9±3.4 (1-14)	10.5±6.2 (4-24)	4.4±2.8 (1-8)	5±3 (0-10)
CT score in each lobe						
Left upper lobe	0.6±0.7 (0-2)	1.1±0.7 (0-2)	1.7±0.7 (0-3)	2.0±1.5 (0-5)	0.8±0.9 (0-2)	0.8±0.6 (0-2)
Left lower lobe	0.9±0.8 (0-2)	1.6±0.8 (0-3)	2.0±0.9 (0-3)	2.1±1.1 (1-4)	1.0±1.0 (0-3)	1.2±0.7 (0-2)
Right upper lobe	0.8±0.8 (0-3)	1.3±0.7 (0-3)	1.9±1.10 (0-4)	2.2±1.3 (1-5)	1.0±0.8 (0-2)	0.9±0.6 (0-2)
Right middle lobe	0.5±0.6 (0-2)	1.0±0.5 (0-2)	1.3±0.9 (0-3)	1.7±1.5 (1-5)	0.4±0.5 (0-1)	0.7±0.8 (0-2)
Right lower lobe	0.8±0.7 (0-3)	1.8±0.8 (0-3)	2.1±0.9 (0-3)	2.2±1.0 (1-4)	1.1±0.6 (0-2)	1.2±0.9 (0-3)

consolidation were less common. This followed in prior reports (6-8). In stage 2 (5-9 days), the CT abnormalities became more diverse; crazy-paving patterns and consolidation increased significantly. In stages 3 and 4, the frequency of consolidation peaked (83.3% and 87.5%, respectively); then it decreased gradually. Again, GGO was the most prominent abnormality in the late stages (5 and 6). Findings of residual disease persisted in 23 (92%) of the 25 patients who underwent imaging in stage 6.

The highest total CT scores were recorded in stages 3 and 4. This result was different from that in Pan et al.'s (6) study; they reported that after 14 days, the infection was brought under control and that the consolidations started to be absorbed. The reason for this difference in results may be that only patients with mild COVID-19 pneumonia were included in Pan et al.'s (6) study. Our finding of the persistence of high CT scores was different finding from that of Pan et al. (6), but it was similar to those of Wang et al. (8). The increase in the incidence of GGO in the late stages was also similar to findings in Wang et al.'s (8) study. Increases in GGO in the late stages were also shown in patients with SARS (9). Moreover, in our study, the incidence of linear lines increased in the late stages (4, 5, and 6). Pan et al. (6) did not observe crazy-paving patterns after 14 days; in our study, in contrast, crazy-paving patterns were observed in stages 4 (25%) and 5 (28.6%).

CT scores were higher in both lower lobes, which followed in previous studies (6,7). Other results in our study that corroborated the results of previous studies included peripheral-subpleural lesions and predominant GGO and consolidation. This pattern of involvement was also similar to those in SARS and Middle East respiratory syndrome (MERS). CT findings in COVID-19 pneumonia showed typical lung damage from viral pneumonia, as in SARS and MERS (9,10).

Study Limitations

This study had two major limitations. First, group analysis of patients with mild and severe pneumonia was not performed. Second, scanning intervals among patients were not uniform because of the retrospective nature of this study.

CONCLUSION

In conclusion, the most common CT finding in COVID-19 pneumonia is bilateral peripheral GGO. On CT, lung involvement increases rapidly after the onset of the symptoms, peaks at approximately 10-14 days and continues at relatively high levels for some time thereafter. CT findings thus show a specific pattern during the disease process. On the basis of these patterns, clinicians can determine whether the disease is progressing or whether the patient is recovering. Knowing which pattern is dominant at which stage can help clinicians predict the course of the disease and determine the prognosis of the patient.

- The most common CT appearances in all stages were GGO, crazy-paving pattern, and consolidation.
- Most of the lesions were peripheral and subpleural in location, and in most patients, involvement was bilateral.
- Residual signs of disease were found in 92% of the patients who underwent CT after the 28th day.

Ethics

Ethics Committee Approval: Ethics Committee of University of Health Seciences Turkey, Prof. Dr. Cemil Tascioglu City Hospital (protocol number: 192) and the Republic of Turkey Ministry of Health, COVID-19 Scientific Research Committee.

Informed Consent: All patients gave informed consent.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.D.Ö., R.Y.B., Design: D.K., Data Collection or Processing: D.K., Analysis or Interpretation: D.K., Literature Search: S.D.Ö., Writing: S.D.Ö., F.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

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