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Spatiotemporal changes of CT manifestations in 110 patients with COVID-19 pneumonia

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Abstract. – OBJECTIVE: The aim of the study was to analyze spatiotemporal changes of CT manifestations in patients with COVID-19 pneumonia.

PATIENTS AND METHODS: In this retrospective review, 110 patients with confirmed COVID-19 by RT-PCR form February 16, 2020, to March 28, 2020 were included. A total of 449 CT scans were reviewed. We analyze the type and distribution of lung abnormalities, and CT general assessment and lesion area statistics were performed. Patients were divided into mild, moderate, and severe disease based on Chinese guidelines: mild (patients with minimal symptoms, CT scans showed no pneumonia or a small area of pneumonia infection), moderate (different extent of clinical manifestations and CT scans showed multiple pneumonia infections in both lungs), severe disease (respiratory distress, CT scans lesion area exceeds 50%, and the lesion contains consolidation). The proportion of patients with mild, moderate and severe diseases was counted.

RESULTS: The CT score and the area involved reached a peak (median 10) on illness days 7-12, and then, continued to be at a high level. The main abnormal pattern after symptoms appeared GGO (36/94 [36%] to 40/65 [62%] in different periods). The proportion of mixed reached its peak on illness days 13-18 (36/93 [39%]). Pure GGO was the most common subtype of GGO (24 of 60 CT scans [40%] to 23 of 33 CT scans [70%]) after symptoms onset. The ratio of GGO with irregular lines and interfaces peaked on illness days 7-12 (6/34 [18%]). The lesions are mainly distributed on both sides and under the pleura. 76/84 (90%) of discharged patients had residual lesions on the final CT scans. 4 confirmed patients' CT scans did not show lesions (on illness days 1-24 days). There were 47 mild cases (42.7%), 46 moderate cases (41.8%), and 7 severe cases (6.3%).

CONCLUSIONS: The degree of lung abnormality on the CT of the patients reached the peak on the 7th to 12th days of the disease. CT performance changes with time have a certain regularity, which may indicate the progress and recovery of the disease. 90% of patients still observed residual lung abnormalities in CT images at the time of discharge. There were 4 confirmed cases where the CT images did not show the lesion; hence, CT cannot be used as a basis for judging COVID-19 as a single tool.

Key Words:
COVID-19, CT images, CT score, symptoms, CT findings.

Abbreviations

COVID-19 = corona virus disease 2019, CT = computed tomography, RT-PCR= Reverse Transcrip-tion-Polymerase Chain Reaction.

Introduction

COVID-19, which was discovered in Wuhan, China, in 2019, broke out in December 2019 and has spread rapidly around the world for more than 16 months[1]. The disease is spreading rapidly around the world. According to real-time statistics released by WHO, as of May 6, 2021, a total of 155,665,214 cases of coronavirus disease 2019 (COVID-19) have been diagnosed, and 3,250,648 deaths have been reported. A total of 220 countries and regions have been affected[1]. CT can help clinicians quickly find the lesions early, and better help clinicians treat patients, so it plays an important role in the diagnosis and treatment of COVID-19[2,3]. Some literature[4-6] showed that CT findings various features, and the main

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abnormalities include GGO and consolidation. Chung et al[7] summarized the chest CT findings of COVID-19 subtype. Pan et al[8] determined the change in chest CT findings associated with COVID-19 from initial diagnosis until patient recovery. However, these studies only include 21 patients, and the analysis was limited to patients with mild COVID-19.

A better understanding of the progress of COVID-19 pneumonia CT manifestations helps inaccurate diagnosis and the stage of the disease. Therefore, we conducted a study to analyze the time changes of continuous CT findings in patients with COVID-19 pneumonia, including mild, moderate, and severe diseases.

The main objective of the study was to analyze the CT manifestations of COVID-19 pneumonia patients over time and studying the changes of symptoms on CT images over time that will help clinicians determine the stage of the disease.

Patients and Methods

This study is a retrospective review, approved by the medical ethics committee of Jiangsu Key Laboratory of Digital Medical Equipment Technology (2020JDMKL0201) and in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The patient signed an informed consent. Patient records and information were anonymized and de-identified prior to analysis.

Patients

In this single-center study, records from patients with COVID-19 were reviewed retrospectively for the period from February 16, 2020, to March 28, 2020. The flow chart of patient enrollment is shown in Figure 1. Inclusion criteria: (1) At least one positive polymerase chain reaction test (RT-PCR) in oropharyngeal swabs after admission; (2) Negative polymerase chain reaction test (RT-PCR) twice when discharged (24 hours apart). The exclusion criteria are: (1) children, (2) death cases, (3) simultaneous COVID-19, and other lung diseases.

The discharge criteria are as follows: two consecutive RT-PCR results are negative at least 24 hours apart. After admission, the CT examination is determined by the clinician based on the clinical situation. We followed up patients until they were discharged or (March 28, 2020) stayed in hospital.

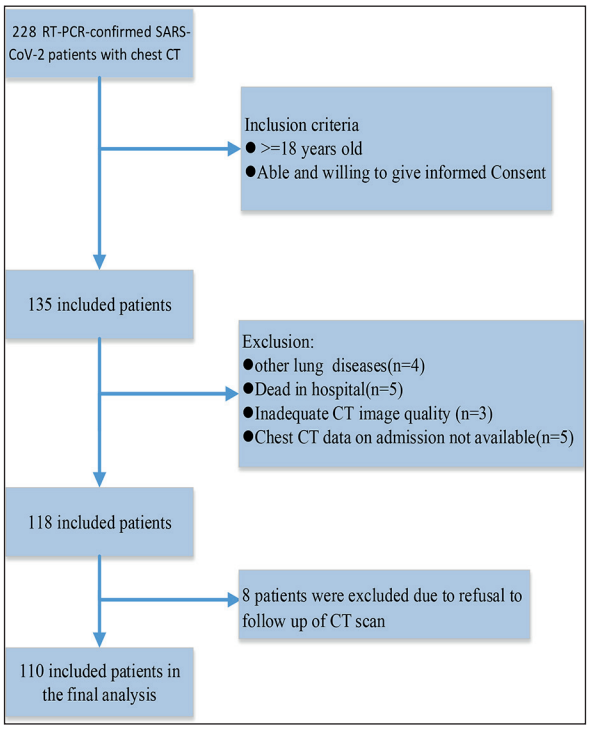

Figure 1. Flow diagram of patients' enrollment.

CT Protocol

Using a 64-row CT system (Philips, Brilliance-64, Eindhoven, Noord-Brabant, Netherlands), the parameters are as follows: detector collimation: 64 × 0.625 mm. The pitch is set to: 0.673; the rotation time is set to: 0.5 s; set the tube voltage: 120 kV; Tube current controlled by AEC; Thickness: 5 mm; using high spatial frequency reconstruction algorithm, continuous reconstruction at 1.5 mm. The scanning parameters are as follows: iterative algorithm, reconstruction layer thickness 2.00 mm, layer spacing 1.00 mm, pitch 0.900, tube voltage is set to 120 kV, tube current using Dose Right intelligent milliamp (Reduce Dose is 20 mAs for Average Adult is 127). All patients were in a conventional supine position with head leaning forward.

CT Scan Image Interpretation

The CT scan of each patient before admission was collected for analysis. Two experienced radiologists read CT images (with 7 years and 5 years of radiology work experience, respectively); the researchers reviewed multiple CT scans of a patient and reached a consistent conclusion. CT images have the characteristics of GGO, consolidation, reticular, mixed (combination of GGO,

consolidation, and reticular)[9]. In addition, GGO subcategories are divided into the following categories: (1) Pure GGO; (2) GGO with interlobular thickening; (3) GGO with interlobular lines; (4) GGO with irregular lines and interfaces. We use the scoring method to quantify CT images[9]. Simply put, the left and right lungs are divided into 3 areas: upper lobe, middle lobe, and lower lobe; the percentage of lung involvement in each area is evaluated by 0-4 points (0 points, 0 % Involved; 1. The participation rate is less than 25%; 2. The participation rate is 25% to 50% or less; 3, 50% to 75% or less; 4, 75% or more). The overall CT score is the sum of the scores of the 6 lung regions. The total score is 24 points.

Clinical Classifications

All patients were classified into mild, moderate, and severe disease according to whether there were clinical symptoms, the severity of pneumonia, respiratory failure, shock, other organ failure based on Chinese guidelines[10].

(1) Mild: mild clinical symptoms, for example, mild cough, CT scans show no pneumonia or a small area of pneumonia infection.
(2) Moderate: long-term fever, respiratory tract, and other symptoms, CT scans show multiple pneumonia infections in both lungs.
(3) Severe disease: respiratory distress, respiratory rate $\geq$ 30 times/min; in resting state, oxygen saturation $\leq$ 93%; PaO2/FiO2 $\leq$300 MMHG, CT scans lesion area exceeds 50%, and the lesion contains consolidation.

Statistical Analysis

Statistical analysis was performed using Matlab software (2018 version for statistical analysis, commercial mathematical software produced by MathWorks, USA). Record The median CT score and the time variation of the number of involved areas. Record the CT morphology distribution of the last CT scan of 84 patients before discharge. Record Temporal changes of the main CT patterns and GGO subtypes. The Kruskal-Wallis rank-sum test was used to compare the median of CT lung quantitative evaluation at different times; the c^2 test was used to compare the frequency of CT scan images at different times.

Results

Patients

Between February 16 and March 28, 2020, 137 patients were admitted to isolation wards. Among them, there were 27 patients with Negative Polymerase Chain Reaction test (RT-PCR), and a total of 110 patients with Positive Polymerase Chain Reaction test participated during our study, the average number of days from the onset of symptoms to the end of the discharge study was 25 days. The clinical statistics of patient symptoms are presented in Table I. A total of 449 CT scans of the chest were performed on 110 patients. Each patient received a median of 4 scans (range: 1-6), and the median scan to scan interval was 6 days (range: 2-18). Therefore, CT scans are performed every 6 days after symptoms appear and ana-

Table I. Demographic characteristics, initial symptoms, and clinical outcomes of 110 patients.

Age, gender, initial symptoms and clinical outcomes	Number of patients (Percentage)
Age (y, mean ± standard deviation)	48 ± 15
Gender (male:female)	57:53
Initial symptoms	
Fever	67 (60.9%)
Hypodynamia	26 (23.6%)
Cough	30 (27.2%)
Chest tightness	12 (10.9%)
Sore throat	10 (9.1%)
Chills	8 (7.3%)
Diarrhea	6 (5.5%)
Anorexia	6 (5.5%)
Headache	8 (7.3%)
Muscle pain	7 (6.4%)
Abdominal pain	4 (3.6%)
Clinical outcomes at the end of study	
Discharged	84 (76.4%)
In admission	26 (23.3%)

lyzed as a group, for patients with illness days ≥ 24, a total of 65 scans are combined together as a group for analysis. Patients were divided into mild, moderate, and severe diseases based on Chinese guidelines. There were 47 mild cases (42.7%), 53 moderate cases (48.1%), and 7 severe cases (6.3%).

Temporal Changes of CT Scores and Numbers of Zones Involved

Figure 2A and Figure 2B show the temporal changes of CT lung quantification. After the onset of symptoms, the median CT score and the number of involved areas increased significantly. On illness days 0-6, the median CT score is 4 (interquartile range, 1-6, p <0.05), and the number of areas involved is 2 (interquartile range,1-3, p<0.05), temporarily at a low level. The median

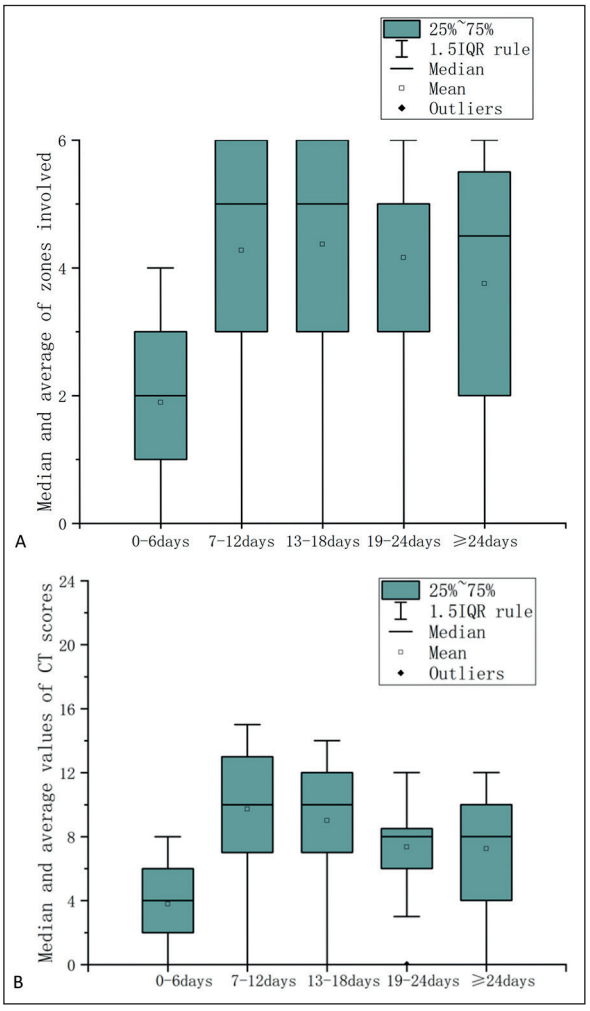

Figure 2. The median CT score and the time variation of the number of involved areas. **A,** Total CT scores. **B,** Numbers of areas involved.

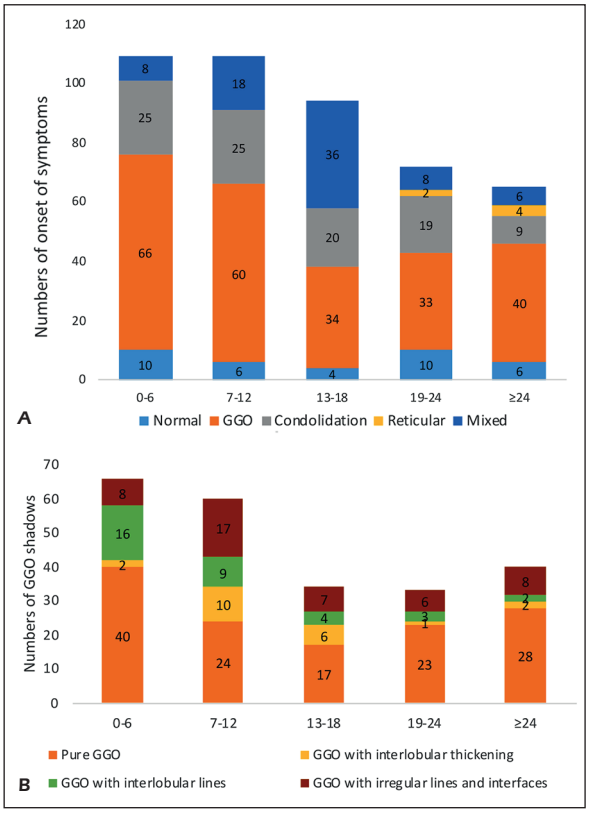

Figure 3. Temporal changes of the main CT patterns and GGO subtypes. **A,**CT scans at different time points from the onset of symptoms. **B,** Subtypes of GGO shadows.

CT score 10 (interquartile range,7-13; p<0.05) and the area of the lesion 5 (interquartile range, 3-6; p <0.05) both reached peaked during illness days 7-12. The peak values were reached on median illness day 9 of the total CT score (interquartile range, 7-14 days, p <0.05).

Changes in Symptoms Based on CT Statistics Over Time

110 patients underwent the first CT scan, of which 10 (9%) had normal CT scan results. These results are presented in Figure 3A. There were 4 cases where no abnormalities were found in multiple scans (probably asymptomatic patients). The other 100 patients have lesions. From the date of CT abnormality to the day of symptom onset on illness days 0-6, the main abnormal patterns after symptoms appear are ground-glass opacities and consolidations. Among them, ground-glass opacities are 60/109 (55%) on illness days 7-12, on illness days 19-24 was 34/94 (45%) (Figure 3A). On illness days (1-6 and 7-12), consolidations are the second major feature, accounting for 25/109 (23%). Normal on illness is 10/110 (9%) on days

0-6, and 4/109 (4%) on illness days 7-12. The incidence of ground glass turbidity decreased significantly from 66/109 (61%) from 0/6 to 33/72 (46%) on illness days 19-24, on illness days 13-18, and the percentage of mixed from 8/109 (7%) rose sharply to 36/94 (38%). On illness days 13-18, the mixed pattern became the second common symptom. The ratio of on illness day ≥ 24 was 6/65 (9%). Reticular is very rare, occurring on illness days 19-24 and on illness day ≥ 24, accounting for 2/72 (2%) and 4/65 (6%). The percentage of frosted glass-like shadows gradually increases from 42/94 (45%) on illness days 13-19 to 40/65 (62%) on illness days ≥ 24 days. Frosted glass shadows always maintain a high proportion.

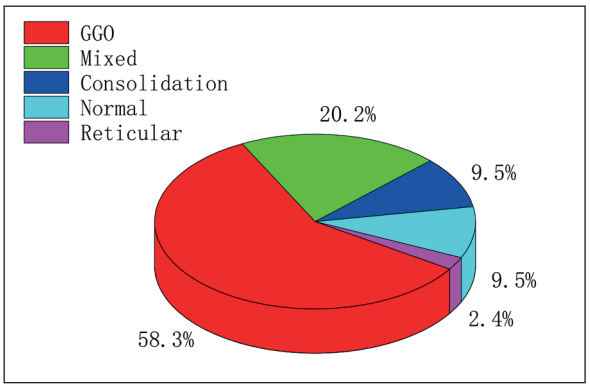

Figure 4. CT morphology distribution of the last CT scan of 84 patients before discharge.

Temporal Change of GGO Subtypes

Pure GGO is the most common subtype of frosted glass shadow after symptoms appear, on illness days 0-6 accounts for 40/66 (61%), on illness days 19-24 accounts for 23/33 (70%) (Figure 3B). On illness days 0-6, GGO with irregular lines and interfaces significantly increased from 8/66 (12%) on illness days 0-6 to 17/60 (28%) on illness days 7-12 and became the second most common pattern of GGO. It is worth noting that the percentage of Pure GGO shows a trend of "declining first and then increasing". 40/66 (61%) on illness days 0-6 decreased to 24/60 (40%, p=0.02), on illness days 7-12, GGO with interlobular lines reached 10/60 (17%), GGO with interlobular thickening reached 9/60 (15%).

CT Findings on Discharge

84 patients were discharged at the end of our study. The last CT scan was performed 2 days before discharge (range: 1-8 days). Of the 84 patients, the last CT scan of 8 patients showed that the lung abnormalities completely disappeared. The remaining 76 patients had residual lesions in the last CT scan. The distribution of CT images is shown in Figure 4. GGO was the main anomaly found in the last CT scan 49/84 (58%), followed by mixed 17/84 (24%). Consolidation ratio was 8/84 (10%). 8/84 (10%) symptoms disappeared completely.

Of the 110 patients included, 20 (18%) had lesions on only one lung during the entire course of pneumonia treatment. 18/20 (90%) patients were discharged (as of the end of the investigation), and 2 patients (27%) completely disappeared on the last CT scan at the end of the study. Figure 5 shows the results of a CT scan of a thirty-three-year-old man with COVID-19 pneumonia from admission to discharge. It can be observed that the initial absorption process then progresses to the final absorption process. Figure 6 shows the results of 4 tests of A 64-year-old female patient with COVID-19 pneumonia. It can be observed that the disease is developing rapidly, with multiple GGO and consolidation. Figure 7 shows a patient 58-year-old woman with COVID-19 pneumonia. GGO, consolidation, mixed, and GGO with irregular lines with interface can be found in the 20-day CT scans observation, and the infection level is still high at the end of the observation.

Discussion

In this study, we described the changes of COVID-19 pneumonia CT symptoms over time. The results showed that after the onset of symptoms, the lung lesion area increased rapidly, reaching a peak around 7-12 days on the day of the disease, and high levels of lung infection lasted a period of time. The CT manifestation of COVID-19 pneumonia is a typical viral pneumonia lung injury[11-13]. This result is consistent with the literature[14-16] 9-13 days reached the peak stage after the onset of the initial symptoms. Afterwards, the persistently high total CT score and the area involved indicate slow absorption of COVID-19 pneumonia. Then, the CT score drops faster after the peak, indicating that the COVID-19 treatment cycle is short.

The most common CT manifestation in the course of COVID-19 pneumonia was GGO. Consolidation is the second most common feature of pre-illness days 12. This is consistent with the findings in previous studies[17-23]. COVID-19

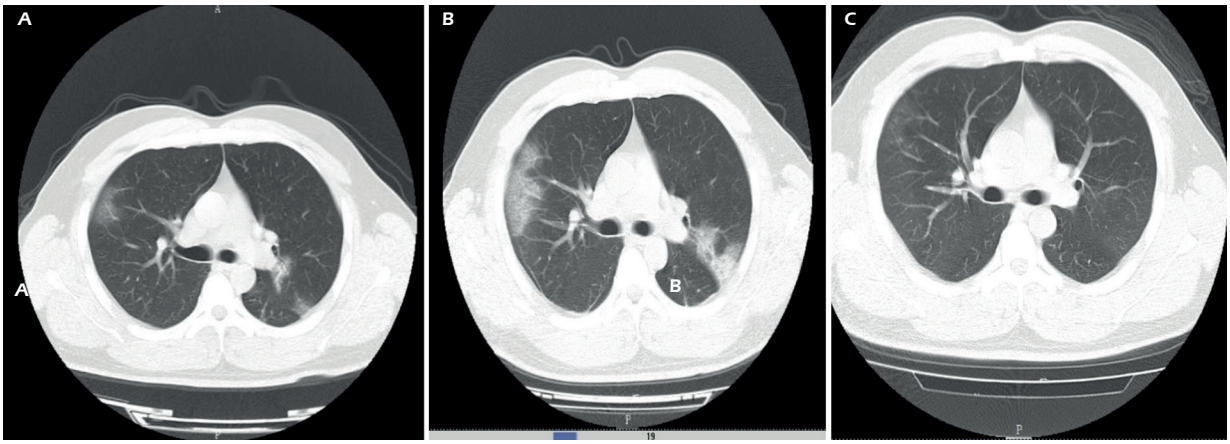

Figure 5. 33-year-old man with COVID-19 pneumonia. **A,** Detection time is January 23, 2020 The chest contours on both sides are symmetrical, and nodular GGO can be seen in the upper half of the lungs. The density is uneven and the edges are blurred. The lower part of the two lungs can be seen GGO. The trachea and bronchi were unobstructed. No abnormalities were observed in the esophagus. **B,** Detection time is January 25, 2020. The chest contours on both sides are symmetrical, and the upper leaves of both lungs can be seen as GGO with uneven density and blurred edges. Bronchial shadows included; cord-like and strip-like density increases were visible in the lower lobe of both lungs. The trachea and bronchi of each leaf segment were unobstructed. Compared with January 23, 2020, the lesions of the two lungs were more advanced than before. **C,** Detection time is February 4, 2020 two pieces of lungs can see the flaky ground-glass shadow disappeared, the trachea and the bronchi of each leaf segment are unblocked.

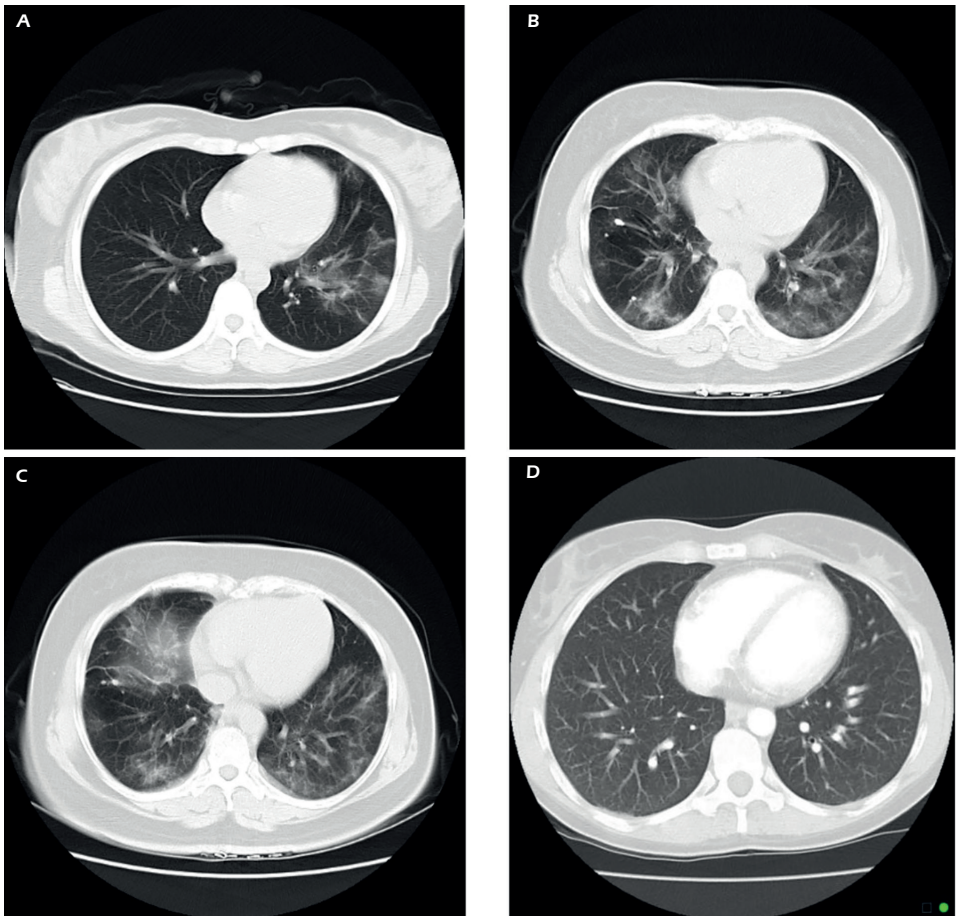

Figure 6. 64-year-old women with COVID-19 pneumonia. **A,** Detection time is February 6, 2020. On the first day of onset, the scan shows multiple simple ground glass-like shadows (GGO) in the lower right lobe. The B scan time was February 16, 2020. The scan on the 10th day of onset shows that GGO appeared in both lungs and increased in degree, and consolidation occurred. CT images of COVID-19 pneumonia **(B)** GGO expanded from a single lung to multiple locations in both lungs. The detection time of **(C)** is February 20, 2020. There are many GGOs with uneven density in both lungs, and the consolidation has also increased. The detection time of **(D)** is February 26, and in 2020, CT scans shows multiple GGOs with uneven density disappear in both lungs.

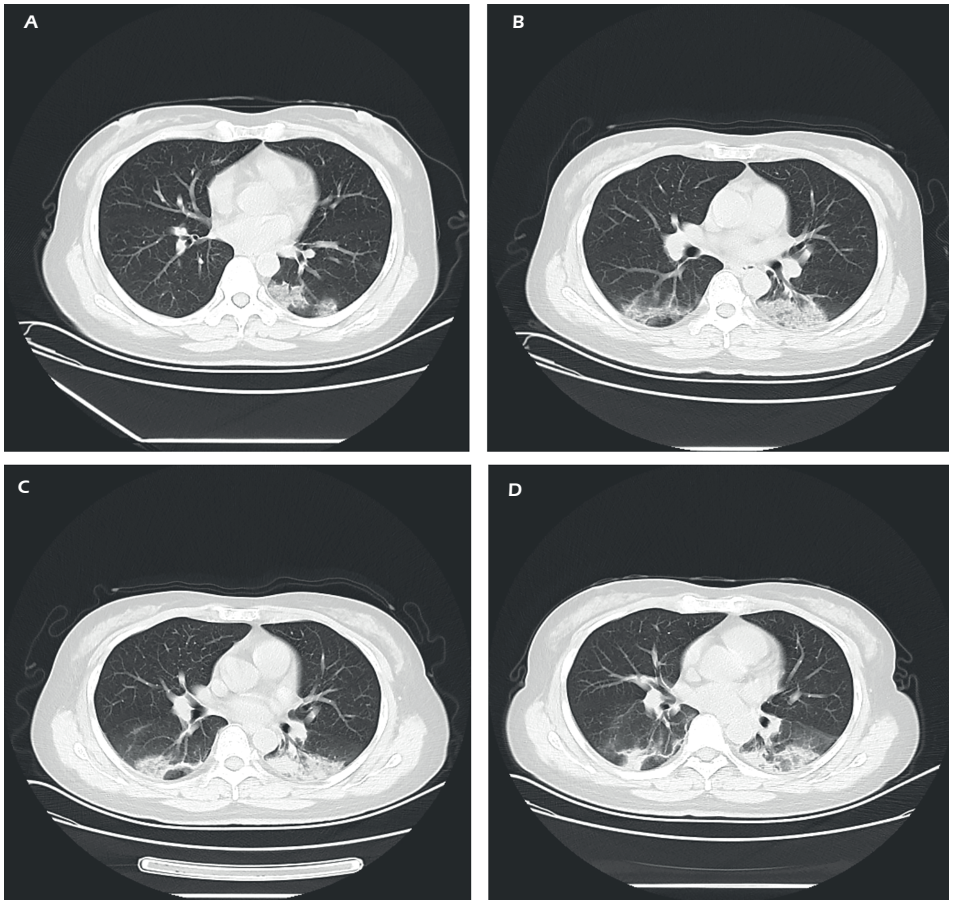

Figure 7. 58-year-old woman with COVID-19 pneumonia. **A,** Detection time is March 1, 2020, CT scans shows multiple GGOs in the lower lobe of the left lung. **B,** Detection time is March 7, 2020, CT scans shows the presence of GGO and consolidation in the lower lobe of the left lung. **C,** Detection time is March 11, 2020, CT scans shows GGO with irregular lines and interfaces appears in the right lung, the left lung has progressed to consolidation, and the lung infection is in mixed. **D,** Detection time is March 20, 2020, CT scans shows GGO and consolidation lesions were partially absorbed, but still at a high level of infection.

pneumonia compared with other viral pneumonia, peripheral distribution, GGO densities, and vascular thickening were more common, central and peripheral lesions, pleural effusion is rare[24]. A comparison of Characteristics of seven common respiratory viral infections is shown in Table II. CT performance on illness days 7-12 and beyond is more diverse than before. For GGO, Pure GGO is the most common subtype in the course of the disease. GGO with irregu-

Table II. Characteristics of seven common respiratory viral infections.

	Typical CT Findings					
	Distribution	Consolidation	GGO	Nodule	Bronchial wall thickening	Pleural effusion
COVID-19	Peripheral,multifocal	+++	+	Rare	Rare	Rare
RSV	Airway	+	+	Centrilobular +++	Rare	Rare
COP	Under the pleura, around the bronchus	+++	Rare	Rare	Rare	Rare
AIP	Diffuse or upper lung	Rare	+++	Rare	+++	Rare
DIP	Lower lung, periphery and under chest mold	Rare	+	Rare	Rare	Rare
Adenovirus	Multifocal	+++	+++	Centrilobular +++	Rare	Rare
H1N1	Lower lung	+++	+++	+++	Rare	+

COVID-19 = coronavirus disease 2019, RSV = respiratory syncytial virus, COP = cryptogenic organizing pneumonia, AIP = acute interstitial pneumonia, DIP = desquamat iveinterstitial pneumonitis, H1N1 = influenza A virus subtype H1N1, + represents severity.

lar lines and interfaces is common after illness days 7-12. Starting from 7-12 on illness days, the percentage of Pure GGO gradually increased significantly. This change in pattern may indicate that inflammation gradually subsided with the re-expansion of the alveoli, thus indicating the absorption or recovery of the disease. These results indicate that CT can help COVID-19's condition judgment after symptoms appear. 90% (76/84) of patients discharged. Many patients still had residual lung abnormalities on their last CT scan when they were discharged. These abnormal images are mainly GGO, and this is consistent with the main CT findings of the previous study[6]. The study included 110 patients, including 57 males and 52 females. There were 47 cases of mild (42.7%), 53 cases of moderate (48.1%), and 7 cases of severe (6.3%). Compared with reference[19], the proportion of mild (30.8%) was higher, the proportion of moderate (59.0%) was lower, and the severe proportion (10.2%) was close. Therefore, more observations and statistics are needed to study the severity of the disease.

Our research has several limitations. Firstly, the sample size was not large enough to observe and track the severe and deadly diseases for a long time. Secondly, due to the large individual differences of each patient, CT scans could hardly be performed regularly, so it was difficult to determine the duration of infection in each stage of the patient. Tertiary, this study excluded death cases due to patients who were close to death usually require mechanical ventilation and CT scans cannot be conducted, thus CT finding in this study cannot be represent for those of entire patients with COVID-19 pneumonia .In addition, this study also found that 4 cases of lung scans showed no signs of infection, it may be that asymptomatic patients, no in-depth research was conducted for them.

Conclusions

In conclusion, the appearance of GGO in both lungs was the most common phenomenon of CT images detected by COVID-19. The score and area of CT abnormality progressed rapidly after the symptoms appear, reaching a peak around 7-12 on illness days, then, the lung abnormality continued to maintain a high level and finally recovered quickly. The time changes of different CT manifestations had specific rules, indicating the progress and recovery of the disease. There were 4 positive RT-PCR cases with no CT findings. This situation was rare and worthy of further study. CT scans indicated the stage of the lesion and the stage of immune repair, which is helpful for prognosis evaluation, but CT was not suitable as an independent screening tool.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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