# ANALYSIS OF BASELINE CT FINDINGS AND EVOLUTION OF SINGLE LESION IN THE EARLY STAGE OF COVID-19

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***ABSTRACT***

***Background:*** *COVID-19 is currently the most concerned epidemic in the world. We conducted a CT follow-up study of a single lesion in the early stage to provide imaging basis for clinicians to accurately diagnose and evaluate the prognosis of COVID-19.*

***Methods:*** *Seventy patients with COVID-19 diagnosed in The Second Hospital of Wuhan Iron and Steel Company were retrospectively analyzed. With the first detection of early single lesion as the baseline lesion, the average interval between 4 follow-up and baseline CT was divided into four stages. The signs of the baseline lesions and their changes in the four stages were analyzed, and their evolution was summarized.*

***Results:*** *We found that most of the baseline lesions were ground-glass opacities (GGO) with subpleural distribution in the lower lobe of the lungs among the 70 patients, and CT signs were different at different stages. In the first stage, baseline lesions progressed in 54 cases (77%) and new lesions were found in 36 cases (51%) . No progressive lesions and new lesions were found in the third stage. In the first three stages, the proportion of fine reticulation decreased gradually, while the proportion of crazy paving pattern and thin GGO gradually increased. Fifty-four cases (77%) were complicated with consolidation, which accounted for the highest proportion in the second stage. After consolidation, the absorption of lesions became slower and the course of disease prolonged. Twenty-two cases (31%) progressed to multiple lesions of the single lobe, and 32 cases (46%) involved both lungs. Single lesion and multiple lesions of single lobe were more easily absorbed than bilateral lung lesions. We also found that patients over 50 years old tend to involve both lungs and the course of disease is relatively longer.*

***Conclusion:*** *The CT imaging features of COVID-19 at different stages can be used to evaluate the progression of the disease.*

***Keywords:*** *Coronavirus infections, pneumonia, tomography, x-ray computer.*

*DOI: 10.19193/0393-6384_2022_1_75*

***Received*** *March 15, 2021;* ***Accepted*** *October 20, 2021*

## Introduction

Multiple cases of acute pneumonia caused by novel coronavirus infections were first found in Wuhan, Hubei Province in December 2019, and subsequently broken out in other regions of China and in many other countries. On February 11, 2020, the World Health Organization officially named it Corona Virus Disease 2019 (COVID-19). It has been shown that COVID-19 has certain characteristic imaging patterns on computerized tomography (CT) scan. The early manifestation is ground-glass opacity (GGO) and it occurs predominantly at subpleural periphery of both lungs[1, 2, 3]. The long axis of the lesion with subpleural distribution is often parallel to the pleura[4], which may be related to the fact that the coronavirus is not distributed based on the lung segment anatomy[5]. Although COVID-19 has been reported to mainly involve the pulmonary interstitium, it may also affect the lung parenchyma

to varying degrees[6]. COVID-19 may progress to the middle and inner zone in the middle and late stages[7]. It has been shown that CT scan plays an important role in the diagnosis and follow-up of the disease[8]. In order to better understand the changes in the CT manifestations of the pneumonia caused by COVID-19, we have selected the early single lesion of the disease as the baseline lesion, followed up with CT to observe and analyze the evolution of the image signs. Our study provides imaging basis for the accurate clinical diagnosis and evaluation of COVID-19.

## Materials and methods

### *Materials*

A retrospective analysis of 70 COVID-19 patients from the COVID-19 affected areas diagnosed by The Second Hospital of Wuhan Iron and Steel Company from January 18, 2020 to March 6, 2020, was performed. All patients were cured and discharged.

The clinical symptoms and laboratory examination during baseline CT scan included 18 cases of fever from 1 to 5 days, 10 cases of fever with cough, 10 cases of chest tightness and chest pain, 8 cases of dry cough, 6 cases of fatigue, and 2 case of lower abdominal pain.

Sixteen cases who contacted with COVID-19 patients showed no clinical symptoms. Among them, 10 cases has developed fever from 1 to 7 days after baseline CT examination, and 2 cases had no clinical symptoms throughout the course. The laboratory examination of 60 cases revealed a decrease in leukocyte count in 10 cases, a decrease in lymphocyte ratio in 20 cases, and an increase of C-reactive protein level in 12 cases.

*The cases in this study had to meet the following criteria :*

• There was an early single lesion at the baseline CT scan;

• At least one positive test of the novel coronavirus nucleic acid;

• Had been cured according to the "A programme for the diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (trial 7th edn)" discharge criteria[9];

• Followed up with CT until the lesions were mostly absorbed.

The case(s) will be excluded from further study if the patient(s) have a severe basic medical history, such as pulmonary tuberculosis, malignant tumor, pulmonary edema, etc.

### *Methods*

Chest high-resolution CT was performed using SOMATOM Definition AS 64 rows (Siemens, German) or uCT530 40 rows spiral CT scanner (United Imaging, China). The SOMATOM CT scan parameters were 120 kV tube voltage, 110 mAs tube current, 512×512 matrix, 1.2 pitch, 8 mm layer thickness, and 8 mm layer spacing. The layer thickness and layer spacing of thin layer reconstruction was 1.0 mm. The uCT530 scan parameters were 120 kV tube voltage, 130mAs tube current, 512×512 scan matrix, 1.0 pitch, 5 mm layer thickness, and 5 mm layer spacing. The layer thickness of thin layer reconstruction is 1.0 mm and the layer spacing is 0.8 mm.

### *Image analysis*

Two senior physicians in the radiology cardiothoracic group read the CT images independently. The baseline was established when an early single lesion was found using CT scan. The interval between each CT follow-up time and the baseline time was recorded, and each interval was divided into different stages of the disease course for analysis. We have examined the location, distribution, size, borders, intra-lesion signs of baseline CT lesions, the absorption and progression of baseline lesions at different follow-up stages, and changes in the distribution of unilateral or bilateral lung lobes.

The density of the lesions, fine reticulation, consolidative opacities, crazy-paving pattern, cable shadows and the presence or absence of concomitant signs such as pleural effusion, were also examined. In case of two different conclusions were made for one image by the two physicians, one conclusion would be assigned to each image through in consensus.

### *Statistical analysis*

Statistical analyses were performed using the SPSS software (version 19, IBM, New York, NY). The basic clinical information and chest CT features were represented as frequency. Quantitative data were presented as means ± standard deviations and ranges, and qualitative data were presented as percentage.

## Results

### *Characteristics of patients*

The patients had an average age of 40±11 years, ranging from 23 to 68 years (4 patients ≥60 years old). Among them, 26 patients were 27-64 years old males

with a mean age of 44±10 years, and 44 patients were 23-68 years old females with a mean age of 38±12 years. 58 and 12 patients were diagnosed as common type and severe type, respectively.

***Baseline CT signs***

The lesions were mainly distributed at subpleural, of which 60 cases were round or patchy GGO and 10 cases were small nodules (Figure. 1). The size of the largest lesion was 3.4 cm × 2.4 cm and the smallest was 0.6 cm × 0.5 cm. The edges of the lesions were mostly blurred, and signs of air bronchus, vascular thickening and fine reticulation can be seen in the lesions. The signs of baseline CT were summarized in Table 1.


**Figure 1:** A 33 years old female exposed to COVID-19 patients, asymptomatic infection.
*(a) A round-shaped GGO is seen in the posterior basal segment of the left lung and the edges are blurred, and small blood vessels can be seen. (b)The first lesion was almost completely absorbed and a new small patchy GGO was seen adjacent to the pleura after 10 days.*

| | Number of cases (Percentage) |
|---|---|
| **Baseline lesion** | Total number of cases 70 |
| Upper lobe of right lung | 4 (6%) |
| Middle lobe of right lung | 4 ( 6%) |
| Lower lobe of right lung | 34 (49%) |
| Upper lobe of left lung | 8 (11%) |
| Lower lobe of left lung | 20 (28%) |
| **Distribution of lesions** | |
| Subpleural | 62 (89%) |
| Along bronchovascular bundle | 8 (11%) |
| **Lesion boundary** | |
| Clear | 2 (3%) |
| Blurred | 68 (97%) |
| **Intralesional signs** | |
| Air bronchial sign | 32 (46%) |
| Thickening of blood vessels | 50 (71%) |
| Fine reticulation | 58 (83%) |

**Table 1:** Baseline CT signs of 70 patients with COVID-19.

***Follow-up CT signs***

Of the 70 patients, there were 4 patients received 1 CT follow-up scan, 24 patients received 2 scans, 24 patients received 3 scans, and 18 patients received 4 scans. A total of 266 CT scans were performed, with an average of 4±1 per person and follow-up of 3±1 times for each person. The time interval between CT follow-ups and the CT baseline was 2 to 44 days.

The interval from the first to fourth CT follow-up was 2 to 15 days (average 5±3 days), 5 to 23 days (average 12±5 days), 8 to 36 Days (average 20±7 days), and 24-44 days (average 33±8 days), respectively, which were divided into four stages in turn.

In the first stage, most cases were in the progressive stage. About 77% of the baseline lesions were progressed and new lesions were found in 51% of the cases.

The second stage was the peak period. In this stage, the lesion consolidation accounted for the highest proportion (49%). The lesions in 54 patients with an average age of 41±12 years had a consolidation in the last follow-up time of 24±10 days. No consolidation was found in the lesions in

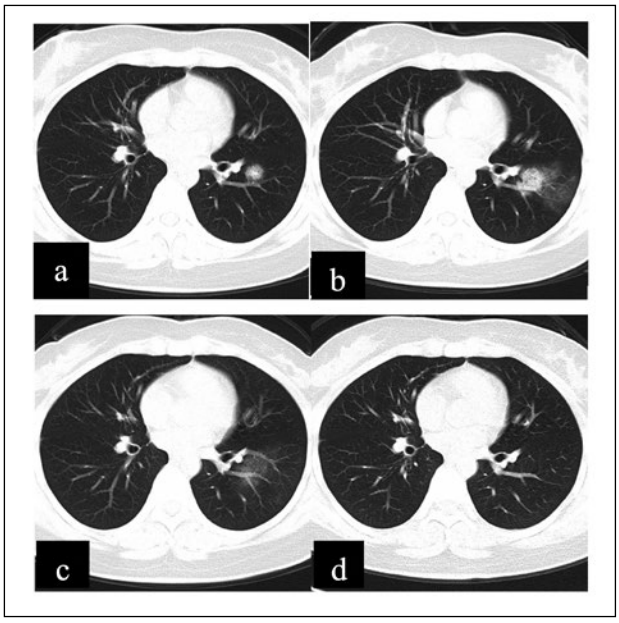


**Figure 2:** A 23 years old female exposed to COVID-19 patients. Fever occurred 2 days after baseline CT examination.
*(a) Baseline CT showed nodular GGO with a diameter of about 1.5 cm in the lower lobe of the left lung. (b) The edges were not clear and fine reticulation was seen within 4 days after the first follow-up. The progressed lesions, the expanded fine reticulation, flaky GGO under the pleura, and vascular shadows were seen. The lesion was limited to the left lower lobe. (c) At the second follow-up 10 days later, the lesions were clearly absorbed, and a thin piece of GGO was seen. (d) At the third follow-up after 36 days, the lesions were completely absorbed.*

16 patients with an average age of 38±9 years in the average last follow-up time of 16±8 days. The third and fourth stage were the absorption stage. There were no progressive lesions or new lesions found in this stage.

Of the 70 baseline lesions, 22 progressed to multifocal lesions of single lobe (Figure 2), and 32 cases involved both lungs (Figure 3).

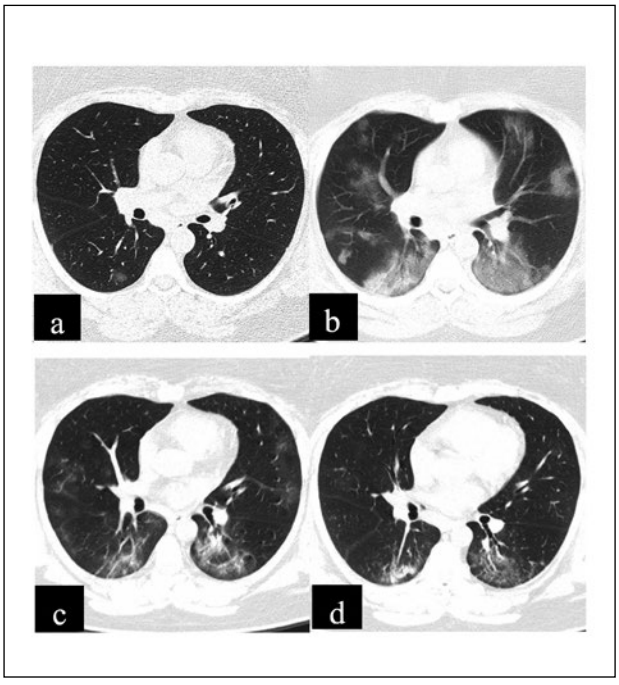


**Figure 3:** A 42 years old female exposed to COVID-19 patients, with intermittent fever for 4 days.
*(a) Baseline CT showed small circular GGO in the right lower lobe. (b) At the first follow-up after 7 days, lesions were obviously progressed. (c) A second follow-up was performed after 15 days. The lower lobe lesions in both lungs were partially absorbed and partially consolidated. The cable shadows may be seen and mainly manifested with the thickened lobular interval. (d) At the third follow-up after 26 days, a little consolidation and thin GGO were seen in the right lower lobe. Crazy-paving pattern mainly with interlobular septal thickening were seen in the lower lobe of the left lung.*

No lesions with multilobar distribution in single lung was found. In the first three stages, the proportions of fine reticulation and density-increasing lesions were the largest in the first stage, and then gradually decreased, while the proportion of crazy-paving pattern and cable shadow gradually increased.

There were 4 cases with pleural effusion. The number of discharged cases at each stage were 4 patients in the first stage, 24 cases in the second and third stages, and 18 cases in the fourth stage. The changes of specific follow-up signs are shown in Table 2.

| CT signs | Stage 1 (n=70) | Stage 2 (n=66) | Stage 3 (n=42) | Stage 4 (n=18) |
|---|---|---|---|---|
| Baseline lesion | | | | |
| Absorption | 16 (23%) | 50(76%) | 42 (100%) | 18(100%) |
| Progression | 54 (77%) | 16(24%) | 0 (0%) | 0 (0%) |
| New lesion | 36 (51%) | 30 (46%) | 0 (0%) | 0 (0%) |
| Distribution | | | | |
| Single-lobe lesion | 28 (40%) | 12 (18%) | 8 (19%) | 4 (22%) |
| Multiple lesions of single-lobe | 22 (31%) | 22 (33%) | 8(19%) | 0 (0%) |
| Double lungs | 20 (29%) | 32(49%) | 26 (62%) | 14 (78%) |
| Fine reticulation | 60 (86%) | 16(24%) | 4(10%) | 0 (0%) |
| Density | | | | |
| Increase mainly | 62 (89%) | 22 (33%) | 8(19%) | 0 (0%) |
| Decrease mainly | 8 (11%) | 44 (67%) | 34 (81%) | 18(100%) |
| Consolidation | 22 (31%) | 32 (48%) | 16 (38%) | 2 (11%) |
| Crazy-paving pattern | 6 (9%) | 24 (36%) | 20 (48%) | 2(11%) |
| Cable shadows | 4 (6%) | 10 (15%) | 18 (43%) | 4 (22%) |
| Pleural effusion | 0 (0%) | 4 (6%) | 4 (10%) | 2 (11%) |

**Table 2:** Changes of CT follow-up signs in 70 patients with COVID-19 in different stages.

## Discussion

In the early stage, the main clinical symptoms of COVID-19 patients were fever and cough. The laboratory tests were mostly normal, and only a few patients had reduced leukocyte counts, reduced lymphocyte ratios, and elevated C-reactive protein level. The imaging signs of COVID-19 might be earlier or later than clinical in the early stage. Very few patients had imaging signs but no clinical symptoms. Chest CT not only has important value in the diagnosis of COVID-19, but also plays an important role in follow-up during treatment[10].

### *Signs of early single lesion at baseline CT*

In this study, the baseline CT lesions of COVID-19 were mostly patchy GGO in the lower lung. Some lesions were round GGO or small nodule opacities and located in the lower lobe of the right lung[11-13]. The subpleural distribution accounted for 89%, partly along the bronchovascular bundle.

The lesions were with blurred edges and air bronchus signs, vascular thickening, and fine reticulation had been observed. Song et al. found that 80% of the COVID-19 cases in a group of 51 patients had air bronchial signs most in the middle of the disease course[14]. However, only 46% of patients of the baseline CT in our group displayed the similar

signs, which might be caused by the small size of the baseline lesions, the smaller baseline GGO lesions, the peripheral distribution, and the insignificant difference in bronchial density. The fine reticulation might be an outcome of increased thin blood vessels shadows[11] and intralobular interstitial thickening[15]. Early single lesion were susceptible to misdiagnosis, which should be combined with clinical history and timely follow-up.

***Follow-up CT signs and evolution***

Because the fourth stage of patients in this group was basically a continuation of the third stage, we focused on the first three stages. Baseline lesions developed rapidly, and the range increased significantly in the short term, or progressed to multiple lesions. Subpleural lesions usually develop laterally, and adjacent lesions were easy to fuse together, showing different patterns of progression.

Pan et al. found that the main evolution signs of a group of 21 cases during the recovery period were GGO, gravel road signs, consolidation, streak shadow, residual GGO[1]. The difference of cases in our group was that the early single GGO was used as the baseline for follow-ups and fine-grid signs were also studied. Pan et al. believed that gravel road signs included thickening of interlobular interstitium and thickening of interlobular interval[1]. However, we noticed that the grids that originated from the interlobular thickening were smaller (fine grids) than those originated from the thickening of the leaflets (large grids). The difference between the two types of gravel road signs can be used to accurately describe the signs of the disease[15].

The fine reticulation and the crazy-paving pattern often occurred together. The former mainly appeared in the progress period and the latter mainly appeared in the absorption period. Xu et al.[16] found that inflammatory infiltration of lymphocyte-based monocytes in the interstitial stroma of COVID-19 patients was found with autopsy. The authors believed that it might appear as GGO on CT in the early stage. With the progress of inflammatory infiltration, fine blood vessels increased and thickened and increased return lymphatic fluid, and mainly manifested as interlobular interstitial thickening and fine reticulation on CT image[15]. As the disease progressed, the density of lesion gradually increase. When the signs of alveolar damage accompanied fibrous mucoid exudation appeared[16], it showed as consolidation on CT images. In the absorption stage, exudates in the alveolar and interstitial were absorbed and the density of consolidation lesions on CT gradually decreased. The residual GGO, cable shadows, and the crazy-paving pattern[17] mainly consisted of interlobular septal thickening could appear. In the first stage of the follow-up, the proportion of lesions progressed, new lesions, fine reticulation and increased density was higher than those in all the other 3 stages, while the proportion of signs of decreased density, crazy paving pattern and cable shadows was lower than those in all the other stages. In the third stage, however, the opposite is true (Table 2). Therefore, the appearance of fine reticulation and increased lesion density may be important signs to evaluate the progress of COVID-19, while signs such as crazy paving pattern and cable shadow are the main signs of the absorption period[11].

The consolidation of most of the lesions in patients from our study was a turning point in the entire course of the disease, which is also the most severe period. This is consistent with the previous conclusions[14]. The consolidation of lesions has the highest proportion in the second stage of the disease, which is basically consistent with the previous report that the peak of COVID-19 was at 9-13 days[1]. In this study, the average last follow-up time of consolidated cases was significantly longer than that of unconsolidated cases, indicating that the absorbed lesions became slower and the course prolonged after consolidation. Lesions are rarely completely consolidated[14]. In most cases, when consolidation appears in the off-center area of lesions, GGO in the marginal region may begin to absorb and fade at the same time. The residual GGO in the absorption phase was different from that in the early stage. The early GGO was more limited and has a slightly higher density, with signs of air bronchus and thickening of the blood vessel visible in the short-term change. The residual GGO in the absorption phase was more scattered with lighter density, blurry boundary, and the dissipation time was longer compared to that in the early stage. Multiple signs may be observed in the same case, and different lesions may appear at different stages of the disease course. Usually, the trend of the disease was evaluated based on which signs were dominant.

We have noticed that there are some shortcomings in this study. For example, because the sample size of cases is small, the results from our study may be biased. In addition, this study is just a retrospective analysis and there is no control group. Second, only common and severely cured patients

but not critically ill or dead patients were included. Third, patients with a basic medical disease were excluded. However, our results strongly suggest that the CT imaging findings of different stages of COVID-19 can be used to evaluate the progression of the disease.

Taken together, the high-resolution chest CT follow-up revealed the early signs of a single lesion of COVID-19 and the complete evolution process. Different signs represent different stages of the course of disease. The signs of fine reticulation and consolidation indicates the progress of the lesion and the peak of COVID-19, respectively, while the signs of crazy paving pattern and cable shadow suggest an improvement of the disease.

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