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Research article

Semi-quantitative analysis for the dynamic chest CT imaging features from onset to recovery in severe and critical COVID-19

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Abstract

Objective: To investigate in the CT manifestations of severe and critical coronavirus disease 2019 (COVID-19) patients.

Methods: Medical data was collected for 2 severe patients and 4 critical COVID-19 patients from onset to their recovery. Three or four CT scans for each patient were taken. The semi-quantitative analysis method was introduced for lesion and its distribution area.

Results: The ground-glass opacities (GGO) and mixed GGO with consolidation were found as the most frequent features. Consolidation followed, and the appearance of stripes which showed an increasing trend before the patient was discharged. Consolidation was associated with clinical severity and disease progression, and the rapid change of the lesion in a short period of time was also a notable feature within 2–3 weeks. After being discharged, the efficacy of treatment could be demonstrated by a follow up CT scan. The distribution of lesion also showed dynamic progress in the follow up CT scan.

Conclusion: CT scans in the whole course provided the entire inflammation information to assess clinical severity, disease progression and the treatment efficacy for COVID-19.

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Keywords: COVID-19; Chest CT features; Pneumonia; Severe type; Critical type

1. Introduction

In December, 2019, a tragic outbreak of a pneumonia of unknown cause occurred in Wuhan city, the capital of Hubei province in China. By Jan 7, 2020, Chinese scientists had isolated the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), from these patients with

virus-infected pneumonia, which was later designated coronavirus disease 2019 (COVID-19) in February, 2020, by WHO. Unfortunately, the COVID-19 pandemic has spread worldwide rapidly and threatened the human health and life seriously [1]. The clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing asymptomatic infection, mild or common upper respiratory tract illness, and severe or critical viral pneumonia with respiratory failure and even death [2]. Although some case series regarding CT manifestations have been published, many studies focused mainly on the common type of COVID-19 in the first diagnosis, or severe and critical types in hospitalization. As an emerging virus-induced pneumonia, the CT manifestations of severe and critical patients remain largely unclear during the whole course including the rehabilitation stage.

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In the current case series study, two severe and four critical types of COVID-19 in Xiangtan Central Hospital, Hunan Province, China, were treated by National TCM master Zhiming Liu in Guang'anmen Hospital, China Academy of Chinese Medical Sciences in Beijing by the Telemedical consultation in February and March, 2020.

CT scans were conducted 3 times during hospitalization for all patients and one follow up in the rehabilitation stage for 4 cases. We aim to explore the dynamic changes of the imaging features and distribution of lung lesions in hospital as well as the day after being discharged from hospital so that we examined the whole course of the disease. A new semi-analysis method was created and used for evaluation of the inflammation for this purpose.

2. Material and methods

In this retrospective case series report, medical data was collected from the Inpatient Department in Xiangtan City Central Hospital, Hunan Province, between January 28, 2020 and February 29, 2020. Real-time reverse transcriptase polymerase chain reaction (RT-PCR) tests for COVID-19 nucleic acid were performed using nasopharyngeal swabs before their admission, and the diagnosis and the discharged criteria for severe or critical type was followed by the COVID-19 Diagnosis and Treatment Guide (version 4,5) of the National Health Commission of the People's Republic of China [2].

The definition is described as the following for the severe and critical types of the disease COVID-19 according to the "Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 4,5)".

- (1) Severe cases adult cases meeting any of the following criteria: ① Respiratory distress (≥ 30 breaths/min); ② Oxygen saturation $\leq 93\%$ at rest; ③ Arterial partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ≤ 300 mmHg (1 mmHg = 0.133 kPa). Cases with chest imaging that shows obvious lesion progression within 24–48 h > 50% shall be managed as severe cases.
- (2) Critical cases meeting any of the following criteria: ① Respiratory failure and requiring mechanical ventilation; ② Shock; ③ With other organ failure that requires ICU care.

All cases (2 in the severe and 4 in the critical stage) underwent CT scans, including the baseline CT imaging, the two follow-up CT scans during hospitalization, and one scan after being discharged. This study was approved by the medical ethical committee of Guang'an Men's Hospital, which waived the requirement for patients' informed consent, referring to the CIOMS guideline.

2.1. Imaging technique

The scans of all patients were conducted using the same CT scanner (Philips, Brilliance 16) in Xiangtan City Central

Hospital. The acquisition parameters were as follows: 120 kVp; 100–250 mAs; pitch, 0.75–1.5; and collimation, 0.625–5 mm respectively. All imaging data was reconstructed by using a medium sharp reconstruction algorithm with a thickness of 2–5 mm. CT images were acquired in the supine position at full inspiration for all patients.

Before being discharged, three chest CT scans were conducted for each case to monitor the severity of the lung inflammation according to the clinical needs. Additionally, four patients had one more scan about one month after being discharged. In this retrospective case series report, CT features for the critical type in 4 and severe types in 2 were demonstrated in detail.

In this case series study, CT findings were semi-quantitatively based on the severity and range of pneumonia lesions on admission and throughout the observation period as an objective indicator of change of inflammation. All patients' chest CT images were independently evaluated by two radiologists with more than 8 years of imaging diagnosis experience. When the diagnosis was inconsistent, they reached a reasonable conclusion after discussion and/or consultation. The optimized semi-quantitative scoring system for CT features was created by referring to the research of previous international experts and the characteristics of new coronavirus pneumonia to assess the severity of pulmonary inflammatory lesions [3,4]. Six CT features included the following imaging features: ground-glass opacities (GGO), consolidation, mixed GGO with consolidation, reticulation, stripe, and effusion. If there is any feature of pneumonia in the lung, the score would be 1. Otherwise, the score would be 0.

Secondly, the lesion distribution in the lung is scored according to the following rule: The bilateral lung lobes were divided into 6 areas, the upper, middle, and lower. The upper-middle boundary in the CT axial section is defined at the level of the tracheal bifurcation, and the middle-lower boundary is the maximum transverse section of the right pulmonary vein. Each lung area is scored visually according to the infiltrative degree of lesions, which is given a score of 1–4. Absence of inflammatory lesions was scored as 0; if the inflammatory area was below 25% the score of 1 is assigned; an inflammatory area from 26% to 50% is give the score 2; likewise an inflammatory area between 51% and 75% is given a score of 3, and an area between 76% and 100% received a score of 4. A higher total score for a patient indicated that the pneumonia was worse.

3. Results

Patient 1, a 67-year-old female patient was diagnosed with critical COVID-19 on admission on February 4, 2020. She was treated by antiviral and supportive interventions, the patient developed fever on February 9 and was started on a non-invasive ventilator. The Chinese herbal decoction was given for a week. Finally, her symptoms disappeared and she was discharged from the hospital on February 23. The continuing

follow up CT was conducted on March 9 after Chinese Medicine (CM) treatment (Fig. 1).

Patient 2, a 55-year-old man was diagnosed as having critical COVID-19 when he was admitted to hospital on 4 February 2020. He received antiviral and supportive treatments. A fever emerged on February 6 which lasted for three days. Chinese herbal decoction was given on February 14 for 9 days. Finally, he recovered and was discharged on February 23. His follow up CT was conducted on March 9 after receiving Chinese Medicine treatment (Fig. 2).

Patient 3, a 67-year-old woman tested positive for COVID-19 nucleic acid on February 2, 2020, and was diagnosed with the severe type on February 4 when she was admitted to the hospital. She acquired antiviral and supportive treatments. She suffered from fever for several times between February 6 and

February 16. She began taking herbal decoction on February 9 for 15 days. Finally, She recovered and was discharged on February 26 (Fig. 3).

Patient 4, a 50-year-old man was admitted to hospital on February 10, 2020 with a diagnosis of severe COVID-19. He was treated by antiviral and supportive treatments. He developed fever symptoms between February 10 and 18. He took a herbal decoction on February 18 for a week. Finally, he felt better and was discharged on February 25. His continuing follow up CT was conducted on March 14 after Chinese Medicine treatment (Fig. 4).

Patient 5, a 37-year-old man was diagnosed as critical COVID-19 when he was admitted to the hospital on 28 January 2020. He developed fever, cough and expectoration for several days with interval. He was treated by antiviral

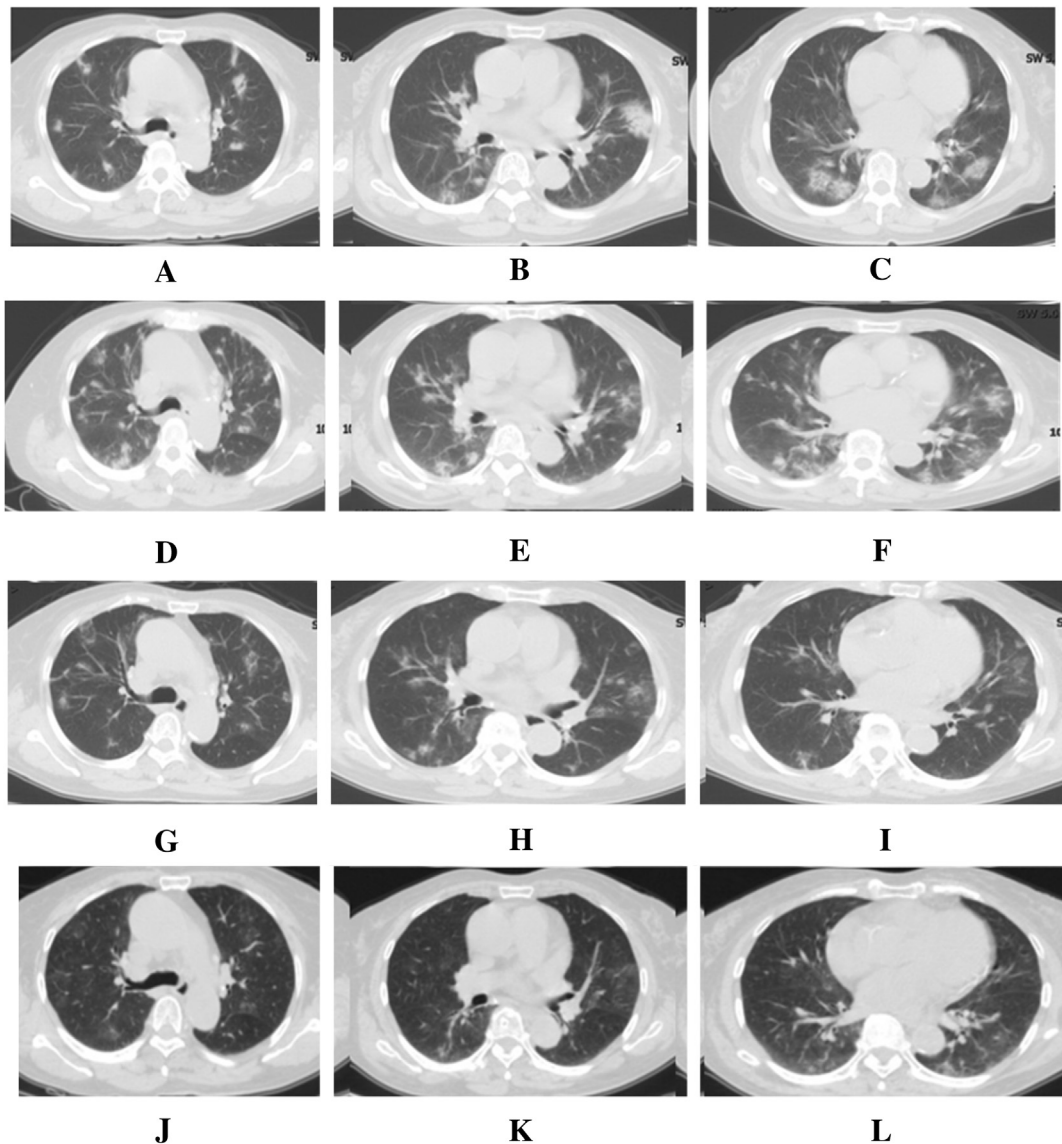


Fig. 1. Three CT scans - Images selected in the upper, middle and lower lung. A–C, Day 6 (Feb.4), the patchy consolidation and mixed density shadow scattered in peripheral area, and the larger ones were in the middle and lower lung. D–F, Day 20 (Feb.18), the original consolidation in middle and lower areas dispersed into the small ground-glass opacities (GGO), and more small patches of GGO and mixed lesions emerged in both lungs. G–I, Day 23 (Feb.21), less small patchy mixing density and GGO remained within both lungs. J–L, Day 40 (Mar.9), the diluted GGO and small nodes remained in both lungs.

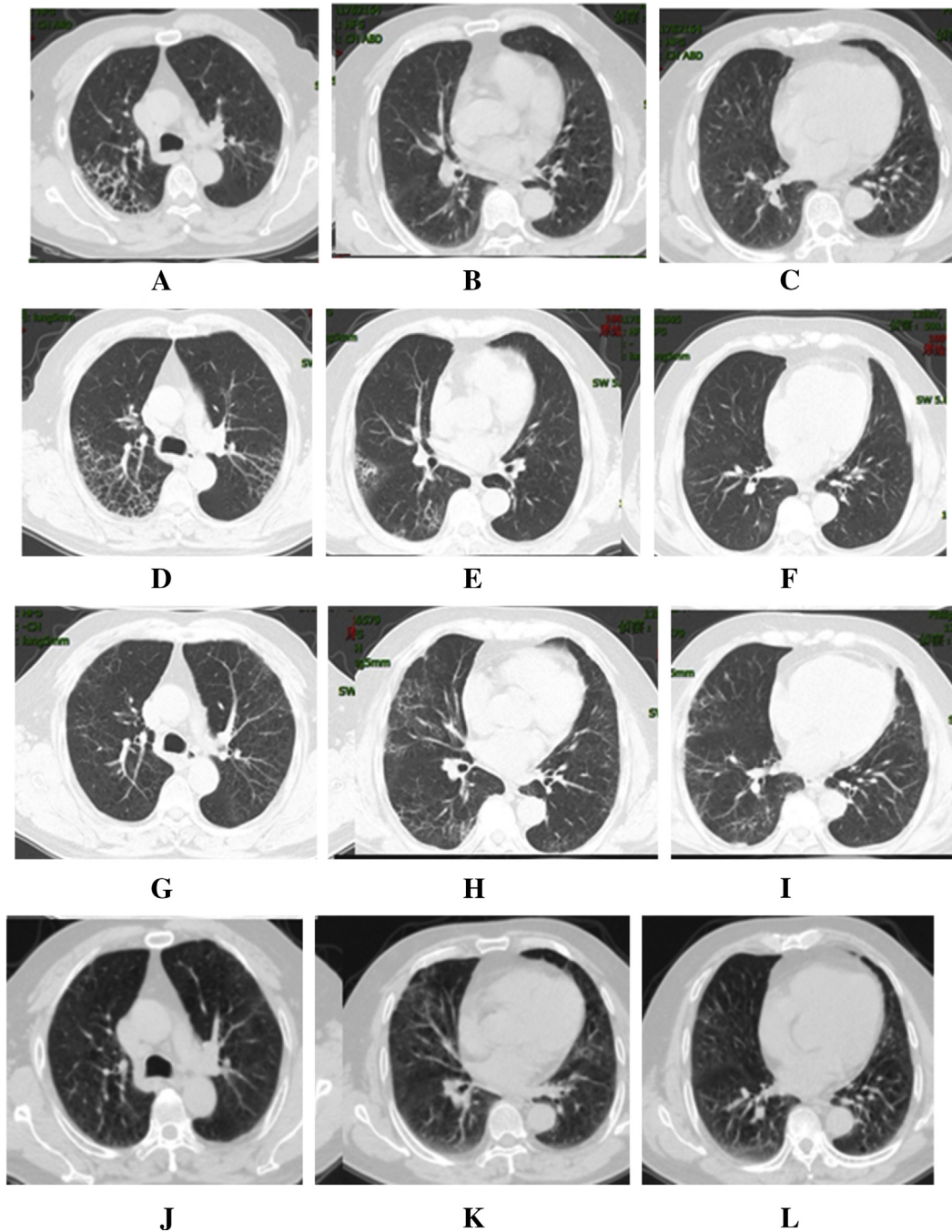


Fig. 2. Three CT scans - Images selected in the upper, middle and lower lung. A–C, Day 7 (February 6), GGO with the coarse reticular in the right upper lung, and the small GGO in the left upper lung. D–F, Day 10 (February 9), the right upper lung reticular lesion became thin and enlarged with mixed GGO, and several new patchy reticulation with GGO emerged in the left upper and right lower lung. G–I, Day 22 (February 21). The reticular in both upper lungs absorbed, but the reticular with GGO enlarged in the right upper and lower lung. J–L, Day 39 (March 9), the diluted GGO and small stripes in both lungs.

and supportive treatments. He began using a non-invasive ventilator on January 31, and received tracheal intubation and invasive mechanical ventilation on February 4. Finally, the herbal decoction was given on February 17 for a week. He recovered and was discharged on February 23 (Fig. 5).

Patient 6, a 67-year-old man was diagnosed as critical COVID-19 on February 13, 2020 when he was admitted to the hospital. He was treated by antiviral and supportive measures.

He developed fever symptoms for more than 12 days. He began using a non-invasive ventilator on February 16. The herbal decoction was given on February 19 for a week. On February 23, the patient's multiple RT-PCR results were negative and he was discharged from the hospital with significant improvement in his symptoms. His continuing follow-up CT was conducted on March 25 after Chinese Medicine treatment (Fig. 6).

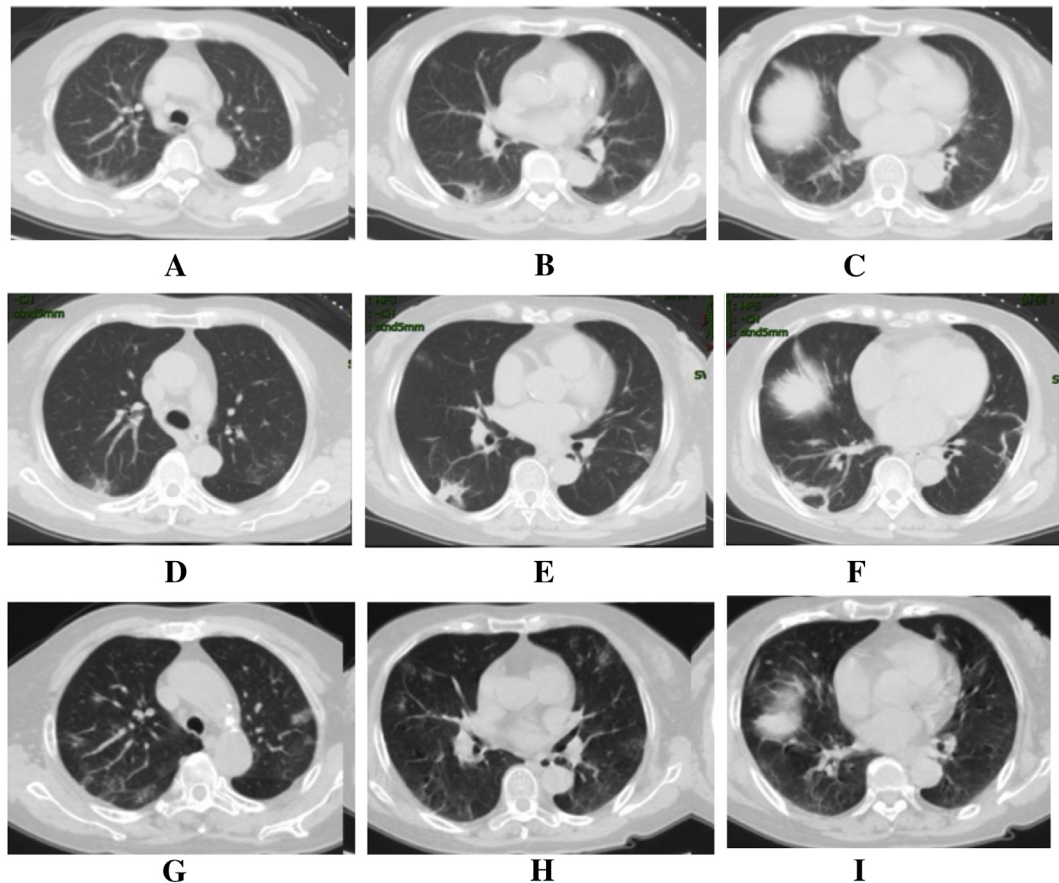


Fig. 3. Three CT scans - Images selected in the upper, middle and lower lung. A–C, Day 7 (February 8), small patchy mixed density and GGO Limited in peripheral areas. D–F, Day 12 (February 13), The lesion became a larger consolidation, parts of GGO disappeared, but several bands showed. All lesions limited in peripheral distribution. G–I, Day 24 (February 25), the new GGO replaced the large consolidation. Smaller patchy GGO, mixed density and stripes emerged in extensive areas in both lungs.

The semi-quantitative method analyzed the detail for the lesion's features and its distribution area (4 final CT scans in the outpatient were not included). GGO and mixed lesions were the most frequent features, consolidation followed, stripe shows increasing trend before discharged, and reticulation was less common.

When the correlation of disease severity and CT scan was explored, the difference was found between the imaging of severe and critical patients as follows: ① the inflammation distribution area was larger in patients with the critical type of COVID-19 than the severe type; ② The confounding of multiple imaging features in the critical patients was more pronounced in the lung field.

The range of lesions dispersed more widely in the second and final times. However, the second ranked the widest for lesions (Table 1, Fig. 7).

The average score in the critical type was higher than the severe type in 3 CT scans.

4. Discussion

The efficient treatment of severe and critical patients with COVID-19, which is approximately 15–20% of all COVID-19

patients, is the key to controlling the high mortality rate. As a modern diagnostic technology, CT is an important routine tool to monitor the inflammation severity of patients after laboratory confirmation of COVID-19 [3].

In this study, we aim to show the evolution of chest CT imaging features in patients with severe and critical COVID-19 across the disease course, to facilitate the cognitions and treatments of this newly emerging life-threatening infection.

Previous studies have mainly explored the CT imaging features in mild and common types in the early stages of COVID 19. Shi and colleagues reported the predominant pattern of ground-glass opacities, with rapid evolution to consolidation at around the first to second week after the onset of symptoms. Several following reports showed that the most common imaging finds were pure GGO, GGO with reticular and/or interlobular septal thickening, and GGO with consolidation. Complete consolidation was relatively less common. The consolidation was also reported involving the disease progression. There were more consolidation lesions and less GGO lesions in the patients with CT interval >4 days than in patients ≤ 4 days after the onset of symptoms. In addition, there were significantly more consolidation lesions and less

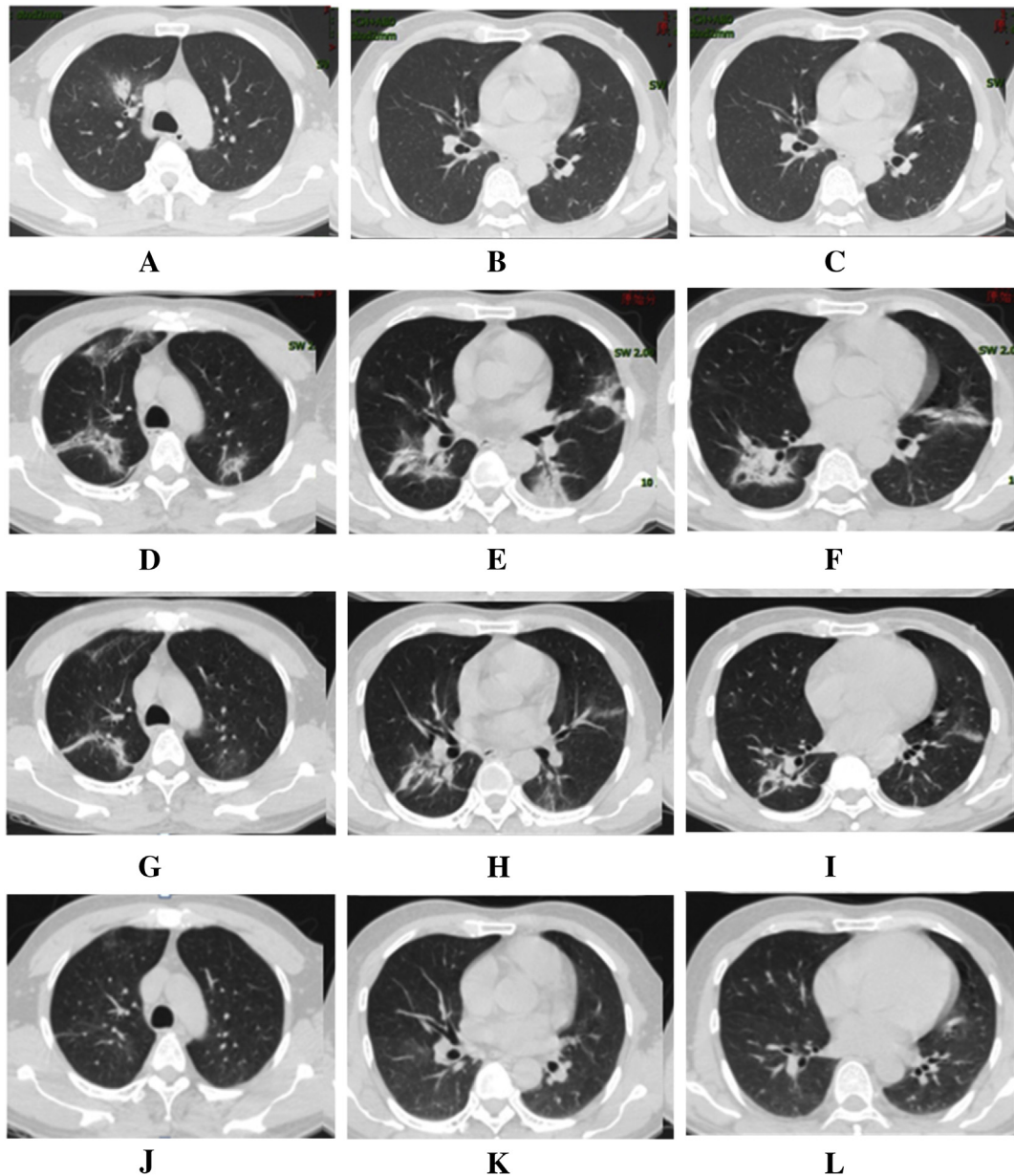


Fig. 4. Three CT scans - Images selected in the upper, middle and lower lung. A–C, Day 4 (February 10), the local consolidation and a small patchy GGO in the right upper lung. D–F, Day 11 (February 17), multifocal consolidations and the mixed lesions scattered in both lungs, accompanied with little stripes and bilateral pleural effusion. G–I, Day 19 (February 25), the consolidation and mixed density partially absorbed and replaced by bands and GGO, the pleural effusion disappeared. J–L, Day 37 (March 14), the most lesions absorbed, and the diluted GGO and small stripes left in both lungs.

GGO lesions in the elder patients than in the younger patients. The predominant distribution was demonstrated in posterior and peripheral part of the lungs. The feature was uncommon in other viral pneumonias, such as SARS and MERS [4–7].

Our study shares most features with the mild and common types. Because our cases were severe and critical types, the involved area was larger, and the features were more complicated. The phenomena were found between severe and critical type reasonably. After analysis using our newly created semi-quantitative method, the average score in the critical type of COVID-19 is higher than the severe type in 3

CT scans respectively. However, there was no significant statistical difference between the two types. The reason may be the small sample size and the big deviation. Moreover, the main four patterns in our imaging findings, pure GGO, GGO mixed with consolidation, and consolidation, stripes and effusion. All these features tended to appear simultaneously in the same patient in the second or third scan, predominately in the second CT scan during 9–20 days after onset. Interestingly, consolidation usually emerged as the main feature in this stage. This phenomenon may relate to the clinical severity and progression. On the other hand, the

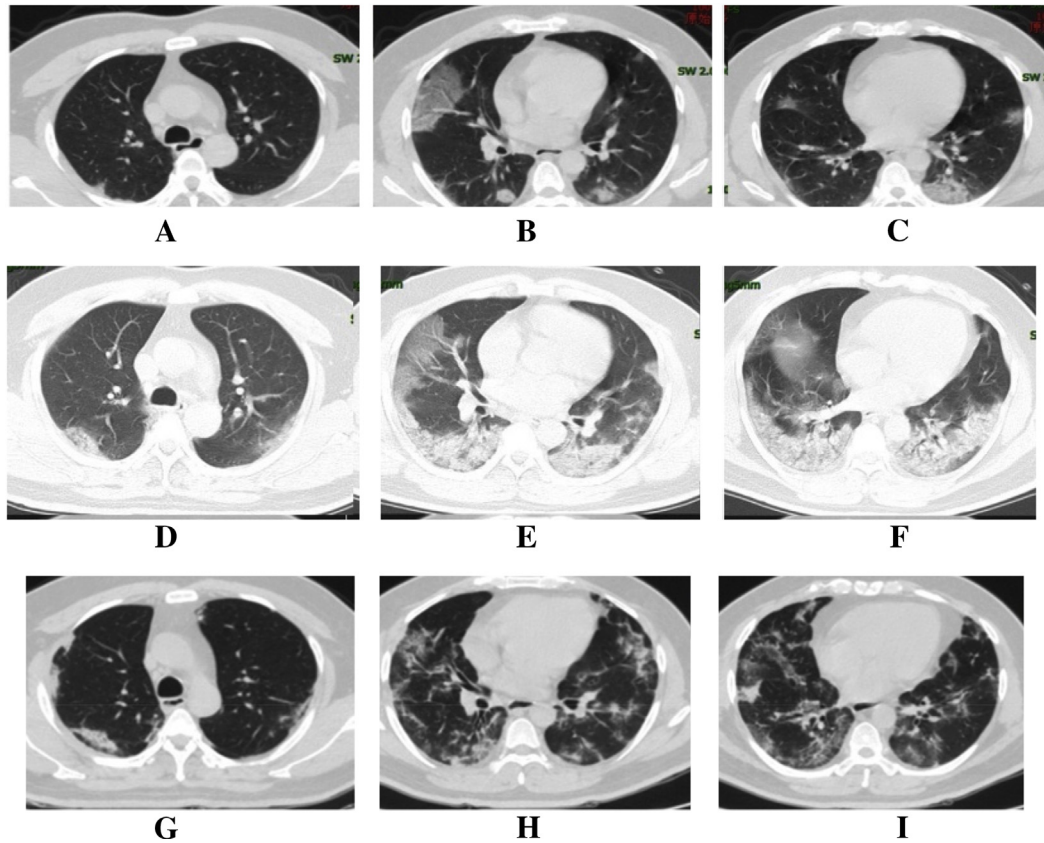


Fig. 5. Three CT scans - Images selected in the upper, middle and lower lung. A–C, Day 6 (January 31), the large GGO in the right upper and middle lung, and limited patchy consolidation and mixed density in both the middle and lower lungs. D–F, Day 9 (February 3), the original GGO enlarged, and the big consolidations showed in both lower lungs extensively. G–I, Day 33 (February 25), the large lesions have been significantly absorbed, but several small patchy consolidations emerged in the right upper lung, the small mixed density and stripes are extensively distributed in both the middle and lower lungs.

feature of stripes emerging showed an increasing trend before being discharged, and it may indicate the absorption of inflammation and fibrosis. Overall, peripheral lesions were more common than central lung lesions. The majority of patients had bilateral posterior lung involvement during the course of the disease. Although the consolidation was absorbed significantly in the CT before being discharged, the range of lesions including GGO and stripes dispersed more widely. Another notable distribution feature of our case is the rapid change of the lesion in a short period of time. Based on multiple CT follow-up scans, it is easy to observe one dramatic change after another over the course of a few days during the hospitalization period. As a result, it is difficult for physicians to assess the progression or deterioration of lesions in specific cases. During the acute phase of SARS-CoV-2 infection, the dramatic changes in the patient's condition also presents a challenge to many experienced clinicians.

The clinical evidence showed that the inflammatory factors associated with diseases mainly containing IL-6 were featureificantly increased, which contributed to the aggravation of the disease around 7–14 days after onset [8,9]. It

was supported that the CT findings are correlated to the storm of inflammatory factors. Recent autopsy and lung replacement pathology reports showed that SARS-CoV-2 mainly causes inflammatory reactions characteristically deep in the airway and at the alveolar level, producing extensive inflammatory exudation and mucus that fills the alveolar cavity [10].

The rapid expansion and change of lung lesions detected by the follow up Chest CT in severe or critical type patients are very helpful for clinicians to change the managements.

In our case series cohort, no one died and the recovery rate was 100%, which may have contributed to the integrated medicine treatments. However, the follow up CT on the day of discharge showed alleviated inflammation, but the substantial lesions were still widely present. Therefore, the treatment of COVID-19 patients after being discharged is of great importance. In our study, 4 in 6 cases luckily conducted the continuing follow up CT after the integrated medicine treatments in half or one month after being discharged, and the lesions showed featureificantly absorbed. The CT scans in the whole course would provide the entire pathological information of COVID-19 [11,12].

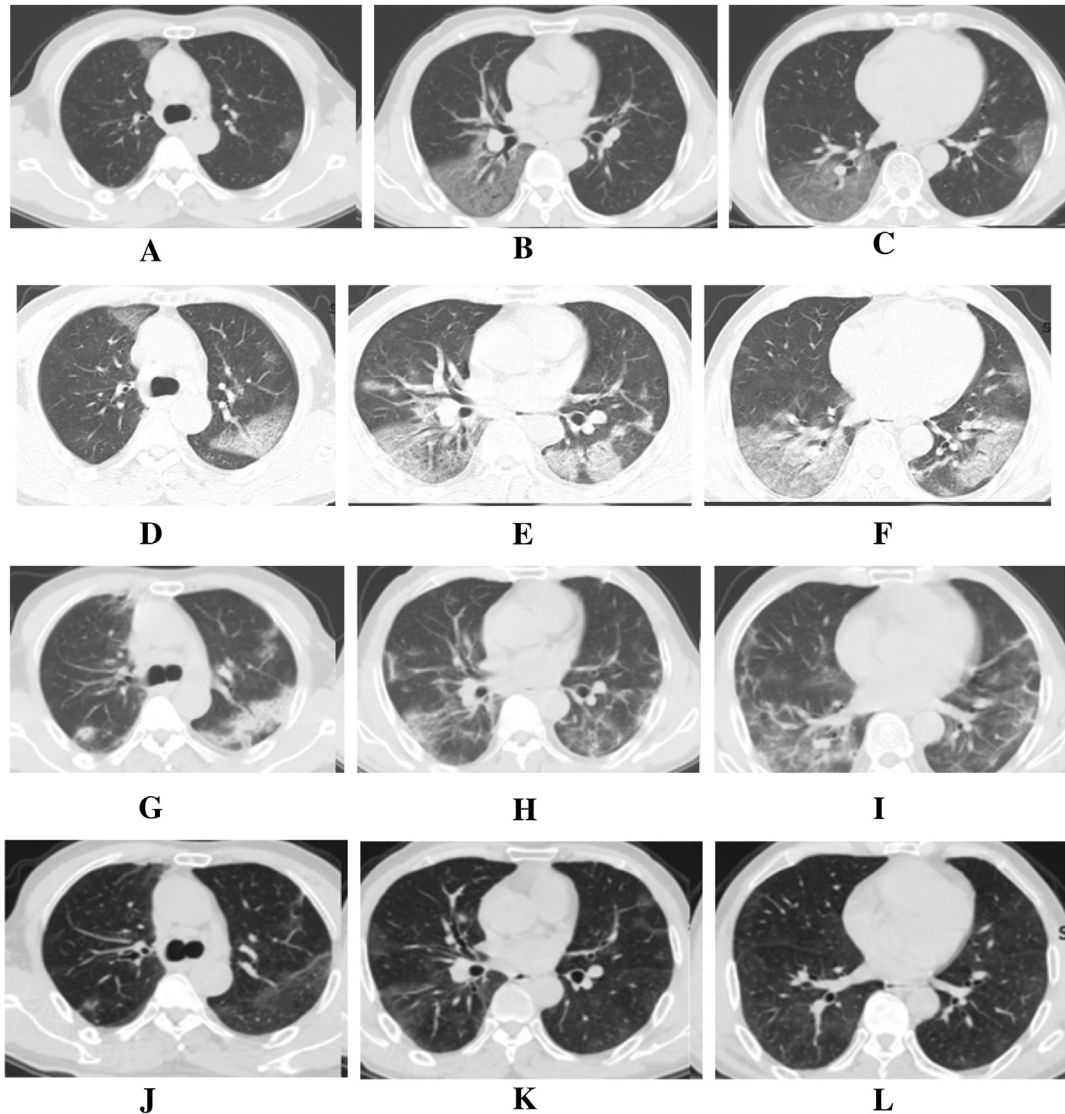


Fig. 6. Four CT scans - Images selected in the upper, middle and lower lung. A–C, Day 12 (Feb. 14), the large lower density GGO in the right lower lung, several small patchy GGO in the right upper and left lower lung. D–F, Day 14 (Feb. 16), the lesions became the mixed density and consolidation in enlarged areas of both the lower lungs and the upper left lung. Also the patchy GGO also increased. G–I, Day 24 (Feb. 26), most of the large lesions in both the lower lungs were absorbed and were replaced with extensive GGO and stripes, but the left upper posterior lung lesion became solid. A small node in consolidation emerged in right upper lung. J–L, Day 52 (Mar.25), the most lesions absorbed, and the small diluted GGO left in both lungs.

Up to now, CT has played a crucial role in the diagnosis and evaluation of COVID-19. The direction for future research is exploring the use of artificial intelligence in CT data. It will provide quantitative information on inflammation to assess

clinical severity, and monitor disease progression, efficacy of specific treatments and predict temporal changes in disease outcomes. CT imaging will help control and prevent acute respiratory distress syndrome and acute lung injury in COVID-19 cases.

Table 1
Percentage of CT features and Score of area for COVID-19 pneumonia (6 cases, 2 severe and 4 critical types).

Characteristics	Item	GGO	Consolidation	Mixed lesions	Reticulation	Stripe	Effusion	Lesion region (mean ± SD)
Severe	1st CT	1/6 (16.7%)	2/6 (33.3%)	2/6 (33.3%)	0/6 (0.00%)	0/6 (0.00%)	0/6 (0.00%)	4.50 ± 1.50
	2nd CT	1/6 (16.7%)	1/6 (16.7%)	2/6 (33.3%)	0/6 (0.00%)	2/6 (33.3%)	0/6 (0.00%)	7.50 ± 1.50
	3rd CT	2/6 (33.3%)	1/6 (16.7%)	1/6 (16.7%)	0/6 (0.00%)	2/6 (33.3%)	0/6 (0.00%)	8.50 ± 2.50
Critical	1st CT	3/6 (50.0%)	3/6 (50.00%)	3/6 (50.00%)	2/6 (33.3%)	0/6 (0.00%)	1/6 (16.7%)	7.75 ± 1.92
	2nd CT	4/6 (66.7%)	3/6 (50.00%)	2/6 (33.3%)	2/6 (33.3%)	1/6 (16.7%)	1/6 (16.7%)	13.75 ± 3.96
	3rd CT	4/6 (66.7%)	3/6 (50.00%)	3/6 (50%)	3/6 (50.00%)	3/6 (50.00%)	2/6 (33.3%)	10.75 ± 2.38

GGO, ground-glass opacities; Mixed lesion, GGO mixed with consolidation.

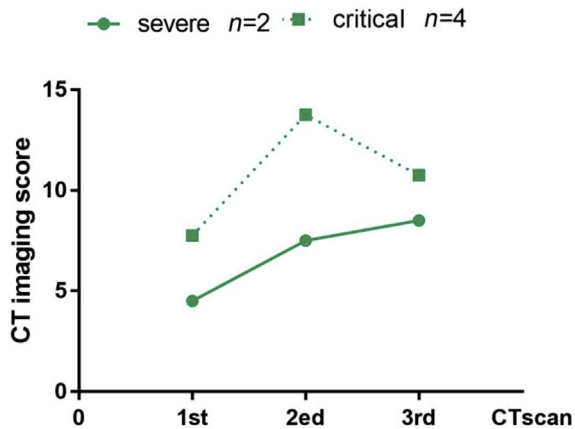


Fig. 7. Score of area for COVID-19 pneumonia in the two groups.

Acknowledgments

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Ethic statement

We obtained the ethics certificate from Guang'anmen Hospital of China Academy of Chinese Medical Sciences. At the same time, the source certificate of the original data has been obtained from Xiangtan Central Hospital.

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Conflict of interest

None.