Radiology

ORIGINAL RESEARCH • THORACIC IMAGING

Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19)

Feng Pan, MD • Tianhe Ye, MD* • Peng Sun, MD • Shan Gui • Bo Liang, MD • Lingli Li, MD • Dandan Zheng, PhD • Jiazheng Wang, PhD • Richard L. Hesketh, MD, PhD • Lian Yang, MD • Chuansheng Zheng, MD, PhD*

From the Departments of Radiology (F.P., T.Y., S.G., B.L., L.L., L.Y., C.Z.) and Emergency Medicine (P.S.), Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, #1277 Jiefang Ave, Wuhan 430022, China; Hubei Province Key Laboratory of Molecular Imaging, Wuhan, China (F.P., T.Y., S.G., B.L., L.L., L.Y., C.Z.); MSC Clinical & Technical Solutions, Philips Healthcare, Beijing, China (D.Z., J.W.); and Department of Radiology, University College London Hospital, London, England (R.L.H.). Received February 9, 2020; revision requested and received February 12; accepted February 13. **Address correspondence to** L.Y. (e-mail: *yanglian@hust.edu.cn*).

* F.P. and T.Y. contributed equally to this work.

Conflicts of interest are listed at the end of this article.

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Background: Chest CT is used to assess the severity of lung involvement in coronavirus disease 2019 (COVID-19).

Purpose: To determine the changes in chest CT findings associated with COVID-19 from initial diagnosis until patient recovery.

Materials and Methods: This retrospective review included patients with real-time polymerase chain reaction–confirmed COVID-19 who presented between January 12, 2020, and February 6, 2020. Patients with severe respiratory distress and/or oxygen requirement at any time during the disease course were excluded. Repeat chest CT was performed at approximately 4-day intervals. Each of the five lung lobes was visually scored on a scale of 0 to 5, with 0 indicating no involvement and 5 indicating more than 75% involvement. The total CT score was determined as the sum of lung involvement, ranging from 0 (no involvement) to 25 (maximum involvement).

Results: Twenty-one patients (six men and 15 women aged 25–63 years) with confirmed COVID-19 were evaluated. A total of 82 chest CT scans were obtained in these patients, with a mean interval (±standard deviation) of 4 days ± 1 (range, 1–8 days). All patients were discharged after a mean hospitalization period of 17 days ± 4 (range, 11–26 days). Maximum lung involved peaked at approximately 10 days (with a calculated total CT score of 6) from the onset of initial symptoms ($R^2 = 0.25$, $P < .001$). Based on quartiles of chest CT scans from day 0 to day 26 involvement, four stages of lung CT findings were defined. CT scans obtained in stage 1 (0–4 days) showed ground-glass opacities (18 of 24 scans [75%]), with a mean total CT score of 2 ± 2; scans obtained in stage 2 (5–8 days) showed an increase in both the crazy-paving pattern (nine of 17 scans [53%]) and total CT score (mean, 6 ± 4; $P = .002$); scans obtained in stage 3 (9–13 days) showed consolidation (19 of 21 scans [91%]) and a peak in the total CT score (mean, 7 ± 4); and scans obtained in stage 4 (≥14 days) showed gradual resolution of consolidation (15 of 20 scans [75%]) and a decrease in the total CT score (mean, 6 ± 4) without crazy-paving pattern.

Conclusion: In patients recovering from coronavirus disease 2019 (without severe respiratory distress during the disease course), lung abnormalities on chest CT scans showed greatest severity approximately 10 days after initial onset of symptoms.

Since December 2019, many gathered cases of "unknown viral pneumonia" have been reported. These cases were initially linked to exposure at the Huanan Seafood Market, Wuhan, China (1). A novel coronavirus capable of infecting humans was formally confirmed on January 6, 2020 (2,3), and termed coronavirus disease 2019 (COVID-19) (2). By February 7, 2020, there were 43 103 confirmed cases of COVID-19 (previously called 2019-nCoV) in 25 countries (4). Similar to other coronaviral pneumonia such as severe acute respiratory syndrome caused by coronavirus and Middle East respiratory syndrome coronavirus, COVID-19 can also lead to acute respiratory distress syndrome (1,5). With the gradual recognition of COVID-19, professional consensus, guidelines, and criteria were steadily established with the aim of preventing transmission and facilitating diagnosis and treatment (6–8).

From the recently published literature, typical radiologic images of COVID-19 demonstrated clear destruction of the pulmonary parenchyma, including interstitial inflammation and extensive consolidation, similar to the previously reported coronavirus infection (1,9–11). However, some patients with COVID-19 consistently demonstrated no hypoxemia or respiratory distress during the course of hospitalization. The purpose of this study was to determine the change in chest CT findings associated with COVID-19 from initial diagnosis until patient recovery.

Materials and Methods

This study was approved by the ethics committees of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, and in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The requirement to ob-

Abbreviations

COVID-19 = coronavirus disease 2019, GGO = ground-glass opacity

Summary

In patients recovering from coronavirus disease 2019 (COVID-19), four stages of evolution on chest CT scans were identified from symptom onset: early stage (0–4 days), progressive stage (5–8 days), peak stage (9–13 days), and absorption stage (≥14 days).

Key Results

- In patients who recovered from coronavirus disease 2019 (COVID-19), initial lung findings on chest CT scans were small subpleural ground-glass opacities (GGOs) that grew larger with crazy-paving pattern and consolidation.
- Lung involvement increased to consolidation up to 2 weeks after symptom onset.
- After 2 weeks, the lesions were gradually absorbed leaving extensive GGO and subpleural parenchymal bands.

tain informed consent for this retrospective study was waived. The anonymous data were collected and analyzed to facilitate better clinical decisions and treatment.

Diagnostic and Discharge Criteria

According to the preliminary diagnosis and treatment protocols from the National Health Commission of the People's Republic of China, COVID-19 was based on the following criteria: *(a)* epidemiologic history (travel and/or residence history in Wuhan or exposure history to patients with fever and respiratory symptoms from Wuhan within 14 days before the onset of illness); *(b)* clinical manifestations (fever, imaging characteristics of pneumonia, and/or normal or decreased white blood cell count or decreased lymphocyte count); and *(c)* laboratory diagnosis (real-time polymerase chain reaction revealed positive detection of COVID-19 in throat swabs or lower respiratory tract) (7,8). Patients with confirmed COVID-19 were hospitalized and isolated for treatment. The discharge criteria were as follows: *(a)* patient was afebrile for more than 3 days, *(b)* respiratory symptoms significantly improved, *(c)* there was improvement in the radiologic abnormalities on chest radiographs or chest CT scans, and *(d)* there were two consecutive negative COVID-19 nucleic acid tests at least 24 hours apart (7).

Patients

In this single-center study, records from patients with COVID-19 were reviewed retrospectively for the period from January 12, 2020, to February 6, 2020. Patients with severe pneumonia during the disease course were excluded. Severe pneumonia was defined as severe respiratory distress (respiratory rate >30 breaths per minute), requirement for oxygen treatment or mechanical ventilation, and oxygen saturation as measured with pulse oximetry of less than 90% on room air (6).

CT Protocol

Chest CT was performed with two commercial multidetector CT scanners (Philips Ingenuity Core128, Philips Medical Systems, Best, the Netherlands; Somatom Definition AS, Siemens Healthineers, Erlangen, Germany) by using a single inspiratory phase. To minimize motion artifacts, patients were instructed on breath-holding. CT images were then acquired during a single breath-hold. For CT acquisition, the tube voltage was 120 kVp with automatic tube current modulation. From the raw data, CT images were reconstructed with a matrix size of 512 × 512 as axial images (thickness, 1.5 mm; increment, 1.5 mm) in transverse slice orientation with either hybrid iterative reconstruction (iDose level 5, Philips Medical Systems) or a pulmonary B70F kernel and a mediastinal B30f kernel (Siemens Healthineers). The mean CT dose index volume (±standard deviation) was 8.4 mGy ± 2.0 (range, 5.2–12.6 mGy).

Chest CT Evaluation

The major CT findings were described by using internationally standard nomenclature defined by the Fleischner Society glossary and peer-reviewed literature on viral pneumonia, using terms including ground-glass opacity (GGO), crazy-paving pattern, and consolidation (12–14). A semiquantitative scoring system was used to quantitatively estimate the pulmonary involvement of all these abnormalities on the basis of the area involved (15). Each of the five lung lobes was visually scored on a scale of 0 to 5, with 0 indicating no involvement; 1, less than 5% involvement; 2, 5%–25% involvement; 3, 26%–49% involvement; 4, 50%–75% involvement; and 5, more than 75% involvement. The total CT score was the sum of the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement).

The distribution of lung abnormalities was recorded as predominantly subpleural (involving mainly the peripheral one-third of the lung), random (without predilection for subpleural or central regions), or diffuse (continuous involvement without respect to lung segments) (16).

Image analysis was performed by three radiologists (C.Z., B.L., and L.Y., with 26, 25, and 22 years of experience in thoracic radiology, respectively) with use of the institutional digital database system (Vue PACS, version 11.3.5.8902; Carestream Health, Oakville, Canada). Final scores were determined by consensus.

Statistical Analysis

Statistical analyses were performed by using software (SPSS, version 24; IBM, New York, NY). Quantitative data are presented as means ± standard deviations and ranges, and qualitative data are presented as the percentage of the total unless otherwise specified. The total CT score of pulmonary involvement as a function of time was quantitively assessed by using the SPSS curve estimation module. The comparisons of nonpaired and paired quantitative data were evaluated by using the Mann-Whitney *U* test and Wilcoxon test, according to the normal distribution assessed by the Shapiro-Wilk test. $P < .05$ was indicative of a statistically significant difference.

Results

Patient Characteristics

A total of 21 patients (six men and 15 women) were included in the study. The mean patient age was 40 years ± 9 (Table 1). The most prevalent symptoms at presentation were fever (18 of 21 patients [86%]) and cough (12 of 21 patients [57%]). Four patients had no chest CT abnormalities at baseline evaluation.

Results of laboratory investigations were often normal, with the most frequent abnormalities being a mildly elevated C-reactive protein level (mean, 17.2 mg/L ± 20.0), erythrocyte sedimentation rate (mean, 33 seconds ± 27), lactate dehydrogenase level (mean, 242 U/L ± 73), and D-dimer level (mean, 0.93 mg/L ± 1.43) (Table 1). The first chest CT scan was obtained a mean of 2 days ± 2 (range, 0–9 days) after the onset of symptoms. A total of 82 chest CT scans were obtained, and each patient had a mean of four CT scans ± 1 (range, 3–6), with a mean interval of 4 days ± 1 (range, 1–8 days) between scans (Fig 1). All patients were discharged after a mean hospital stay of 17 days ± 4 (range, 11–26 days).

Table 1: Characteristics of the Patient Cohort

Parameter	Value
Age (y)	40 ± 9 (25–63)
Sex*	
M	6 (29)
F	15 (71)
Initial symptoms*	
Throat pain	4 (19)
Cough	12 (57)
Expectoration	6 (29)
Fever	18 (86)
Low-grade fever (37.5°–38.0°C)	6 (29)
Moderate-grade fever (38.1°–39.0°C)	7 (33)
High-grade fever (>39.1°C)	5 (24)
Chills	6 (29)
Fatigue	11 (52)
Loss of appetite	9 (43)
Myalgia	5 (24)
Chest pain	2 (9.5)
Laboratory investigations	
White blood cell count (G/L)	4.9 ± 1.0 (3.1–6.9)
Neutrophil count (G/L)	3.1 ± 0.8 (2.1–4.6)
Lymphocyte count (G/L)	1.4 ± 0.5 (0.7–2.5)
Lymphocyte percentage (%)	28 ± 8 (15–42)
C-reactive protein (mg/L)	17.2 ± 20.0 (3.1–88.6)
Erythrocyte sedimentation rate (sec)	33 ± 27 (5–93)
Alanine aminotransferase level (U/L)	42 ± 31 (12–107)
Aspartate aminotransferase level (U/L)	32 ± 20 (15–95)
Lactate dehydrogenase level (U/L)	242 ± 73 (156–377)
D-dimer level (mg/L)	0.93 ± 1.43 (0.17–4.70)
Time between onset of initial symptoms and first scan (d)	2 ± 2 (0–9)
No. of chest CT scans in each patient	4 ± 1 (3–6)
Interval between adjacent scans (d)	4 ± 1 (1–8)
Hospitalization period (d)	17 ± 4 (11–26)
Interval between onset of initial symptoms and discharge (d)	19 ± 4 (12–26)

Note.—Except where indicated, data are means ± standard deviations, with ranges in parentheses.
* Data are numbers of patients (n = 21), with percentages in parentheses.

Chest CT Evaluation

GGO, crazy-paving pattern (GGO with superimposed inter- and intralobular septal thickening), and consolidation were the most frequent CT findings in mild COVID-19 (Fig 2). No mediastinal lymphadenopathy was observed. In most patients (18 of 21), the total CT score increased approximately 10 days after the onset of symptoms and then gradually decreased (Fig 3, *A*). The total CT score peaked at 10 days after the onset of initial symptoms (Fig 3, *B*), with a calculated total CT score of 6 at 10 days.

On the basis of quartiles of chest CT scans and degree of lung involvement from day 0 to day 26 after disease onset, four stages were identified from the onset of initial symptoms (Fig 3, *B*): stage 1 (0–4 days, 24 scans), stage 2 (5–8 days, 17 scans), stage 3 (9–13 days, 21 scans), and stage 4 (≥14 days, 20 scans). In each group, the lower lobes were more inclined to be involved with higher CT scores. The CT scores of bilateral lower lobes in particular reached significant differences compared with those in the corresponding upper and middle lobes in stage 3 and 4 (mean values for stage 3 and 4: left lower lobe vs left upper lobe, 2 ± 1 vs 1 ± 1 [P = .002 and P = .004, respectively]; right lower lobe vs right upper lobe and right middle lobe, 2 ± 1 vs 1 ± 1 [$P < .001$ and P = .002, respectively] and 1 ± 1 [P = .001 and P = .003, respectively]). The total CT score in stage 2 was greater than that in stage 1 (mean, 6 ± 4 vs 2 ± 2; P = .002) (Table 2).

The distribution of lesions and major CT findings were compared at the four stages of the course (Table 3). Overall, subpleural lesions were more common than central lung lesions. Most chest CT scans showed bilateral lung involvement during the course of the disease. The most common CT findings in stage 1 were GGO (18 of 24 scans [75%]) with partial crazy-paving pattern (six of 24 scans [25%]) and consolidation (10 of 24 scans [42%]) (Figs 4, 5). In stage 2, the GGO (14 of 17 scans [82%]) extended to more pulmonary lobes with more crazy-paving pattern (nine of 17 scans [53%]) and consolidation (eight of 17 scans [47%]). In stage 3, consolidation (19 of 21 scans [90%]) was the main finding, with an obviously decreased ratio of GGO (15 of 21 scans [71%]) and crazy-paving pattern (four of

21 scans [19%]). In stage 4, the consolidation (15 of 20 scans [75%]) was partially absorbed without any crazy-paving pattern.

Discussion

The purpose of this study was to determine the change in chest CT findings associated with coronavirus disease 2019 (COVID-19) from initial diagnosis until patient recovery. We studied patients with COVID-19 at approximately 4-day intervals from the onset of symptoms until recovery. Patients with complicated pneumonia, defined as severe respiratory distress (respiratory rate >30 breaths per minute), requirement for oxygen treatment or mechanical ventilation, or oxygen saturation as measured with pulse oximetry of less than 90% on room air, were excluded. In patients without severe respiratory disease, the major pulmonary CT findings of COVID-19 were ground-glass opacities, crazy-paving pattern, and consolidation predominantly in subpleural locations in the lower lobes. The number and severity of lesions seen at chest CT increased in the first 10 days (peaking at approximately 10 days). Subsequently, there was a short plateau phase and a gradual decrease in abnormalities.

Patients in our study had multiple chest CT scans at different time points (at least three), which provided reliable data on the dynamic radiologic pattern. The typical mild COVID-19 mainly starts as small subpleural unilateral or bilateral GGOs in the lower lobes, which then develops into the crazy-paving pattern and subsequent consolidation. After more than 2 weeks, the lesions are gradually absorbed with residual GGO and subpleural parenchymal bands. In these patients who recovered from COVID-19, four stages of lung involvement were defined on CT scans.

In stage 1 (early stage, 0–4 days after the onset of initial symptoms), GGO was the main radiologic demonstration (Fig 2, *A*) and was distributed subpleurally in the lower lobes unilaterally or bilaterally. In our cohort, four patients had normal CT findings (total CT score = 0) (Fig 3, *A*). However, repeat chest CT showed lung abnormalities in these four patients.

In stage 2 (progressive stage, 5–8 days after the onset of initial symptoms), the infection rapidly aggravated and extended to a bilateral multilobe distribution with diffuse GGO, crazy-paving pattern, and consolidation.

In stage 3 (peak stage, 9–13 days after the onset of the initial symptoms), the involved area of the lungs slowly increased to peak involvement and dense consolidation became

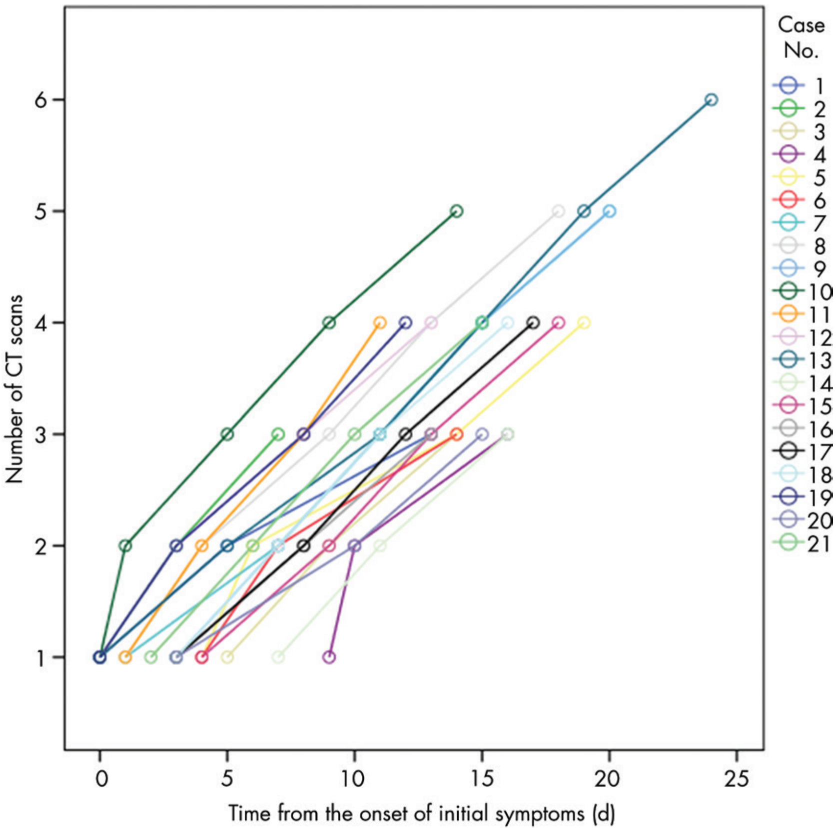

Figure 1: Timeline of the chest CT scans.

Figure 2: Chest CT findings of coronavirus disease 2019 (COVID-19). Transaxial images show, *A*, ground-glass opacity (GGO), *B*, crazy-paving pattern (GGO with superimposed inter- and intralobular septal thickening), and, *C*, consolidation. All images were obtained with a window level of −600 and window width of 1600.

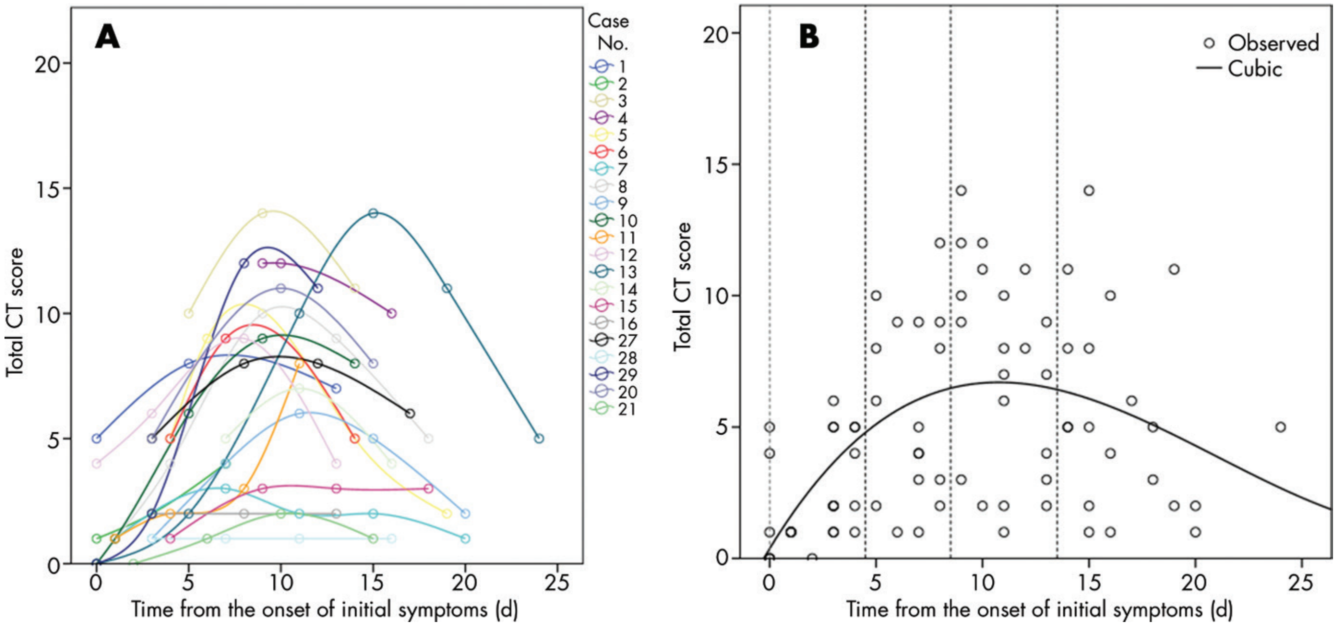

Figure 3: Change in lung involvement on chest CT scans from time of onset of initial symptoms. *A*, Graph shows dynamic changes in total CT score for each patient. *B*, Graph shows peak total CT lung involvement occurred at day 10 (curve fitting equation: $y = 0.001 \times x^3 - 0.083 \times x^2 + 1.329X + 0.373$, where x is the time from onset of the initial symptoms and y is the total CT score of the pulmonary involvement; $R^2 = 0.25$, $P < .001$). Quartiles of chest CT scans between 0 and 26 days from symptom onset are shown as stages 1–4.

Table 2: Summary of Pulmonary Involvement in the Four Stages

Parameter	Stage 1 (24 scans)	Stage 2 (17 scans)	Stage 3 (21 scans)	Stage 4 (20 scans)
Total CT score	2 ± 2 (0–6)	6 ± 4 (1–12)*	7 ± 4 (1–14)	6 ± 4 (1–14)
No. of involved lobes	2 ± 2 (0–5)	3 ± 2 (1–5)*	4 ± 2 (1–5)	3 ± 2 (1–5)
CT score according to lobe				
Left upper lobe	0 ± 1 (0–2)	1 ± 1 (1–3)	1 ± 1 (0–3)	1 ± 1 (0–3)
Left lower lobe	1 ± 1 (0–3)	1 ± 1 (0–5)*	2 ± 1 (0–4)†	2 ± 1 (0–5)†
Right upper lobe	0 ± 1 (0–2)	1 ± 1 (0–2)*	1 ± 1 (1–3)	1 ± 1 (0–2)
Right middle lobe	0 ± 1 (0–2)	1 ± 1 (0–2)*	1 ± 1 (0–2)	1 ± 1 (0–2)
Right lower lobe	1 ± 1 (0–2)	2 ± 1 (0–4)*	2 ± 1 (0–4)‡	2 ± 1 (0–4)‡

Note.—Data are means ± standard deviations, with ranges in parentheses.

* Mann-Whitney *U* test showed significant difference between stage 1 and stage 2 ($P < .05$).

† Wilcoxon test showed significant difference between the left lower lobe and the left upper lobe ($P < .05$).

‡ Wilcoxon test showed significant difference between the right lower lobe and the right upper and right middle lobes ($P < .05$).

more prevalent. Findings included diffuse GGO, crazy-paving pattern, consolidation, and residual parenchymal bands.

In stage 4 (absorption stage, ≥14 days after the onset of initial symptoms), the infection was controlled and the consolidation was gradually absorbed. However, in this process, extensive GGO could be observed as the demonstration of the consolidation absorption (Fig 5, *D*). Noticeably, the crazy-paving pattern was no longer observed in this stage, likely as a result of recovery. On the basis of the total CT score, the absorption stage extended beyond 26 days (our last days of follow-up) from the onset of initial symptoms.

Limitations of this study include the retrospective nature of our analysis and lack of a comparison group with severe COVID-19. Most of the patients with severe pneumonia and acute respiratory distress syndrome are still hospitalized (17). Therefore, the analysis was limited to patients with mild COVID-19.

In summary, most patients who recovered from coronavirus disease 2019 showed the greatest severity of lung disease on CT scans obtained at approximately 10 days after the initial onset of symptoms. Signs of improvement at chest CT began at approximately 14 days after the onset of initial symptoms.

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Table 3: Distribution and Frequency of Major CT Findings according to Stage

Parameter	Stage 1 (*n* = 24)	Stage 2 (*n* = 17)	Stage 3 (*n* = 21)	Stage 4 (*n* = 20)
Distribution of pulmonary lesions				
No lesion	4 (17)	0 (0)	0 (0)	0 (0)
Peripheral	13 (54)	10 (59)	13 (62)	14 (70)
Random	7 (29)	6 (35)	7 (33)	5 (25)
Diffuse	0 (0)	1 (5.9)	1 (4.8)	1 (5.0)
Involvement of the lesions				
No involvement	4 (17)	0 (0)	0 (0)	0 (0)
Single lobe	10 (42)	4 (24)	3 (14)	4 (20)
Bilateral multilobe	10 (42)	13 (76)	18 (86)	16 (80)
Ground-glass opacity				
No	6 (25)	3 (18)	6 (29)	7 (35)
Yes	18 (75)	14 (82)	15 (71)	13 (65)
Crazy-paving pattern				
No	18 (75)	8 (47)	17 (81)	20 (100)
Yes	6 (25)	9 (53)	4 (19)	0 (0)
Consolidation				
No	14 (58)	9 (53)	2 (10)	5 (25)
Yes	10 (42)	8 (47)	19 (90)	15 (75)

Note.—Data are numbers of chest CT scans, with percentages in parentheses.

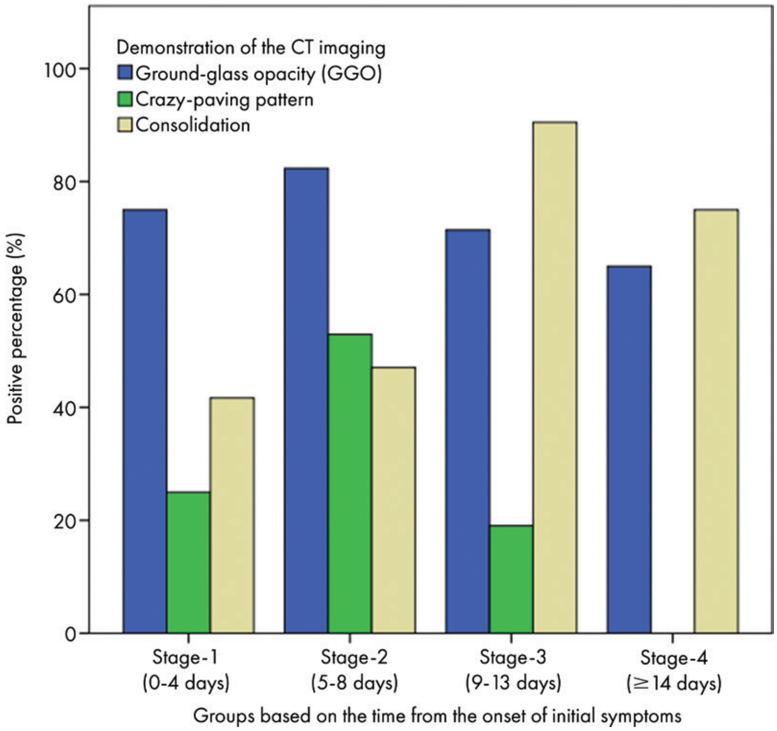

Figure 4: Bar graph shows frequency of major CT findings at different stages.

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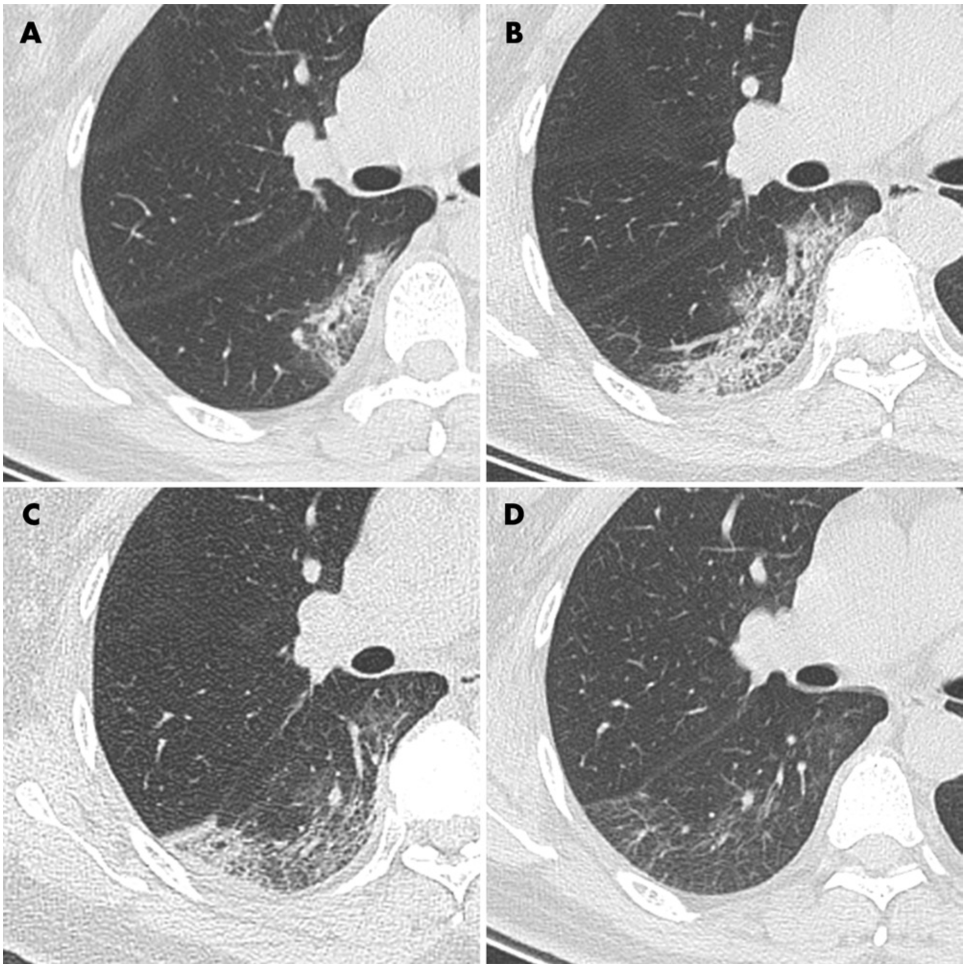

Figure 5: Typical evolution of CT findings in a 47-year-old woman who presented with persistent fever (38.8°C) for 3 days. *A*, CT scan obtained at presentation (day 3 from symptom onset) shows a small region of subpleural ground-glass opacity (GGO) with partial consolidation in right lower lobe. *B*, Scan obtained on day 7 from symptom onset shows an enlarged region of GGO with superimposed inter- and intralobular septal thickening (crazy-paving pattern) with partial consolidation. *C*, Scan obtained on day 11 from symptom onset shows partial resolution of the initial GGO, with a new area of subpleural consolidation. *D*, Scan obtained on day 20 from symptom onset shows continued resolution with minimal residual GGO. Parenchymal bands are observed. All images were obtained with a window level of −600 and window width of 1600.

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