Temporal changes in the chest based on findings from imaging in severe patients with novel coronavirus pneumonia

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Abstract. The aim of the present study was to observe the temporal changes in the chest based on findings from imaging in severe patients with novel coronavirus pneumonia. A total of 33 severe confirmed cases (20 male patients and 13 female patients) were enrolled in the present study between January 31, 2020 and March 10, 2020. Chest imaging findings and clinical data were collected and analyzed. The median age was 65 years (age range, 25-90 years). As of April 7, 2020, 24 patients were discharged, and 9 patients died. With regards to the clinical manifestations, 28 patients had fever, 17 patients had a cough and 15 patients had shortness of breath. Of these, 29 patients had underlying health conditions. Ground glass opacities, consolidation and interlobular septal thickening were the most common and typical chest computerized tomography (CT) scan abnormalities. A total of 6/33 (18.2%) patients had 1 affected lobe, 6/33 (18.2%) patients had 2 affected lobes, 5/33 (15.2%) patients had 3 affected lobes, 9/33 (27.3%) patients had 4 affected lobes and 7/33 (21.2%) patients had 5 affected lobes in the initial chest CT scan. The mean interval time between two consecutive CT examinations was 4.5 days (range, 3-9 days). Most severe patients exhibited some degree of aggravation based on the CT findings in the 3 weeks from illness onset. After 3 weeks from illness onset, these severe survivors demonstrated improvements in the chest CT findings, which included complete absorption or only a few remaining fibrous stripes. Chest CT manifestations of patients infected with novel coronavirus pneumonia were diverse and varied. Severe patients had imaging features of rapid progression and slow absorption. Monitoring of chest imaging findings is vital to detect any changes in a timely manner.

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Introduction

In December 2019, novel coronavirus disease 2019 (COVID-19; now termed severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) infection was first reported in Wuhan, Hubei Province, China. Since then, it has become a global pandemic. The basic reproduction number (R0) of COVID-19 reported by Wu *et al* (1) was estimated to be 2.68, indicating >two new cases were generated by a SARS-CoV-2 infected patient. Asymptomatic carriers can also infect healthy individuals (2). Recent studies have reported that the mortality rate of COVID-19 fluctuates between 4.3 and 11% (3,4). Up to March 27, 2021, there were >125 million infected individuals and 2.77 million deaths worldwide. Given the higher mortality rate and enormous infectivity of COVID-19, it is vital to detect suspected cases, evaluate the disease severity and track patients with COVID-19 pneumonia in a timely manner.

Nucleic acid detection of SARS-CoV-2 remains the gold standard for diagnosing COVID-19 using reverse transcription PCR (5). Chest radiology evaluation is often key to identify suspected patients with COVID-19 (6). Prompt recognition of COVID-19 is invaluable to ensure timely treatment, and rapid patient isolation is crucial for containment of this communicable disease (6). Fang *et al* (7) reported that the sensitivity of nucleic acid detection was 71%, whereas the sensitivity of computerized tomography (CT) scans for SARS-CoV-2 infection was 98% in the early stages of infection (within 3 days of the disease onset). Based on the current understanding that chest imaging features may precede the clinical symptoms, imaging examination is critical to detect suspected SARS-CoV-2 infected patients (8). Ground-glass opacities (GGO), reticular and/or interlobular septal thickening, consolidation and bilateral lung involvement are the most frequent CT features observed (9). To date, two reports (8,10) have described the temporal radiological changes of COVID-19 pneumonia for mildly and moderately affected patients.

At present, there are a limit number of published data regarding the temporal profile of CT images. Therefore, the present study examined the temporal changes in CT images in severe cases of COVID-19 pneumonia.

Materials and methods

Study design and patients. The present retrospective study was performed in Xiangyang No. 1 People's Hospital (Xiangyang, China), and consisted of 33 severe patients (20 male patients and 13 female patients) who had been diagnosed with COVID-19 in our hospital between January 31 and March 10, 2020. The median age was 65 years (range, 25-90 years). The diagnostic criteria and the severity of COVID-19 were determined according to the guidance provided by the National Health Commission of the People's Republic of China and the National Administration of Traditional Chinese Medicine (11). The confirmed infected patients who met the following criteria were regarded as severe patients: i) Respiratory distress with a respiratory rate ≥30 breaths per minute; ii) oxygen saturation ≤93% under resting conditions; and iii) arterial blood oxygen partial pressure (PaO_2)/fraction of inspiration oxygen (FiO_2) ≤300 mmHg. In addition, those patients who had a rapid progression >50% on CT imaging within 24-48 h were also enrolled in the present study. Children, pregnant women and patients who were infected with other viruses or bacteria were excluded from the present study. The present study was approved by the Ethics Commissions of Xiangyang No. 1 People's Hospital (approval no. 2020GCP011). All enrolled patients provided informed oral consent for the use of their samples in scientific research.

Data collection. Clinical and laboratory data were extracted from the electronic medical records of patients by two physicians with extensive experience (Mr. Helun Cai and Mrs. Yan Dong). Sex, age, underlying diseases, symptoms and laboratory findings, including leukocyte, lymphocyte, procalcitonin (PCT) and C-reactive protein (CRP) counts, were collected at admission.

CT scans and evaluation. The time points of chest CT follow-up was based on the development of COVID-19 in each individual patient. All CT findings were reviewed by two radiologists (Mr. Yong Wang and Mrs. Lisha Wang). Imaging findings were reviewed independently, and final decisions were reached by consensus.

The following CT features were evaluated: GGO, patchy/punctate GGO, consolidation, fibrous stripe and irregular solid nodules. The affected maximum cross-section of each lobe was used to assess its score on CT scans. The score of each lobe was evaluated according to the following criteria (10): i) 0, no involvement; ii) 1, ≤25% involvement; iii) 2, 25-50% involvement; iv) 3, 50-75% involvement; and v) 4, >75% involvement. The degree of aggravation in follow-up CT scans was evaluated according to the following criteria (12): i) 1, minimal aggravation to a lobe; ii) 2, mild aggravation to a lobe; iii) 3, moderate aggravation to a lobe; and iv) 4, severe aggravation to a lobe. The total scores were the sum of each lobar score. The initial evaluation was the basis for the subsequent evaluation in the present study. Therefore, the features in the initial chest CT scan were highlighted.

Statistical analysis. Statistical analysis was performed using SPSS version 22 (IBM, Corp.). Continuous variables are expressed as the mean ± standard deviation or as the median and range. Categorical variables are expressed as frequency rates and percentages.

Results

Patient clinical characteristics. As shown in Table I, the most prevalent symptoms were fever (84.6%), cough (51.5%) and shortness of breath (45.5%). Of the recruited patients, 25 had hypertension, 9 patients had diabetes, 6 patients had cardio-cerebrovascular diseases, 3 patients had chronic obstructive pulmonary disease and 10 patients had >1 comorbidity. On admission, the majority of patients had a normal leukocyte count (28/33) and a decreased lymphocyte count (27/33). CRP and PCT levels were above the normal range in 25 patients and 9 patients, respectively. By April 7, 2020, 24 patients had been discharged, and 9 patients had died. The days from the symptom onset to admission ranged from 1-10 days. The hospital days were 13-35 days for survivors and 6-20 days for non-survivors.

Initial chest CT findings in severe patients with COVID-19 pneumonia. As shown in Table II, of the 33 patients, 6 (18.2%) patients had 1 affected lobe, 6 (18.2%) patients had 2 affected lobes, 5 (15.2%) patients had 3 affected lobes, 9 (27.3%) patients had 4 affected lobes and 7 (21.2%) patients had 5 affected lobes. Additionally, 29 (87.9%) patients had GGOs, 20 (60.6%) patients had patchy GGO, 22 (66.7%) patients had patchy consolidation, 9 (27.3%) patients had fibrous stripes and 3 (9.1%) patients had irregular solid nodules. The total lung severity score ranged from 1-14, with a mean score of 7.

Follow-up chest CT findings in severe patients with COVID-19 pneumonia. As shown in Table III, five stages of lung CT scans were determined: Initial stage (n=33), the first follow-up stage (n=33), the second follow-up stage (n=28), the third follow-up stage (n=27) and the fourth follow-up stage (n=5). In total, 9 non-survivors underwent at least two chest CT scans and 24 survivors underwent >three chest CT scans during hospitalization (data not shown). The mean interval time between two consecutive chest CT scans was 4.5 days (range, 3-9 days) (data not shown). At the first follow-up, no patients demonstrated improvement, 2 (6.1%) of the 33 patients demonstrated minimal progression, 9 (27.3%) demonstrated mild progression, 13 (39.3%) demonstrated moderate progression and 9 patients (27.3%) demonstrated severe progression. At the second follow-up, 28 patients received a CT scan and 5 patients were excluded (4 patients died and 1 severe patient received an X-ray). Of these, 2 of the 28 patients (7.1%) demonstrated disease improvement, 5 (17.9%) demonstrated minimal progression, 10 (35.7%) demonstrated mild progression, 8 (28.6%) demonstrated moderate progression and 3 (10.7%) demonstrated severe progression. At the third follow-up, 27 patients received CT scans, of which 5 patients died, and 1 patient was discharged. Of these, 22 of the 27 patients (81.5%) demonstrated improvement, 2 (7.4%) demonstrated minimal progression, 2 (7.4%) demonstrated mild progression, 1 (3.7%) demonstrated moderate progression and no patients demonstrated severe progression. At the fourth follow-up, only 5 patients received a CT scan (19 patients were discharged and 9 patients died). Of the 5 patients, 2 (40%) demonstrated no changes, and 3 (60%)

Table I. Demographic characteristics of the enrolled patients (n=33).

Clinical characteristics	Patients
Age, years	73±15 (25-90)
Sex	
Female, n (%)	13 (39.4)
Male, n (%)	20 (60.6)
Hospital admission	
Survivors, days	13-35
Non-survivors, days	6-20
Days from symptom onset to hospital admission	1-10
Clinical outcomes	
Discharged, n (%)	24 (72.3)
Died, n (%)	9 (27.3)
Symptoms	
Fever, n (%)	28 (84.8)
Cough, n (%)	17 (51.5)
Shortness of breath, n (%)	15 (45.5)
Underlying disease	
Hypertension, n (%)	25 (75.8)
Diabetes, n (%)	9 (27.3)
Cardio-cerebrovascular disease, n (%)	6 (18.2)
COPD, n (%)	3 (9.1)
Comorbidity	
Acute respiratory distress syndrome, n (%)	9 (27.3)
Acute renal injury, n (%)	7 (21.2)
Shock, n (%)	5 (15.2)
Laboratory data	
PCT increase, n (%)	9 (27.3)
CRP increase, n (%)	25 (75.8)
Lymphocyte decrease, n (%)	27 (82.8)
Leukocyte normal, n (%)	28 (84.5)

COPD, chronic obstructive pulmonary disease; PCT, procalcitonin; CRP, C-reactive protein.

Table II. Initial CT findings of the enrolled patients (n=33).

Parameters regarding CT findings	Patients
Number of affected lobes	Number (%)
1	6 (18.2)
2	6 (18.2)
3	5 (15.2)
4	9 (27.3)
5	7 (21.2)
Total CT score, mean ± SD	7±4
CT features	Number (%)
GGOs	29 (87.9)
Patchy GGOs	20 (60.6)
Patchy consolidation	22 (66.7)
Fibrous stripes	9 (27.3)
Solid nodules	3 (9.1)

GGO, ground-glass opacities; CT, computerized tomography.

demonstrated disease improvement. After ~3 weeks of disease onset, the presence of fibrous stripes and the decreased extent and density of consolidation or GGO indicated that these patients had improved (Fig. 1). In detail, Fig. 1 shows a typical temporal process of CT findings in a severe patient (a 54-year male patient) with novel coronavirus pneumonia. Scattered ground glass opacities were observed in the initial stage, and then an increased range of opacities and density of consolidation were observed 5 days after admission. Moreover, fibrous stripes began to appear at 3 weeks after admission, along with a deceased extent and density of consolidation or GGOs.

Discussion

In the present study, the majority of severe patients were elderly adults (>60 years old, 23 elderly patients). Fever, cough and shortness of breath were the most common clinical manifestations. Additionally, the temporal changes in the chest CT findings of severe patients with COVID-119 pneumonia were observed. GGO, consolidation and interlobular septal thickening were the most common CT abnormalities. Severe patients with COVID-19 pneumonia had features of rapid progression and slow absorption on chest CT images. Follow-up CT examination may assist in observing progression and identify patients at risk in a more timely manner.

CoVs constitute a large family of viruses that possess a single-strand, positive sense RNA genome 26-32 Kb in length. As well-known causes of severe infections, two major zoonotic pathogenic CoVs, SARS-CoV and Middle East Respiratory Syndrome CoV (MERS-CoV) caused a global outbreak with far-reaching effects on public health during 2002-2003 and in 2012, respectively (13-15). COVID-19 is a new subtype in the CoV family, which is 82% similar to SARS-CoV in genetic structure (4). Although the mortality rate of COVID-19 is less than that of SARS-CoV and MERS-CoV infection, the total number of COVID-19 infections is increasing rapidly and has far exceeded the previous CoV outbreaks. Asymptomatic pneumonia with SARS-CoV-2 infection has been reported (16), and asymptomatic patients are also a major source of transmission. Therefore, early detection and management of these asymptomatic patients is of great significance.

It has been previously reported that CT findings have a higher sensitivity than PCR in the early stage of COVID-19 (4). Fang *et al* (7) reported the sensitivity of nucleic acid detection was 71%, whereas the sensitivity of CT scans for SARS-CoV-2 infection was 98% in the early stage (within 3 days from the onset of disease). Chest CT scans are a key screening tool for the diagnosis of patients suspected of being infected or suffering from asymptomatic pneumonia.

In the present study, findings from imaging of COVID-19 pneumonia are consistent with typical viral pneumonia manifestations. The images demonstrated that the majority of patients showed multifocal GGO along with or without

Table III. Qualitative changes at follow-up chest CT examination in enrolled patients (n=33).

	Follow-up CT findings			
Disease progression	First (n=33)	Second (n=28)	Third (n=27)	Fourth (n=5)
No change, n (%)	0	0	0	2 (40.0)
Disease improvement, n (%)	0	2 (7.1)	22 (81.5)	3 (60.0)
Minimal progression, n (%)	2 (6.1)	5 (17.9)	2 (7.4)	0
Mild progression, n (%)	9 (27.3)	10 (35.7)	2 (7.4)	0
Moderate progression, n (%)	13 (39.3)	8 (28.6)	1 (3.7)	0
Severe progression, n (%)	9 (27.3)	3 (10.7)	0	0

CT, computerized tomography.

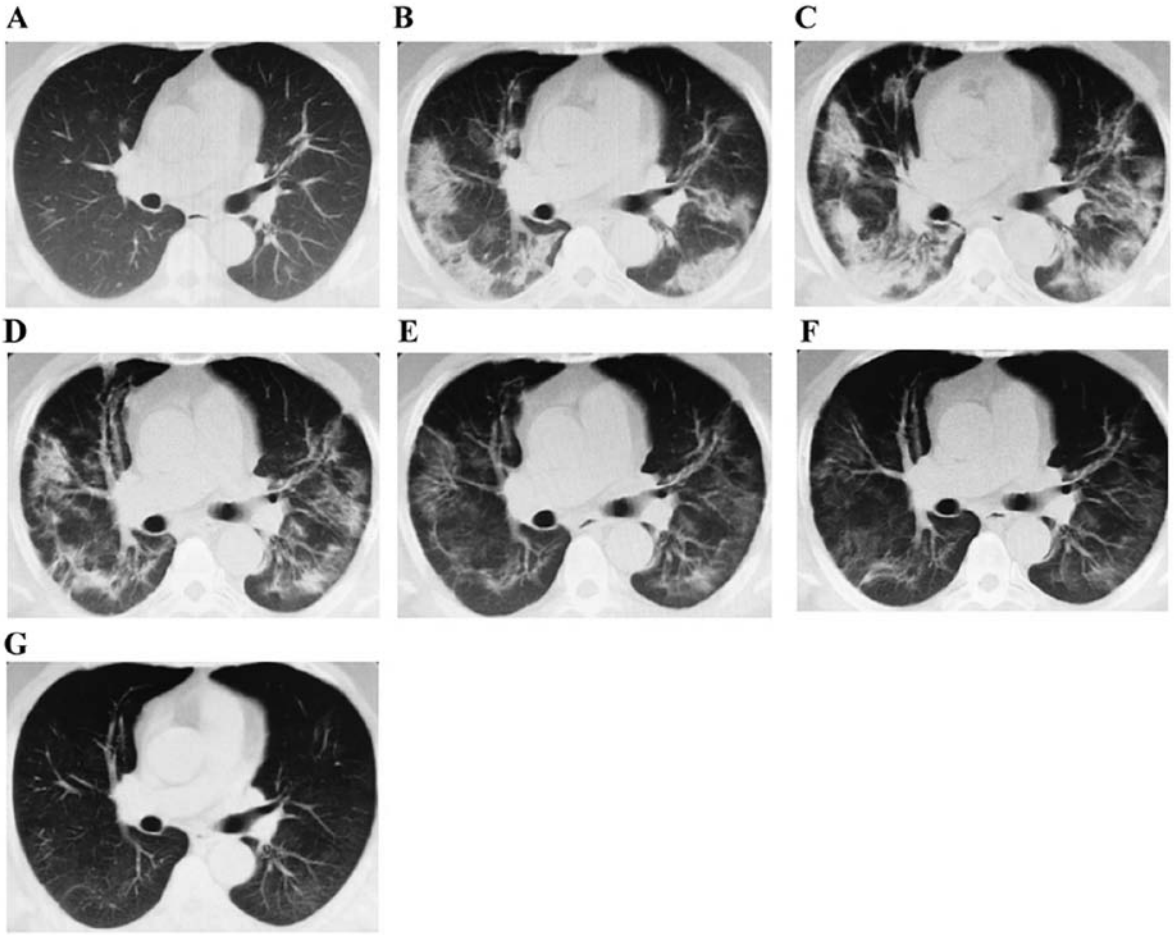

Figure 1. Temporal profiles of CT imaging findings of a 54-year-old male patient with novel coronavirus pneumonia. (A) Initial CT imaging findings obtained on January 25, 2020, showed scattered ground glass opacities. (B) First follow-up CT image, which showed an increasing range of opacities and density of consolidation on January 30, 2020. (C) Second follow-up CT image on February 8, 2020. (D) Third follow-up CT image on February 18, 2020. (E) Fourth follow-up CT image on February 27, 2020. (F) Fifth follow-up CT image on March 5, 2020. (G) Sixth follow-up CT image on April 9, 2020. CT, computerized tomography.

consolidation and bilateral involvement on CT findings in the early stages of the disease, which is different from previous findings in patients with SARS-CoV (typically unifocal lung lesion) (17). The lesions were primarily distributed under the pleura during the initial stage and became random or diffuse during the course of the disease in these severe patients. Other CT abnormalities, such as pneumothorax and pleural effusion were also observed in the present study (data not shown). Imaging findings of viral pneumonia are varied and rapid. As the disease progressed, the extent and density of GGO increased gradually and consolidation began to appear. These patients showed improvement at the third follow-up CT examination (~3 weeks after the onset of disease), which included the presence of a fibrous stripe and a decreased extent and density

of consolidation or GGO. At the fourth follow-up (~4 weeks after the onset of disease), most severe patients showed notable improvement, including complete absorption or only a few fibrous stripes remaining. Based on the fact that patients who have recovered from MERS-infected pneumonia have residual fibrotic changes, it was hypothesized that the patients with COVID-19 pneumonia may also respond and heal in a similar manner (18). In the present study, irregular solid nodules were found during the early stage, enlarged and merged nodules during the middle stage, and reduced and absorbed nodules at the later stage in a few severe patients (data not shown). Initial CT scans were performed for all patients at admission. However, the days from symptom onset to hospital admission were different among these patients. Therefore, the present study tracked the temporal profiles of CT based on the development of COVID-19.

In the present study, severe cases were primarily observed in elderly patients. It has been reported that CT score was positively correlated with age, the level of inflammatory biomarkers, severity of disease, underlying co-morbidities and disease progression (19). Lymphopenia was observed in most patients with COVID-19, which may be associated with the immunosenescence and the high mortality rates. However, the exact relationship between lymphopenia, immunosenescence and high mortality rates requires further study. Underlying comorbidities is another factor that affects COVID-19 outcomes, particularly in elderly patients with COVID-19. These clinical features have been extensively confirmed by numerous other reports (19,20). Psychiatric disorders are also a major factor of higher mortality rates. The majority of elderly patients had mild cognitive impairment and frailty, which may underlie the high mortality rates in elderly patients (21).

The present study has several limitations. First, chest X-ray findings were not included in the present study. For severe patients with invasive respiratory support, chest X-rays are the major tool used to understand the dynamic changes in a timely manner, thus the present study may be missing important results. A large white lung was observed in a patient who succumbed to the disease, which led to decreased scores at the follow-up stages. Second, the slice thickness of CT scans was 5 or 8 mm for these patients, which may have meant subtle features were missed. Third, the number of enrolled patients was relatively small. Xiangyang No.1 People's Hospital (Hubei, China) was one of the designated hospitals for COVID-19. Some patients were admitted to other hospitals, and the number of critically ill patients was limited.

In summary, the present study demonstrated the dynamic changes of CT findings in severe patients with COVID-19 pneumonia, with the intention of highlighting changes and possible clinical manifestations in the lungs following infection. Severe patients with COVID-19 pneumonia had features of rapid progression and slow absorption on chest CT imaging. Chest CT scans are vital for the early detection of suspected cases, evaluation of the disease severity and follow-up of patients with COVID-19 pneumonia.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

PL, HC and YD conceived and designed the study. PL, HC and YD consulted the literature, contributed to the writing of the manuscript and final edits. LW and YW produced the figures. PL, HC, YD and JH contributed the interpretation of the data and the critical revision of the manuscript. All authors had accessed the authenticity of all raw data and taken responsibility for the authenticity of all data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Commissions of Xiangyang No. 1 People's Hospital (approval no. 2020GCP011; Xiangyang, China). All enrolled patients provided informed oral consent for the use of their samples in scientific research. Clinical data for all enrolled patients were collected. This study did not interfere with the diagnosis and treatment of each patient. The personal information of each patient will not be disclosed.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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