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CHEST

Chest computed tomography findings of coronavirus disease 2019 (COVID-19) pneumonia

Fangfang Fu[1] · Jianghua Lou[1] · Deyan Xi[2] · Yan Bai[1] · Gongbao Ma[3] · Bin Zhao[4] · Dong Liu[5] · Guofeng Bao[6] · Zhidan Lei[1] · Meiyun Wang[1]

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Abstract

Objective To retrospectively analyze the chest computed tomography (CT) features in patients with coronavirus disease 2019 (COVID-19) pneumonia.

Methods From January 9, 2020, to February 26, 2020, totally 56 laboratory-confirmed patients with COVID-19 underwent chest CT. For 40 patients, follow-up CT scans were obtained. The CT images were evaluated for the number, type and distribution of the opacity, and the affected lung lobes. Furthermore, the initial CT scan and the follow-up CT scans were compared.

Results Forty patients (83.6%) had two or more opacities in the lung. Eighteen (32.7%) patients had only ground-glass opacities; twenty-nine patients (52.7%) had ground-glass and consolidative opacities; and eight patients (14.5%) had only consolidation. A total of 43 patients (78.2%) showed two or more lobes involved. The opacities tended to be both in peripheral and central (30/55, 54.5%) or purely peripheral distribution (25/55, 45.5%). Fifty patients (90.9%) had the lower lobe involved. The first follow-up CT scans showed that twelve patients (30%) had improvement, 26 (65%) patients had mild-moderate progression, and two patients (5%) had severe progression with "white lungs." The second follow-up CT showed that 22 patients (71%) showed improvement compared with the first follow-up CT, four patients (12.9%) had aggravated progression, and five patients (16.1%) showed unchanged radiographic appearance.

Conclusions The common CT features of COVID-19 pneumonia are multiple lung opacities, multiple types of the opacity (ground-glass, ground-glass and consolidation, and consolidation alone), and multiple lobes especially the lower lobe involved. Follow-up CT could demonstrate the rapid progression of COVID-19 pneumonia (either in aggravation or absorption).

Key Points

- *The predominant CT features of COVID-19 pneumonia are multiple ground-glass opacities with or without consolidation and, with both lungs, multiple lobes and especially the lower lobe affected.*
- *CT plays a crucial role in early diagnosis and assessment of COVID-19 pneumonia progression.*
- *CT findings of COVID-19 pneumonia may not be consistent with the clinical symptoms or the initial RT-PCR test results.*

Keywords Coronavirus · Pneumonia · Thoracic diseases · Tomography, spiral computed

Fangfang Fu and Jianghua Lou contributed equally to this work.

✉ Meiyun Wang
mywang@ha.edu.cn

[1] Department of Medical Imaging, Henan Provincial People's Hospital & People's Hospital of Zhengzhou University, 7 Weiwu Road, Zhengzhou 450003, Henan Province, China

[2] Department of Radiology, Taikang People's Hospital, Zhoukou, Henan, China

[3] Department of Radiology, Gongyi People's Hospital, Zhengzhou, Henan, China

[4] Department of Radiology, Xincai People's Hospital, Zhumadian, Henan, China

[5] Department of Radiology, The First Affiliated Hospital of Soochow University, Suzhou 215006, Jiangsu, China

[6] Department of Radiology, Yihe Hospital in Zhengzhou, Zhengzhou, Henan, China

Abbreviations

COVID-19	Coronavirus disease 2019
CT	Computed tomography
MERS	Middle East Respiratory Syndrome
RT-PCR	Real-time fluorescence polymerase chain reactions
SARS	Severe acute respiratory syndrome
SARS-CoV-2	Severe acute respiratory syndrome corona virus 2
WHO	World Health Organization

Introduction

In mid-December 2019, a cluster of unidentified pneumonia cases named coronavirus disease 2019 (COVID-19) emerged in Wuhan, Hubei, China, with clinical symptoms resembling viral pneumonia. Real-time fluorescence polymerase chain reaction (RT-PCR) of respiratory specimens revealed a novel beta corona virus to be present, which has subsequently been named severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) by the World Health Organization (WHO) [1–5]. COVID-19 pneumonia is characterized by fast spread, wide epidemic range, and major respiratory dysfunction. The number of reported cases rose rapidly and by 26 February 2020, there were more than 78,100 confirmed cases (65,596 in Hubei Province) with 2718 deaths (2104 in Hubei) reported, and with an additional 2019 suspected cases in China [6]. In addition, 2918 confirmed cases had appeared in many other countries throughout the world [6]. Global attention was soon focused on the situation because of the increasing number of new cases and the high death rate associated with SARS-CoV-2 infection. Early diagnosis will enable patients to be isolated and treated in good time, essential for avoiding the spread of disease, improving prognosis, and reducing mortality. Thus, early diagnosis of COVID-19 pneumonia is of great significance.

Medical imaging techniques have a potentially important role to play in early diagnosis and managing the treatment of patients infected with SARS-CoV-2. Chest X-rays have a potentially useful role to play in revealing the presence of pathology affecting the lung [7–9]. However, small lesions may not be detected and the greater resolving power of CT is likely to particularly important for early diagnosis of patients with a negative chest X-ray and high clinical suspicion of COVID-19.

Thus, the aim of this study was to evaluate retrospectively the CT features in patients with COVID-19 pneumonia at our institution and to compare the CT findings during different periods of the disease.

Materials and methods

Patients

This retrospective study was conducted with the institutional review board approval, and written informed consent was waived.

Patients admitted to our hospital and who were suspected to have COVID-19 pneumonia were screened according to the guideline for the diagnosis and treatment of COVID-19 [5]. Suspected patients were defined as the cases with any epidemiological history and any 2 of the following clinical manifestations, or 3 of the following clinical manifestations if without clear epidemiological history: (1) epidemiology history: (i) a travel or residence history of Wuhan and its surrounding areas, or other communities with case reports in other cities within 14 days before symptom onset; (ii) contact with COVID-19 cases who have a positive result of the RT-PCR test within 14 days before symptom onset; (iii) contact with patients who have fever or respiratory symptoms from Wuhan and its surrounding areas, or other communities with case reports in other cities within 14 days before symptom onset; (iv) clustered symptom onsets. (2) Clinical manifestations: (i) fever and/or respiratory symptoms; (ii) imaging manifestations of pneumonia; (iii) normal or decreased white blood cell count, or decreased lymphocyte count in the early stages of the disease. As of February 26, 2020, all the respiratory specimens from 85 suspected patients were tested by using RT-PCR. Finally, 56 patients (33 males and 23 females) were confirmed to be infected with SARS-CoV-2. The ages of the patients ranged from 19 to 67 years with a mean of 42.9 years.

CT imaging

CT scans were acquired for the 56 patients in the supine location on one of three different scanning systems. One unit (uCT 780, United Imaging Healthcare) was used with the following parameters: 1.0-mm section thickness, 5-mm gap, 120 kV, and 150 mA. Another unit (Optima CT520; GE Healthcare) was used with the following parameters: 1.3-mm section thickness, 10-mm gap, 120 kV, and 180 mA. A third unit (Discovery CT750, GE Healthcare) was used with the following parameters: 1.25-mm section thickness, 10-mm gap, 120 kV, and 180 mA.

A follow-up scan was performed in 40 patients and a second follow-up scan was performed in 31 patients, and a third follow-up scan in 25 patients. The average time between the initial and first follow-up scan was 4.5 days (range 2 to 8 days), between the first and second follow-up scan was

4.5 days (range 2 to 14 days), and between the second and third follow-up scan was 5.6 days (range 2 to 17 days).

For reporting, the CT images were displayed with standard lung (window width, 1000 to 2000 HU; window level − 700 to – 500 HU) and mediastinal (window width 300 to 400 HU; window level 30 to 50 HU) settings.

Image interpretation

Three radiologists (with 21, 13, and 9 years of experience in thoracic radiology, respectively) independently reviewed all CT images using a viewing console and finally reached a decision in consensus.

The CT scans were assessed for the presence of ground-glass opacities, consolidation, thickened small vessels within opacity, crazy-paving pattern, interlobular septal thickening, air bronchograms, and fibrous stripes. The potential presence of pleural effusion or thoracic lymphadenopathy and any other abnormalities were also noted. The number of opacity in both lungs is classified according to the following: 0, 1, 2, 3, or more. Abnormalities were magnified and examined for interlobular septal, intralobular interstitial thickening, etc.

Ground-glass opacification was defined as increased lung parenchymal attenuation that did not obscure the underlying vessels [10]. Consolidation was defined as opacification with the underlying vessels was obscured [10]. Lymphadenopathy was defined as lymph node size (short-axis dimension) of ≥ 10 mm [11]. The outer one-third of the lung was defined as peripheral, and the rest of the lung was defined as central.

The extent of disease at CT was also assessed. Each of the lung lobes (total of five lung lobes) was evaluated and classified for the degree of involvement that was on grounded on the following: None corresponded to score 0 (0%), minimal to score 1 (1–25%), mild to score 2 (26–50%), moderate to score 3 (51–75%), and severe to score 4 (76–100%). Summation of the five lobe scores provided overall lung involvement (range of possible scores, 0–20) [12].

Results

Clinical parameters and selected laboratory tests

One patient confirmed with SARS-CoV-2 infection failed to enroll in the group of COVID-19 pneumonia due to presenting normal appearance on lung CT images. Finally, a total of 55 patients with SARS-CoV-2 infection were enrolled in this study. These 55 patients had a median age of 45 years (range 20 to 67 years) and comprised 33 males with median age of 42 years (range 20 to 67 years) and 22 females of median age 47 years (range 26 to 66 years). The clinical characteristics and results of selected laboratory tests for the 55 patients are presented in Table 1.

CT findings

Of the 55 patients, forty (72.7%) had 3 or more opacities, six (10.9%) had 2 opacities, nine had 1 opacity (16.4%). Eighteen patients (32.7%) had only ground-glass opacities (Fig. 1);

Table 1 Clinical characteristics and results of laboratory tests in patients with COVID19 pneumonia

Characteristic	All patients ($n = 55$)
Age, years	45 (20–67)
Sex	
Men	33 (60%)
Women	22 (40%)
Epidemiological history	55 (100%)
Recent travel or residence history of Wuhan	27 (49.1%)
Contact with COVID-19 cases	28 (50.9%)
Clustered onsets	16 (29%)
Fever	50 (90.9%)
Maximal temperature	
< 37.3 °C	1 (2%)
37.3–38.0 °C	23 (46%)
38.1–39.0 °C	22 (44%)
> 39.0 °C	4 (8%)
Myalgia or fatigue	13 (23.6%)
Pharynx discomfort	2 (0.04%)
Cough	21 (38.1%)
Sputum production	6 (10.9%)
Hemoptysis	0
Shortness of breath	8 (14.5%)
Diarrhea or vomiting	1 (0.02%)
Headache	6 (10.9%)
White blood cell count (× 10^9/L)	
< 4	21 (39.3%)
4 ~ 10	32 (57.1%)
> 10	2 (3.6%)
Lymphocyte count (× 10^9/L)	1.0 (0.38–2.58)
Reduced lymphocyte count	35 (63.6%)
Normal lymphocyte count	20 (36.4%)
CRP (mg/L)	10.96 (1.3–217.17)
Increased CRP	50 (90.9%)
Normal CRP	5 (9.1%)

Note: Data are median (range), *n* (%), or *n*/*N* (%), where *N* is the total number of patients with available data

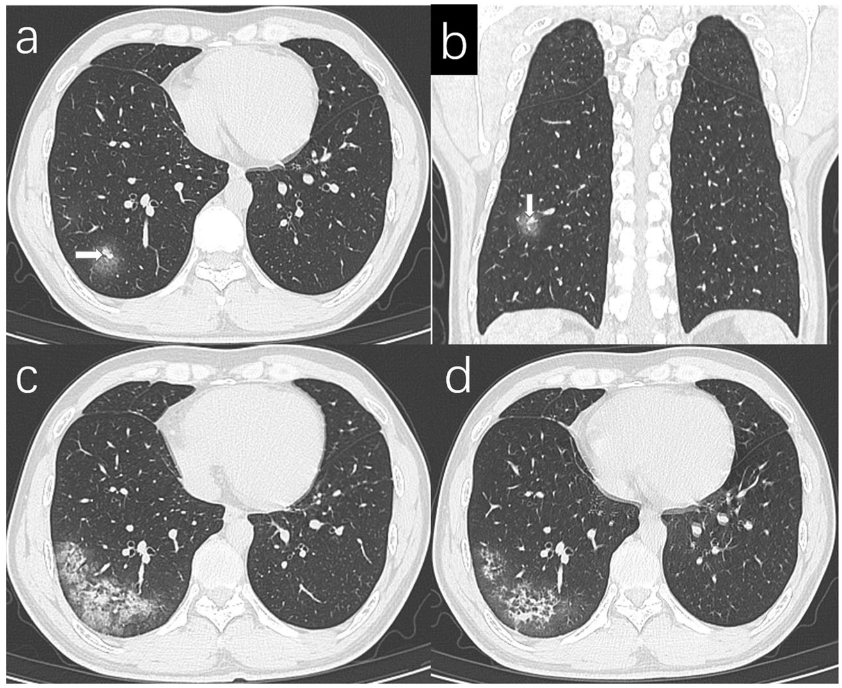

Fig. 1 A 29-year-old woman with COVID-19 pneumonia. **a**, **b** Axial CT image and coronal CT image showed ground-glass opacification accompanied with thickened small vessels (arrow) in right lower lobe on day 9 after symptom onset; **c** The first follow-up CT image (5 days after initial CT) showed the ground-glass opacification obviously enlarged mixed with consolidation. **d** The second follow-up CT image (4 days after initial CT) showed the opacification gradually absorbed, and the density of lesion reduced

twenty-nine patients (52.7%) had ground-glass opacities and consolidation (Fig. 2); and eight patients (14.6%) had only consolidation (Fig. 3). In addition, forty-five patients showed thickened small vessels accompanied with opacities (Figs. 1 and 4). Nine patients (16.4%) demonstrated crazy-paving patterns (Fig. 5). Twenty-one patients (38.2%) had associated the interlobular septal thickening in the zones of ground-glass attenuation or adjacent to zones of consolidation (Fig. 2a). Twenty-nine patients (52.7%) demonstrated air bronchograms (Figs. 4 and 6). Only one patient (2%) showed a small amount of unilateral pleural effusion. None of the patients had evidence of thorax lymphadenopathy.

With regard to the distribution of opacities, the opacities were present in both peripheral and central regions for 30 patients whereas the opacities were present in merely peripheral for 25 patients (Table 2). No opacity was present in a purely central region. The total lung involvement score ranged from 1 to 19, with a mean score of 4.6. The patient with the highest lung severity score was admitted to an intensive care unit.

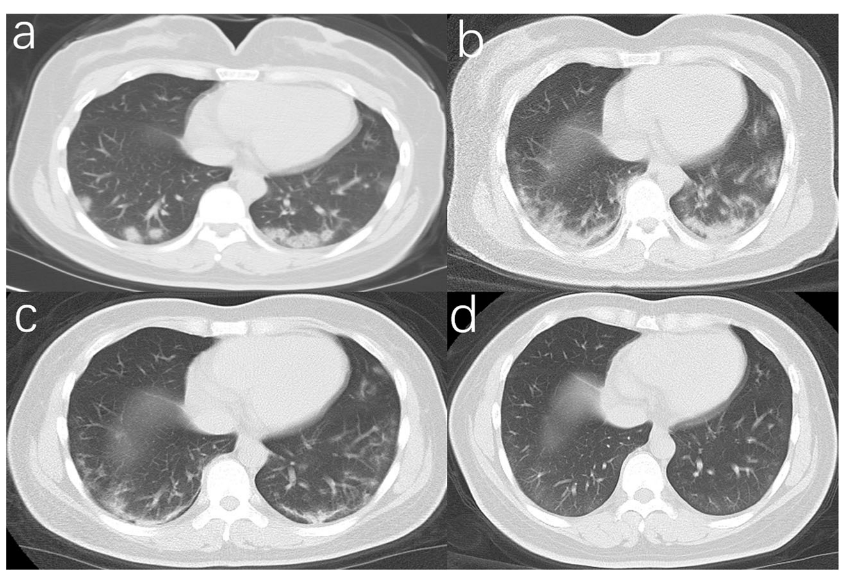

Fig. 2 A 31-year-old woman with COVID-19 pneumonia. **a** Axial CT image showed multifocal consolidations with a peripheral distribution in the bilateral lower lobes and a patchy ground-glass opacification in the left lower lobe day 3 after symptom onset. **b** The first follow-up CT image (7 days after initial CT) showed that the lesions had increased in extent and the density became heterogeneous. **c** The second follow-up CT image (10 days after initial CT) showed previous opacifications being dissipated. **d** The third follow-up CT image (18 days after initial CT) showed further resolution of the lesions

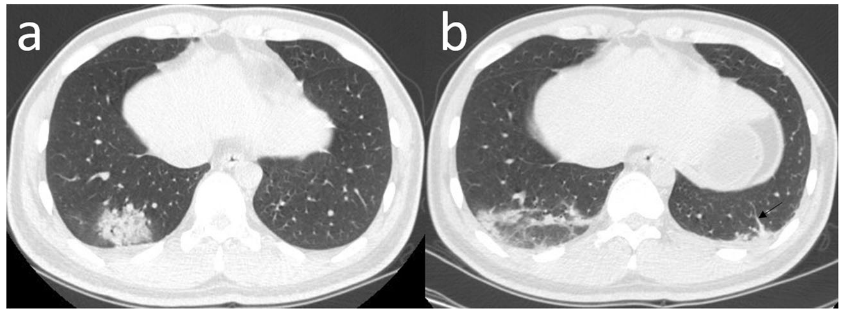

Fig. 3 A 23-year-old man with COVID-19 pneumonia. **a** Axial CT image showed consolidation in the right lower lobe on day 8 after symptom onset. **b** A follow-up CT image (6 days after initial CT) shows that the consolidation area of the right lower lobe was gradually absorbed and a fibrous stripe was presented in left lower lobe (arrow)

In the majority of patients both lungs were affected (only in 12 patients (21.8%) was one lung affected) and usually it was also the case (i.e., in 43 patients (78.2%)) that more than one lobe was affected, with the lower lobe more often affected (50 patients (90.9%)) than the upper (39 patients (70.9%)) and lastly the middle (28 patients (50.9%)) lobe (see Table 2).

By February 26, 2020, 40 (72.7%) patients had been cured and discharged from the hospital, with an average interval between symptom onset and discharge of 19 days (range 11–34). Nevertheless, the other 15 patients were not followed up and the follow-up CT scans were not obtained because these patients were transferred to other hospitals for treatment after hospitalization in our hospital.

CT image changes at follow-up

During hospitalization, follow-up CT scans were performed in 40 patients (Table 3), a second follow-up scan in 31 patients, and a third follow-up scan in 25 patients. Through follow-up CT scans of 40 patients, we observed two evolution patterns of COVID-19 as follows: (1) radiographic improvement, seen in 12 (30%) patients with an average interval between symptom onset and discharge of 17.7 days (range 12–26) and (2) initial progression, followed by radiographic improvement, seen in 28 (70%) patients (Figs. 1, 2, 4, and 5) with an average interval between symptom onset and discharge of 19.3 days (range 11–34).

The first follow-up CT scans showed that twelve of 40 (30%) patients had improvement (Fig. 3), 26 (65%) patients had mild-moderate progression (Figs. 1, 2, and 4), and two (5%) patients had severe progression (i.e., "white lungs") (Fig. 5) who were admitted to the ICU. Compared with the initial CT scans, the first follow-up scans showed that the numbers of patients with both lungs affected increased from 31 to 34, with all lobes involved increased from 13 to 15 and with 3 lobes involved from 4 to 9 (Table 3). The number of patients in which imaging features were present both peripherally and centrally also increased from 22 to 28. Furthermore, the numbers of patients with ground-glass and consolidative opacities increased from 19 to 32 and the number of patients with interlobular septal thickening from 16 to 31. In addition, the number of patients with fibrous stripes increased from 3 to 13 (Table 3).

Of the 31 patients with a second follow-up CT scan, 22 patients showed improved radiographic appearance with opacities gradually absorbed (Figs. 1, 2, and 4) and the fibrous stripes and pleural thickening noted compared with the first follow-up CT scan, five patients showed unchanged radiographic appearance, and four patients showed further progression with increasing number of ground-glass opacities and consolidation (Fig. 6).

Of the 25 patients with a third follow-up CT scan before discharge, all patients showed improved radiographic

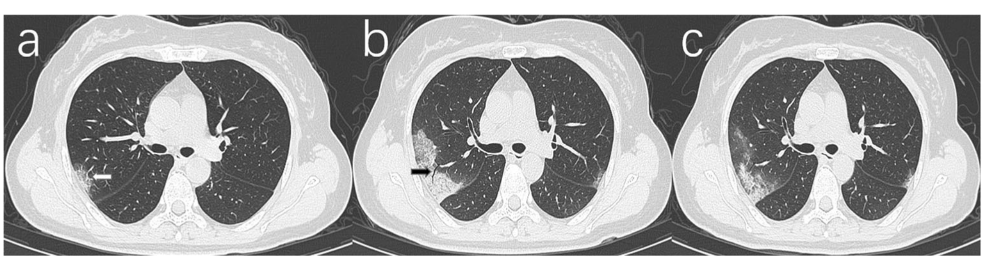

Fig. 4 A 51-year-old woman with COVID-19 pneumonia. **a** Axial CT image showed ground-glass opacification accompanied with thickened small vessel (arrow) in the posterior segment of upper lobe on day 5 after symptom onset; **b** The first follow-up CT image (7 days after initial CT) showed the ground-glass opacification obviously enlarged mixed with local consolidation and air bronchogram in the opacification (arrow). **c** The second follow-up CT image (10 days after initial CT) showed the lesion gradually absorbed, and the density of lesion reduced

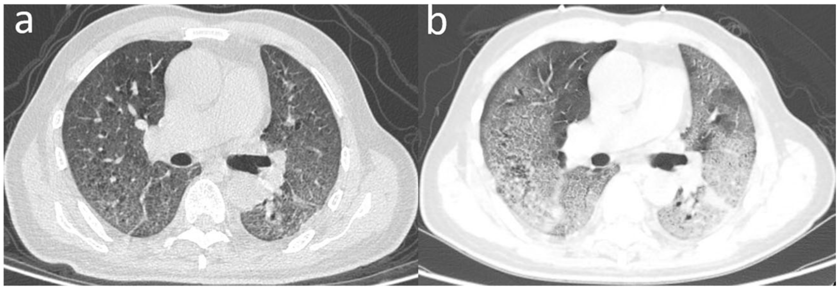

Fig. 5 A 65-year-old man with COVID-19 pneumonia. **a** Axial CT image showed bilateral multiple patchy ground-glass opacities in both lungs on day 12 after symptom onset; **b** Follow-up CT image (5 days after initial CT) showed diffuse ground-glass opacities associated with interlobular septal thickening presenting as a "crazy paving" pattern and focal consolidation affected all the lobes and the lungs progressed to the "white lung" stage

appearance with opacities gradually absorbed and reduced compared with the second follow-up CT scan (Figs. 2 and 6).

Correlation of chest CT findings and clinical symptoms

All the patients with abnormal initial CT scans were symptomatic. However, three patients with obviously abnormal CT showed mild clinical symptoms only presenting pharyngeal discomfort. Additionally, after receiving treatment, 30 patients (75%) showed that follow-up CT changes were consistent with the clinical symptoms changes, while the other 10 patients (25%) showed that follow-up CT changes were not consistent with the clinical symptoms changes. The clinical symptoms of these 10 patients were significantly improved, but their follow-up CT images showed progression.

Correlation of initial chest CT findings and the initial RT-PCR test result

Of the 55 patients, 53 (96.4%) patients showed that the initial chest CT findings were consistent with the results of initial RT-PCR tests. Nevertheless, 2 patients with a Wuhan exposure history presenting expected features on CT images had a negative result on the initial but not a follow-up RT-PCR test.

Discussion

The first cases of COVID-19 pneumonia occurred in Wuhan, Hubei Province, China, in December 2019. Since then, there have been many cases of COVID-19 pneumonia with human-to-human transmission by close contacts in other cities and provinces in China and in other countries around the world

Fig. 6 A 49-year-old man COVID-19 pneumonia. **a** Image obtained on day 1 after symptom onset showed ground-glass opacification in the right lower lobe. **b** The first follow-up CT image (4 days after initial CT) showed the original ground-glass opacification were consolidated and enlarged. In addition, a new lesion was found in the right middle lobe. **b** The second follow-up CT image (9 days after initial CT) showed that lung opacities increased and more segments of both lung lobes were affected. **d** The third follow-up CT image (24 days after initial CT) showed that lung opacities were being dissipated into ground-glass opacities and a fibrous stripe (arrow) was presented

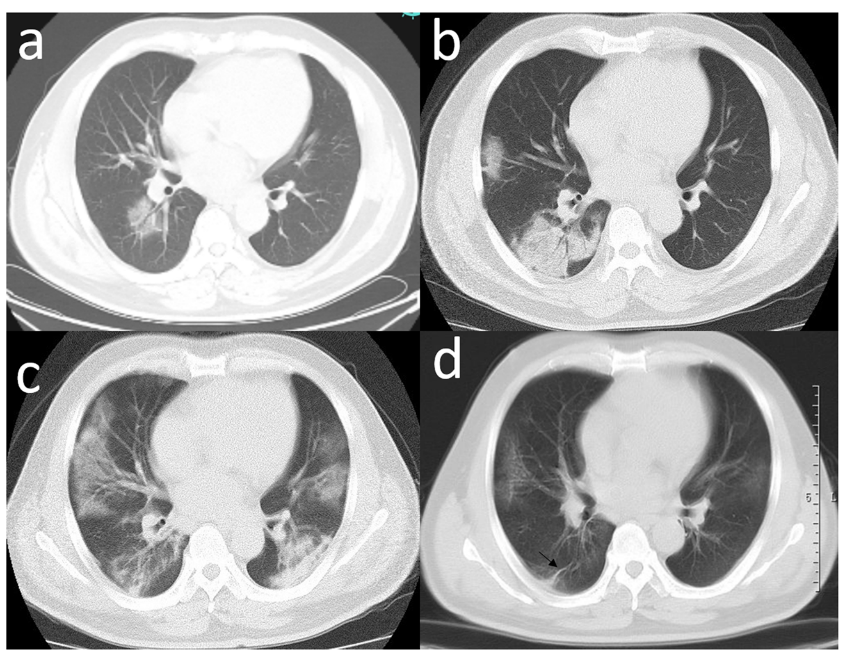

Table 2 Number and percentage (%) of patients with specific diagnostic features on CT images

Characteristic	Initial CT scan, no. of patients* ($n = 55$)
Affected lung	
Right lung	6 (10.9)
Left lung	7 (12.7)
Both lung	42 (76.4)
Affected lung lobes	
Upper lobe	39 (70.9)
Middle lobe	28 (50.9)
Lower lobe	50 (90.9)
1 lobe affected	12 (21.8)
2 lobes affected	8 (14.5)
3 lobes affected	6 (10.9)
4 lobes affected	11 (20.0)
All lobes affected	18 (32.7)
Distribution	
Central	0
Peripheral	25 (45.5)
Both central and peripheral	30 (54.5)
Opacity	
Ground-glass	18 (32.7)
Ground-glass with consolidation	29 (52.7)
Consolidation	8 (14.5)
Other findings	
Thickened small vessels within opacity	45 (81.8)
Crazy-paving pattern	9 (16.4)
Interlobular septal thickening	21 (38.2)
Air bronchograms	29 (52.7)

*Numbers in parentheses are percentages

[11]. The clinical symptoms of the disease are very similar to 2003 SARS-CoV with patients frequently developing acute respiratory distress syndrome and which may lead to death. We have thus been interested to analyze the CT features and the evolution of COVID-19 pneumonia to provide a reference for early diagnosis, timely isolation, and treatment.

Our preliminary investigation has revealed some common findings on lung CT images obtained from patients with COVID-19 pneumonia. Firstly, the number of opacities is often more than one. The types of opacities including ground-glass without consolidation and ground-glass with consolidation are very often seen. Moreover, small vessels often identified to be thickened within the opacities. Secondly, multiple lung lobes and especially the lower lobe are often involved. Thirdly, the opacities may be distributed peripherally and centrally or peripherally but never occur just centrally. Other findings including a crazy-paving pattern, interlobular septal thickening, and air bronchograms may sometimes be seen. Nevertheless, the appearance of the CT features also depends on the stage of COVID-19 pneumonia.

In the early stage of the disease, CT images predominantly show unilateral or bilateral ground-glass opacities accompanied with enlarged small vessels. Sometimes, ground-glass with focal consolidation can be seen. In terms of distribution, the lower lobe and peripheral (i.e., subpleural area) are most commonly affected. The early involvement of the peripheral and subpleural regions may be related to the pathological mechanism of viral pneumonia, such as the early involvement of bronchioles and parenchyma around the bronchioles, and then the involvement of whole pulmonary lobule and diffuse alveolar damage [13].

As the disease progresses, CT images show enlargement of opacities and an increased number of new ground-glass opacities affecting more and larger regions of multiple lung lobes. Furthermore, some of the original ground-glass opacities begin to consolidate. Thus, ground-glass opacities and consolidation are commonly seen. At this stage, if the patients could not receive effective treatment promptly or if the immunity is low, COVID-19 pneumonia may be life-threatening. CT images may show diffuse opacities to be present in both lungs and

Table 3 Comparison of CT image features in initial and first follow-up scans

Characteristic	Initial CT scan, no. of patients ($n = 40$)	The first follow-up CT scan, no. of patients ($n = 40$)
Affected lung		
Right lung	5	3
Left lung	4	3
Both lung	31	34
Affected lung lobes		
Upper lobe	29	31
Middle lobe	15	18
Lower lobe	37	37
1 lobe affected	6	5
2 lobes affected	10	4
3 lobes affected	4	9
4 lobes affected	7	7
All lobes affected	13	15
Location		
Central	0	0
Peripheral	18	12
Both central and peripheral	22	28
Opacity		
Ground-glass	13	4
Ground-glass with consolidation	19	32
Consolidation	8	4
Other findings		
Interlobular septal thickening	16	31
Air bronchograms	20	28
Fibrous stripes	3	13

in severe cases so-called white lung manifestation. However, there are fewer patients in the stage. In the study, only two cases showed "white lungs." If the patient accepts effective treatment or if immunity is enhanced, pneumonia will be gradually absorbed and the opacity will be diminished [14]. The disease will improve, possibly leaving the lung fibrous stripes and thickened pleural. In the present study, 40 patients were cured and discharged and before discharge, the RT-PCR test result for each patient was negative and the appearance of opacities in both lungs was improved and their size obviously diminished.

Nevertheless, we found that COVID-19 pneumonia has many similar CT features to those reported with SARS [15, 16] and MERS [17, 18]; thus, it is difficult to distinguish COVID-19 pneumonia from them. Our findings were in accordance with the present studies [12, 19]. It is not surprising since the responsible viruses of SARS and MERS are also coronaviruses and viruses in the same viral family have similar pathogenesis.

However, there are interesting new findings. Firstly, the features on CT images of some patients may not be consistent with the results of RT-PCR tests. For example, two patients with a Wuhan exposure history who showed expected features on CT images had a negative result on the initial but not on a follow-up RT-PCR test. Therefore, when the result of the RT-PCR test is negative for a patient with CT features typical of viral pneumonia and history of potential exposure, the patient should be isolated, closely observed, and undergo further RT-PCR testing.

Besides, we occasionally found that the CT findings of some patients may not be consistent with their clinical symptoms. For example, three patients with mild clinical symptoms only showed pharyngeal discomfort but because one of their family members had been diagnosed with COVID-19 pneumonia, they underwent CT scans. Their CT images revealed multiples opacities to be present in the lungs, and subsequently, they also tested positive for SARS-CoV-2 on a RT-PCR test. In addition, some patients showed obvious improvements of symptoms after receiving treatment but the follow-up CT suggested there would have been a significant progression. Therefore, for some suspicious patients with mild clinical symptoms, CT examination is recommended for the detection of lesions, early diagnosis, and assessment of the disease progression. Moreover, follow-up CT scans should be performed for evaluating the efficacy of treatment during hospitalization.

Incidentally, we additionally found that COVID-19 pneumonia showed obvious characteristics of crowd aggregation, especially family aggregation in that sixteen patients who were members of just five families were all infected with SARS-CoV-2.

There are limitations to our study that should be noted. Firstly, the sample size is relatively small and the reported CT features of COVID-19 pneumonia should be considered preliminary rather than definitive. Secondly, follow-up CT scans were only obtained for 40 of the 55 patients and thus the full range of disease appearance may not be represented. Thirdly, the relatively small sample size may account for why no children are included in this study. Whether children may be less likely to become infected or, if infected, display milder symptoms is obviously an important question to be addressed in future studies.

In conclusion, the predominant finding on CT images obtained for patients with COVID-19 pneumonia is multiple ground-glass opacities with or without consolidation and, with both lungs, multiple lobes and especially the lower lobe affected. Although CT findings alone may not be sufficient for definitive diagnosis of COVID-19 pneumonia, in combination with epidemiological history, laboratory test results, and clinical symptoms, the diagnosis of COVID-19 pneumonia could potentially be made in newly referred cases.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Meiyun Wang.

Conflict of interest The authors of this manuscript declare no relationships with any companies.

Statistics and biometry No complex statistical methods were necessary for this paper.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap No similar study subjects or cohorts have been previously reported.

Methodology
- Retrospective
- Diagnostic or prognostic study
- Performed at multiple institutions

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