



Analyzing the Early CT findings and Clinical Features of 12 Patients with 2019 Novel Coronavirus Disease (COVID-19) in China

Xianwu Xia¹, Liang Sheng¹, Tiejun Yang¹, Guobing Zhang¹, Li Ding¹, Jianmin Shen^{1,*} and Jihong Feng^{2,**}

¹Department of Radiology, Municipal Hospital Affiliated to Medical School of Taizhou University, Zhejiang, Taizhou, China

²Department of Oncology, Municipal Hospital Affiliated to Medical School of Taizhou University, Zhejiang, Taizhou, China

*Corresponding author: Department of Radiology, Municipal Hospital Affiliated to Medical School of Taizhou University, 381-1 Middle Zhongshan Rd., Jiaojiang District, Taizhou, Zhejiang Province, 318000, China. Tel: +86-13905768989, Email: sjm_60@126.com

**Corresponding author: Department of Oncology, Municipal Hospital Affiliated to Medical School of Taizhou University, China 381-1 Middle Zhongshan Rd., Jiaojiang District, Taizhou, Zhejiang Province, 318000, China. Tel: +86-15157689870, Email: jh_f@163.com

Received 2020 April 06; Revised 2020 April 15; Accepted 2020 April 22.

Abstract

Background: Regarding the outbreak of highly contagious the 2019 Novel Coronavirus (2019-nCoV) in various countries and regions, data have been needed on the early chest CT images and clinical characteristics of the affected patients.

Objectives: To explore the early clinical and computed tomography (CT) characteristics of the 2019 Novel Coronavirus Disease (COVID-19) patients to improve the diagnostic level of this contagious respiratory disease.

Methods: An analysis retrospectively was implemented on the radiological features and clinical characteristics of 12 patients with COVID-19 who had undergone chest CT scanning in the designated hospital from Jan 23, 2020, to Feb 18, 2020. The clinical data on general information, epidemiological, cardinal symptoms, blood test, and CT imaging characteristics were obtained.

Results: According to the relevant diagnostic criteria, the patients were divided into two groups: mild (2 cases), and ordinary type (10 cases). The main symptoms of 2019-nCoV pneumonia were fever (9/12) and cough (8/12) with or without respiratory and other systemic symptoms. The blood test of the patients showed that most of the white blood cell count was normal (10/12), decreased lymphocyte count (6/12), and increased hypersensitive C reactive protein (hs-CRP) (5/12). In the early stage of COVID-19, the chest CT images showed patchy mixed ground-glass opacity (GGO) (8/12), mainly distributed in the periphery and posterior part of both lungs. The internal density of image lesion area was uneven, and lesions primarily manifested as “crazy-paving pattern” (8/12), with grid-like, interlobular septal thickening, thickened bronchovascular bundle and air bronchus sign and multiple fibrosis. A few cases showed pulmonary atelectasis (1/12), bilateral pleural effusion (1/12), no mediastinal or bilateral hilar lymph node enlargement.

Conclusions: The clinical characteristics of 2019-nCoV pneumonia are similar to those of common viral pneumonia. The chest CT images may be helpful for the early detection of novel coronavirus pneumonia.

Keywords: COVID-19, Pneumonia, Tomography, X-Ray Computed

1. Background

The initial cluster of severe pneumonia cases that triggered the COVID-19 epidemic was identified in Wuhan, China, in December 2019 (1, 2). As of Mar 28, 2020, a considerable number of confirmed cases of novel coronavirus infection are reported in the world's countries and regions, including 82,236 patients in China and 516,951 patients outside of China. Despite the extensive implementation of control measures, human-to-human transmission has driven the rapid spread of the virus throughout the world and result in the number of confirmed and suspected cases of COVID-19 has risen, in just the past few weeks, with extraordinary speed. The “2019 novel Coron-

avirus” (2019-nCoV) or SARS-CoV-2 formally named by the World Committee on Virus Classification. There has been evidence that SARS-CoV-2 is highly contagious, with an average incubation period of 5.2 days and a basic regeneration number (R0) of 3.77 at the initial stage of the epidemic (3). The SARS-CoV-2 is propagated primarily via close contact, and exhaled droplets, with the incubation period usually from 1 - 14 days, can cause the symptoms, including fever, dry cough, fatigue, dyspnea, and so on in the pathogenesis of different stages of patients with COVID-19. At present, although the diagnosis of COVID-19 still depends on nucleic acid detection (4), its sensitivity is low, and some cases found in the clinic need to be confirmed by multiplex nucleic acid testing (5). It is worth noting that these

patients who were later diagnosed had positive lesions in the early stage of the CT image. Although the CT characteristics of COVID-19 that have been reported in the literature (5-10), due to the lack of sufficient autopsy specimens and pathological comparison, the understanding of its early CT changes is still not comprehensive enough. Therefore, early identification of COVID-19 is very important to control the epidemic and spread of the disease.

2. Objectives

In order to further improve the understanding of the CT features of COVID-19, the clinical features and imaging findings of 12 cases of early novel coronavirus pneumonia diagnosed in our hospital were retrospectively analyzed. The purpose of this study was to assess the performance of the early chest CT in the diagnosis of patients with COVID-19 from viral pneumonia.

3. Methods

3.1. Patient Population

The Ethics Committee of the Municipal Hospital Affiliated to Medical School of Taizhou University waived the need for informed consent for this study. This study consisted of 12 patients with COVID-19 pneumonia who met the inclusion criteria. We retrospectively analyzed 12 patients confirmed infected by the novel coronavirus from Jan 20 to Feb 23, 2020. Laboratory findings of COVID-19 were confirmed in the first admission hospital and verified by the Taizhou Center for Disease Control and Prevention (CDC). The patients with COVID-19 were confirmed to be infected by a real-time polymerase chain reaction (RT-PCR). The COVID-19 respiratory samples were tested using novel coronavirus ORF1ab/N gene nucleic acid detection kit (batch number: P732200130, manufacturer: Suzhou Tianlong Biotechnology Co., Ltd.). Two of the trained researchers recorded clinical data, including date of onset of symptoms, laboratory examinations, and other information. The general data and clinical features included age, sex, history of epidemiological exposure, clinical symptoms, blood routine (five classifications), hypersensitive C-reactive protein, and history (Table 1).

3.2. CT Scanning Protocol

The American GE Optima 540 16-layer spiral CT scanner was used. The patients were scanned with supine position, advanced head, and breath-holding after inspiration. The scanning range was from the tip of the lung to the bottom of the lung. The scanning parameters were as follows: tube voltage 120 kV, tube current 300 mA, pitch 1.75 mm, matrix

512 × 512, slice thickness 5 mm, visual field 350 mm × 350 mm, axial reconstruction Bone Plus, slice thickness 1.250 mm. The CV of Ct value was less than 5%, and the detection limit was 500 copies/mL.

3.3. CT Viewing and Evaluation

All CT images were analyzed by two trained chest radiologists with 10 - 15 years of experience, in a consistent manner. In case of disagreement, it is meticulously examined and reached a decision in consensus by the chief physician of the cardiothoracic group.

Image analysis, focused on the lesion features of each patient, included location, distribution, size, shape, number, density, internal structure, margin, degree of lung involvement, remaining lung manifestations and extrapulmonary manifestations (e.g., lymph node enlargement of mediastinal and/or bilateral hilar, pleural effusion). The description standards of CT performance parameters are as follows: (1) The location of lesion: the periphery, the center, the periphery, and the center are affected at the same time; the anterior and the posterior were involved at the same time (on the transverse CT image, draw a horizontal line across the midline of the axilla, divided into the anterior part and the posterior part. The outer third of the lung is defined as the peripheral type, and the rest is identified as the central type). (2) Lesion distribution: single lung lobe, multiple lung lobes, double lung lobe, and lung lobe are divided into the left lung (upper lobe, lower lobe) and right lung (upper lobe, middle lobe, lower lobe). (3) Lesion size: the length of the largest lesion was < 1 cm, 1 - 3 cm, > 3 cm. (4) Lesion morphology: nodules, patches, pulmonary segments, lobes (nodules less than 3 cm in diameter). (5) The number of lesions: 1, 2, 3, and more were multiple. (6) Lesion density: ground-glass opacity (GGO), consolidation, mixed GGO and consolidation type (according to the standard of Fleischner Society (11): ground-glass opacity is a slightly high-density shadow with vascular shadow; consolidation is a high-density opaque shadow in the lung, covering blood vessels and trachea wall shadow; GGO and consolidation type has both ground-glass opacity and solid components). (7) Internal structure: cavity, reticular, interlobular septal thickening, bronchial air sign, calcification, and internal vascular changes. (8) Edge of lesion: clear and blurred. (9) There are potential lung diseases such as emphysema or fibrosis. (10) Enlargement of lymph nodes: yes or no (enlargement of lymph nodes was defined as short diameter of supraaxial lymph nodes > 1cm). (11) Pleural effusion: yes or no. (12) CT's method for evaluating the degree of pulmonary involvement (12): both lungs were divided into 20 segments, 10 in the right lung and 10 in the left lung (Two segments in the posterior segment of the tip

Table 1. General Data and Clinical Features of 12 Newly Treated Patients with COVID-19 Pneumonia

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12
Epidemic history	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Incubation period	15	6	2	8	Not clear	8	Not clear	Not clear	4	11	11	22
Gender	Female	Female	Male	Female	Male	Male	Female	Female	Male	Female	Male	Female
Age	24	45	75	19	32	70	67	68	28	78	80	39
Symptom time (d)	/	3	4	1	3	1	1	1	3	1	2	4
Temperature([U+2103])	Normal	38.3	38.4	37.9	38.2	37.7	39.5	37.5	38.4	37.9	Normal	37.5
Cough	None	Yes	Yes	Yes	Yes	None	None	Yes	None	Yes	Yes	Yes
Expectoration	None	None	None	None	Yes	None	None	None	None	None	None	None
Sore throat	None	None	Yes	None	None	Yes	None	None	None	None	None	None
Nausea, vomiting	None	None	None	None	None	None	None	None	None	None	None	Yes
Diarrhea	None	None	None	None	None	Yes	None	None	None	None	None	None
Chest tightness	None	None	None	None	None	None	None	None	None	None	None	Yes
fatigue	None	None	None	None	None	None	None	None	Yes	None	Yes	Yes
OD	None	None	PPA	None	AIDS	None	None	HBP	None	HBP	HBP	PT

Abbreviations: AIDS; acquired immune deficiency syndrome; HBP, high blood pressure; OD, other diseases; PPA, postoperative pituitary adenoma; PT, postoperative teratoma.

of the upper lobe of the left lung, two segments in the superior and inferior lingual segment of the left lobe, and two segments in the anterior basal segment of the lower lobe of the left lung). If more than half of the lung segment with the largest lesion area on the axial thin slice CT is involved, the lung segment is recorded as one point, and if the lung segment is involved and the part is not more than half, it is recorded as 0.5 point. The scores were mild: 0-6, medium: 7-12, heavy: > 12.

4. Results

4.1. Clinical Characteristics

A total of 12 patients with COVID-19 pneumonia were entered into the study, including five males (41.7%) and seven females (58.5%), aged from 19 to 80 years old, with an average of 38 years old. The general data, main clinical symptoms of 12 patients with COVID-19 are shown in Table 1. In 9 cases with definite contact history and contact time, the median incubation period was eight days (2 - 22 days). The contact time cannot be determined in 3 cases. There was no clinical symptom in one case (fever occurred 2 days later). There were 11 cases with clinical symptoms, nine cases with fever (75.0%), eight cases with cough (66.7%), three cases with fatigue (25.0%), and 1 case with other symptoms such as expectoration, sore throat, chest tightness, abdominal pain, diarrhea, nausea and vomiting (8.3%). The laboratory findings of 12 patients with COVID-19 are shown in Table 2. Routine blood tests were performed for 12 patients. Laboratory results showed that white blood cells were normal in 10 cases (83.3%), increased in one case (8.3%), slightly decreased in one case (8.3%), neutrophil percentage was normal in 11 cases (91.7%), lymphocyte percentage decreased in four cases (33.3%), the absolute number

of lymphocytes decreased in six cases (50.0%), hypersensitive C-reactive protein increased in five cases (41.7%). All patients were diagnosed with a positive nucleic acid test at least two times. According to COVID-19's diagnosis and treatment plan (trial version 6) (4) clinical classification criteria, two cases of 12 patients with COVID-19 were mild (16.7%), and 10 cases were ordinary type (83.3%).

4.2. CT Findings of COVID-19 Pneumonia

The early features of chest CT of 11 patients with COVID-19 pneumonia are shown in Table 3. Among the 12 patients with COVID-19, 11 patients underwent chest CT within 1 - 4 days after the onset of clinical symptoms, and only one asymptomatic patient, which have been received chest CT scanning, developed a fever 2 days later. Chest X-ray was performed in 3 of 12 patients with COVID-19, and the examination showed that there were negative in all 3 cases. Among the 12 cases, 1 case had a normal chest CT (GGO appeared in both lungs of CT 2 days later). The early CT features of 11 patients with COVID-19 are shown in Table 2. In the early stage, the shape of chest CT could be nodular (1, 9.1%) (Figure 1), patchy (10, 90.9%) (Figure 2), mainly subpleural and posterior of the periphery of the lung (8, 72.7%) (Figure 3), and involving both lungs more frequently (7, 63.6%). The density is mainly mixed ground-glass opacity (8, 72.7%) (Figure 2), followed by pure ground-glass opacity (2, 18.2%) (Figure 4) and solid shadow (1, 9.1%) (Figure 4). Most of the inner density was uneven, manifested as "crazy-paving pattern" (8, 72.7%), with grid changes (7, 63.6%) (Figure 2), interlobular septal thickening (8, 72.7%) and air bronchial sign (7, 63.6%) (Figure 5). Bronchovascular bundle thickening (8, 72.7%) (Figure 2) and fibrosis (8, 72.7%) (Figure 4). Segmental atelectasis occurred in 1 case (9.1%) (Figure 2). 1 case (9.1%) had a small amount of pleural

Table 2. Laboratory Findings of 12 Newly Treated Patients with COVID-19 Pneumonia^a

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12
WBC	Normal	Normal	Normal	11.7	Normal	Normal	3.31	Normal	Normal	Normal	Normal	Normal
NEUTP	Normal	Normal	Normal	81.7	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
LYMPHP	Normal	18.3	10.3	14.5	Normal	Normal	Normal	Normal	Normal	Normal	15.8	Normal
LYMPHN	Normal	1.07	0.78	Normal	1.04	Normal	0.87	Normal	1.03	1.03	Normal	Normal
CRP	Normal	Normal	98.3	Normal	Normal	70.72	18.87	27.01	Normal	Normal	11.47	[U+65E0]
NAD	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive	Positive

Abbreviations: CRP, hypersensitive C-reactive protein; LYMPHN, lymphocyte number; LYMPHP, lymphocyte percentage; NAD, nucleic acid detection; NEUTP, neutrophil percentage; WBC, white blood cell.
^aTest normal reference value: WBC: 3.5 ~ 9.5 × 10⁹/L; NEUTP: 40 ~ 75%; LYMPHP: 20% ~ 50%; LYMPHP/N 11 ~ 3.2 × 10⁹/L; CRP: 0 ~ 8mg/L

effusion. There were no cavities, calcification, enlargement of mediastinal, and hilar lymph nodes.

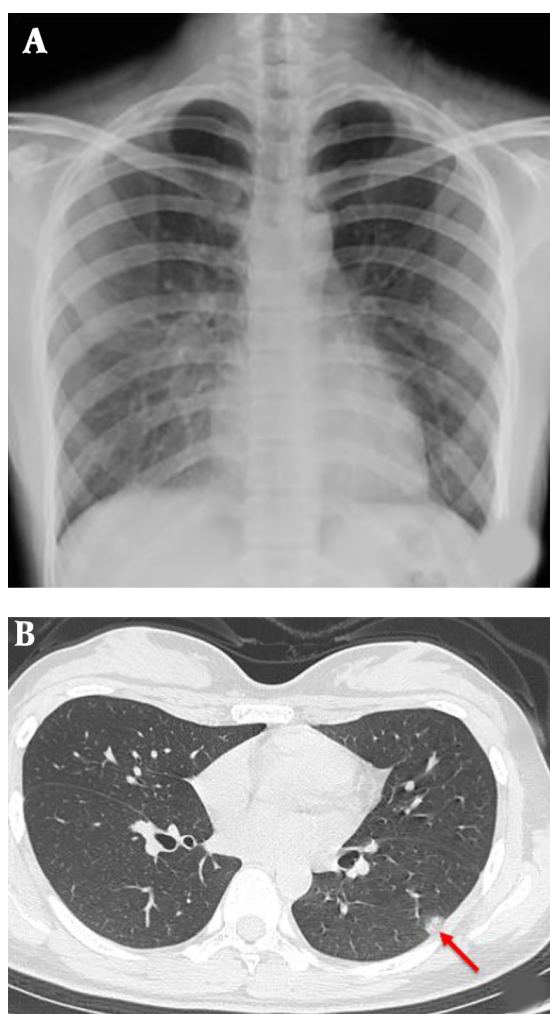


Figure 1. Female, 24 years old, come from Wuhan city, without clinical symptoms (have a fever after 2 days). No obvious abnormality was found in chest X-ray (A). Solid nodule of the left lower lobe with halo sign in chest CT (B). (window level-600, window width-1600).

5. Discussion

At present, the epidemic of COVID-19 is currently affecting multiple countries and may cause feelings of fear and helplessness. Once the medical resources run out, the mortality rate will increase rapidly. At present, confirmed cases in European and American countries present a comprehensive outbreak of the situation, the World Health Organization (WHO) has characterized coronavirus as a global pandemic, calling on each country to take urgent and active action. However, there is no specific drug treatment or vaccine for COVID-19 pneumonia. In light of the urgent clinical demand, early detection, early isolation, and early treatment are very necessary. According to the latest guidelines for diagnosis and treatment issued by the Chinese government (4), the diagnosis of COVID-19 pneumonia could be confirmed by RT-PCR or gene sequencing. However, this detection method lacks sufficient sensitivity, good stability, and relatively long processing time is conducive to the control of the disease epidemic. It is reported (13) that the total RT-PCR positive rate of pharyngeal swab samples is about 30% to 60%. In addition, there are several defects in RT-PCR detection, such as limited sample collection and transportation, inconsistent performance of the kit, and so on. In the current emergency, the low sensitivity of RT-PCR means that a certain amount of patients with COVID-19 may not be confirmed and, therefore, unable to isolate and receive appropriate treatment in a timely manner. Because of the highly contagious nature of the virus, these patients pose a high risk of infecting more people. Reports also showed that chest CT present pulmonary abnormalities in patients with COVID-19 with clinical symptoms and negative RT-PCR results (14, 15). AI et al. (16) compared chest CT results of 1,014 patients with suspected COVID-19 with the initial and series of RT-PCR results and found that chest CT is more sensitive than RT-PCR in the diagnosis of COVID-19. Therefore, in the current outbreak phase, chest CT imaging may be a more practical and rapid method to diagnose and evaluate COVID-19.

Novel coronavirus (SARS-CoV-2) is highly contagious and easy to spread from person to person (1, 3). COVID-19

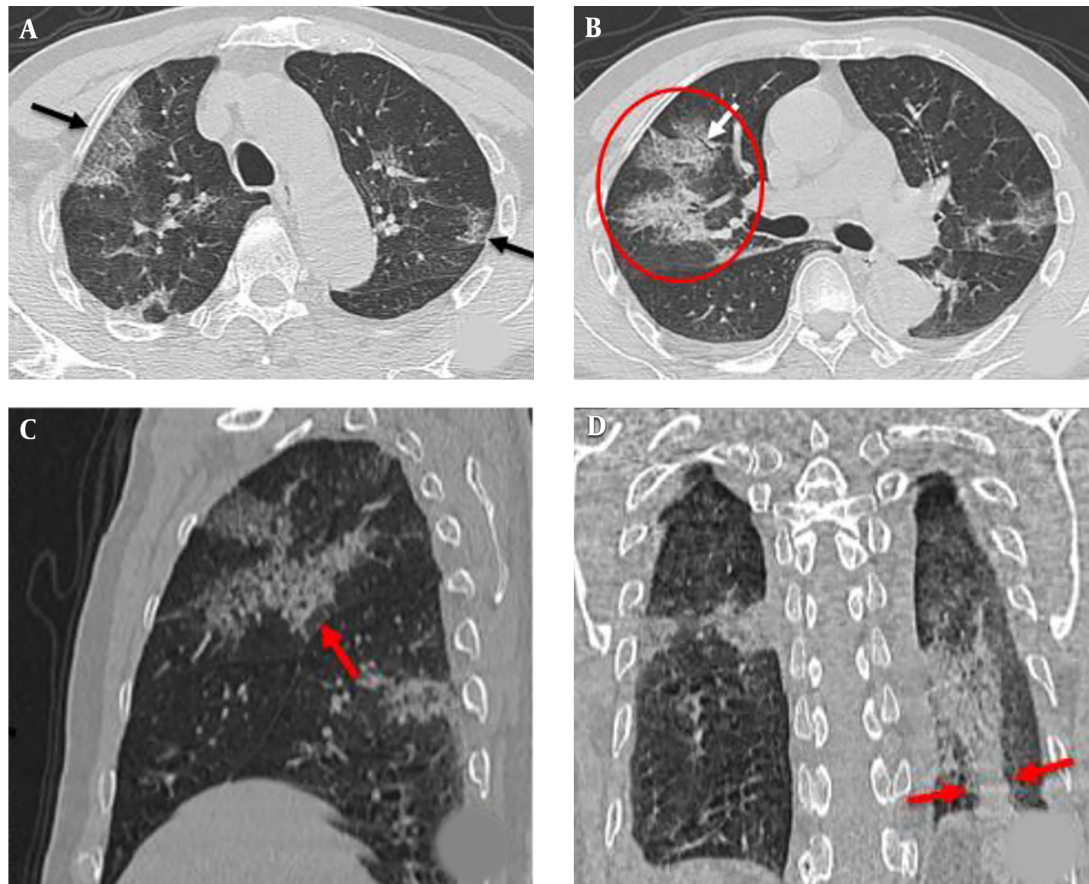


Figure 2. Male, 75 years old, contacted with patients with COVID-19 six days ago and had a fever for four days. Chest CT showed patchy mixed GGO, scattered under the pleura and presented interlobular septal thickening (black arrow) (A), bronchiectasis (white arrow) (B) in transverse images, and in sagittal position (C), vascular thickening and segmental atelectasis (red arrow) in coronal images (D). (CT image window level-600, window width-1600).

is common in adults and rare in children (17). In this study, 12 patients with COVID-19 pneumonia are all adults with a history of epidemiological contact, so it is very important to inquire about the history of epidemiology in fever clinics of medical institutions outside the epidemic area. Li et al. (3) found that the incubation period of COVID-19 was 5.5 d (4.1 - 7.0 d). This study found that the median incubation period was 8 d (2 - 22 d). Therefore, epidemic contacts need to be observed in isolation for 14 days (4). At present, it is reported in the literature (1, 10) that the vast majority of patients with COVID-19 have respiratory symptoms such as fever, cough, diarrhea, and vomiting are rare. In this study, the symptoms of 12 patients with COVID-19 at the onset of illness were fever (81.8%) and cough (54.5%), a few fatigues occurred in 3 cases (25.0%), and some patients had symptoms such as expectoration, pharyngalgia, chest tightness, abdominal pain, diarrhea, nausea and vomiting (1 case, 8.3% each), which was consistent with the lit-

erature report. Laboratory examination showed that most of the white blood cells were normal (81.8%), the absolute number of lymphocytes decreased slightly (54.5%), and hypersensitive C-reactive protein could be increased (45.5%). These clinical features are similar to those of SARS-CoV and MERS-CoV infection (10, 18, 19). For the patients with epidemiological history and these clinical features, we should be vigilant and carry out chest CT examination and nucleic acid detection in time.

Chest X-ray in patients with early COVID-19 may be negative or show only a little patchy increased density (20). In this study, it was found that the chest X-ray examination of 3 patients was negative, and the lesions were found by further examination of CT. It is suggested that an ordinary chest X-ray may lead to the omission of early lesions. Therefore, chest CT screening is recommended for patients with fever, especially those with a history of epidemiology.

The main features of pulmonary CT in patients with

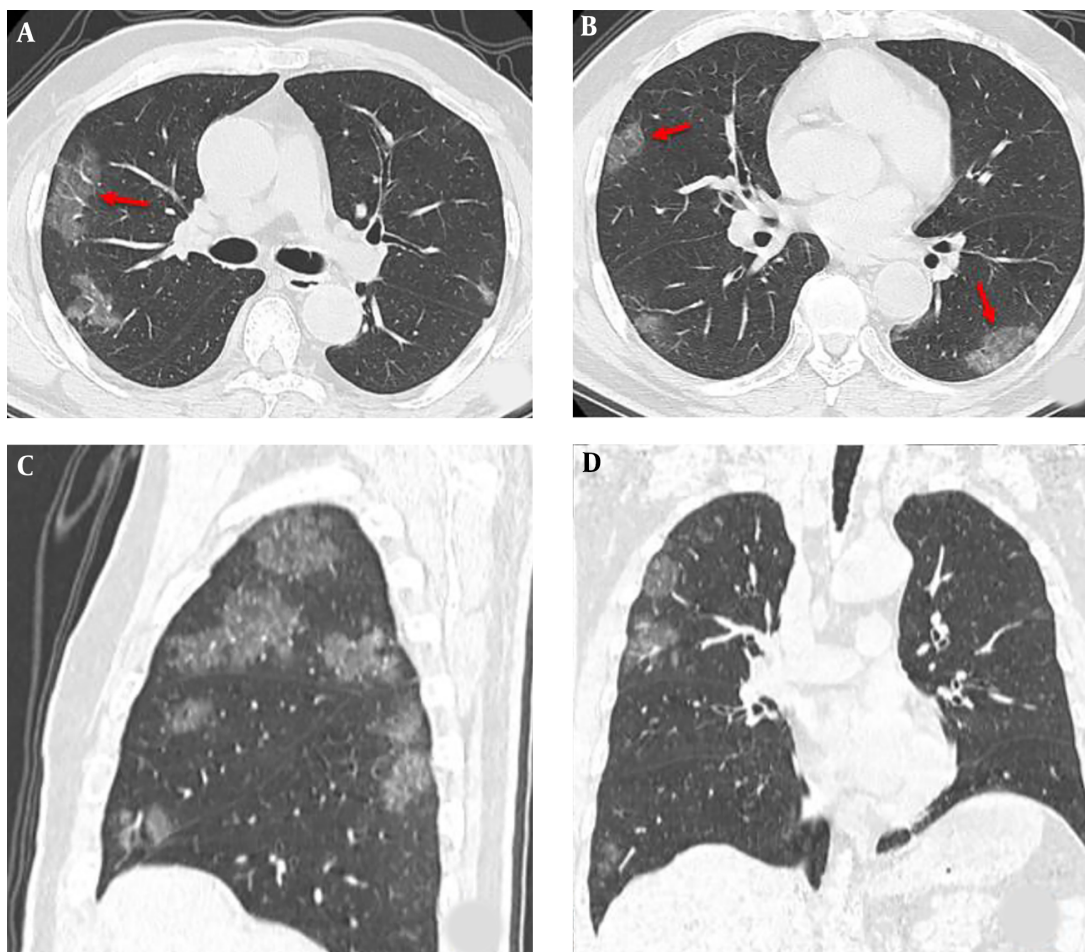


Figure 3. Male, 70 years old, contacted with patients with COVID-19 nine days ago and had a fever for one day. Patchy ground-glass opacity was scattered under the pleura of both lungs, showing fireworks-like changes, and vascular shadows were seen in transverse images (A and B) or sagittal position (C) or coronal images (D). (window level-600, window width-1600).

early COVID-19 were nodular and patchy consolidation shadow, pure ground-glass opacity and mixed ground-glass opacity, most of which were multiple lesions, which were usually distributed around the bronchovascular bundles of both lungs and/or under the pleura (6, 8, 21-25). In this study, 11 cases of early COVID-19 pneumonia showed patchy mixed ground-glass opacity at the periphery and posterior part of the lung on CT. Most of the inner density was uneven, manifested as “crazy-paving pattern” (72.7%), with grid changes (63.6%), interlobular septal thickening (72.7%), and air bronchial sign (63.6%), bronchovascular bundle thickening (72.7%), and fibrosis (72.7%). Yan et al. (26) found that the S protein of coronavirus binds to human ACE2 to replicate, and the ACE2 receptor mainly exists in alveolar epithelial cells. Hence, the CT imaging findings of patients with COVID-19 are mainly alveolar exudation

ground-glass opacity. Tian et al. (27) reported that the early pathological changes of SARS-CoV-2 pneumonia found in two cases of lung tumor resection were interstitial lymphocyte infiltration, alveolar type II epithelial injury, pulmonary edema, and non-protruding hyaline membrane. On the other hand, Xu et al. (28) postmortem pathology showed diffuse alveolar injury, formation of transparent membrane, exfoliation of the alveolar epithelium, exudation of the alveolar cavity and scattered monocytes, dilatation of small blood vessels, and transparent membrane, which may be the pathological basis of the white lung on CT in advanced patients. These two studies found pathological changes at different stages of COVID-19 pneumonia. Referring to the previous SARS pneumonia report (29), we believe that ground-glass opacity may be caused by alveolar wall injury and alveolar serous inflammatory exuda-

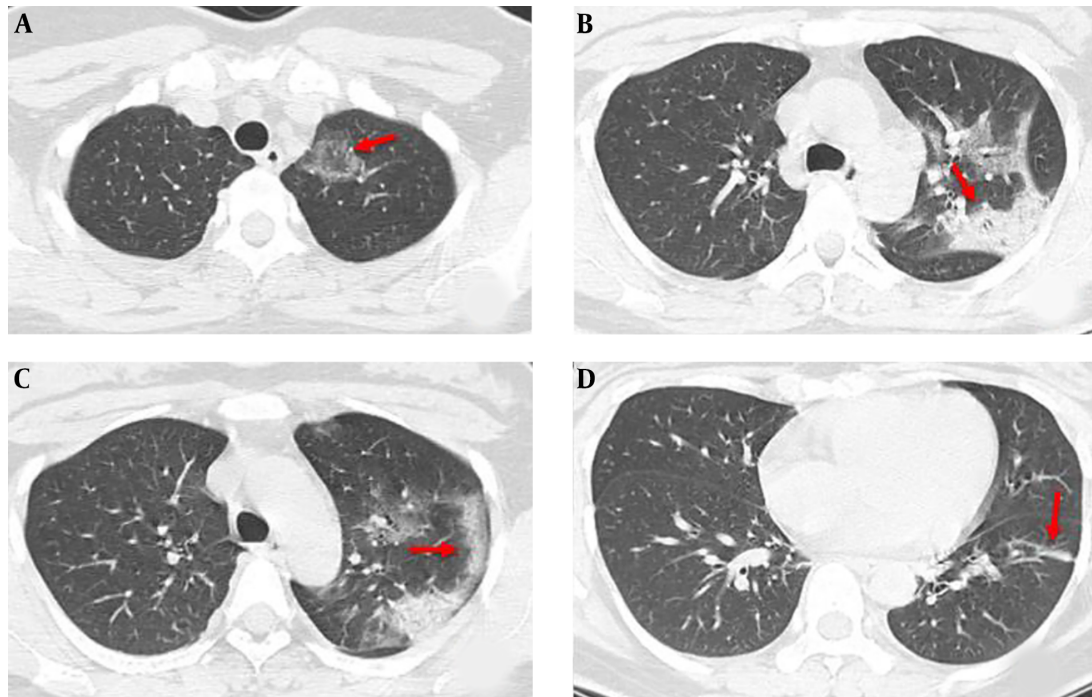


Figure 4. Female, 67 years old, came from Wuhan city, close contact time is not clear, have a fever for one day. There is a patchy ground-glass shadow in the upper lobe of the left lung, showing an anti-halo sign (A). The lesion showed consolidation of the lung (B). Subpleural mixed ground-glass opacity, interlobular septum thickening, with "crazy-paving pattern" (C). Left lower lobe fibrous cord shadow (red arrow) (D). (all CT images window level-600 and window width-1600).

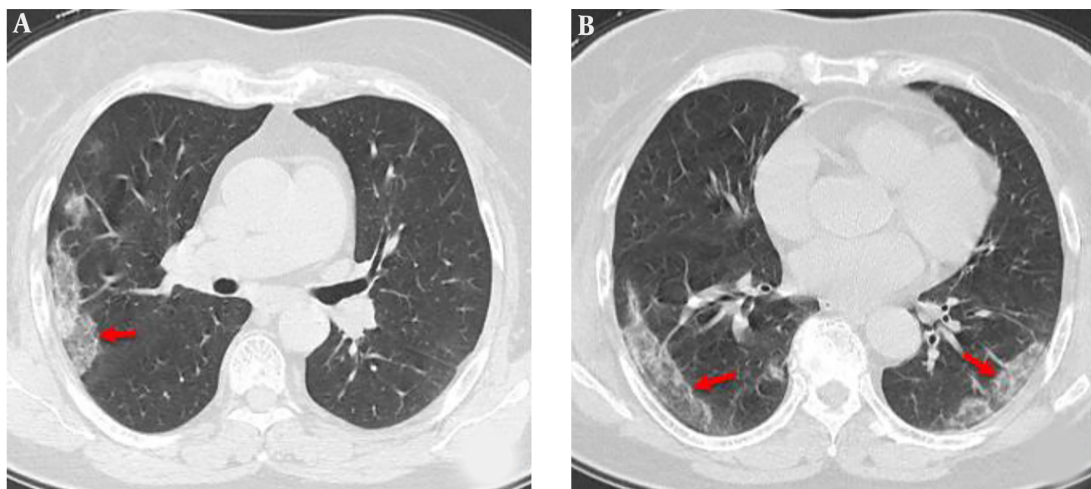


Figure 5. Female, 68 years old, come from Wuhan, close contact time is not clear, fever for one day. Both lungs scattered under the pleura mixed ground-glass opacity, interlobular septum thickening, with "crazy-paving pattern" (A and B). (window level-600 and window width-1600 in all CT images).

tion, followed by interstitial inflammation leading to interlobular septal thickening and "crazy-paving pattern," and increased alveolar inflammatory exudation in the center of the lesion leads to consolidation. Tian et al. (27) believe that the pathological characteristics of COVID-19

are very similar to SARS and MERS coronavirus infection. According to the similarity between SARS-CoV-2 virus and SARS coronavirus as high as 85%, we speculate that the CT performance of COVID-19 is similar to that of SARS.

A study by Pan et al. (7) showed that the initial chest

Table 3. Early Features of Chest CT of 12 Patients with COVID-19 Pneumonia

Characteristics	All, No. (%)
Location	
BL	7 (63.6)
LLLL	1 (9.1)
LLRL	1 (9.1)
ULLLL	1 (9.1)
LLBL	1 (9.1)
Distribution	
Rear periphery	8 (72.7)
Scattered	3 (27.3)
Number	
Single	1 (9.1)
Two	2 (18.2)
Multiple	7 (63.6)
Long diameter, cm	
< 1	1 (9.1)
1-3	2 (18.2)
> 3	8 (72.7)
Shape	
Nodular	1 (9.1)
Patchy	10 (90.9)
Density	
pGGO	2 (18.2)
Solid	1 (9.1)
mGGO	8 (72.7)
Grid shape	
IST	8 (72.7)
ABS	7 (63.6)
BBT	8 (72.7)
Fibrosis	8 (72.7)
Margin	
Well-defined	6 (54.5)
Ill-defined	5 (45.5)
DLI	
Mild	10 (90.9)
Moderate	1 (9.1)
Severe	0
Atelectasis	1 (9.1)
Cavity	0
Calcification	0
Emphysema	0
ELN	0
Pleural effusion	1 (9.1)

Abbreviations: ABS, air bronchial sign; BBT, bronchovascular bundle thickening; BL, bilateral lungs; DLI, degree of lung involvement; ELN, enlarged lymph nodes; IST, interlobular septal thickening; LLBL, the lower lobe of bilateral lung; LLLL, lower lobe of the left lung; LLRL, the lower lobe of right lung; mGGO, mixed ground-glass opacity; pGGO, pure ground-glass opacity; ULLLL, the upper and lower lobe of the left lung

CT of patients with COVID-19 pneumonia revealed a small ground-glass opacity under the pleura, and then gradually became solid and enlarged, and a “crazy-paving pattern”

appeared. Jiang et al. (23) also reported that 17 cases of sub-clinical CT were characterized by small ground-glass nodules or ground-glass opacity along the subpleural and/or bronchovascular bundles, without solid nodules. In this study, it was found that the early chest CT of one patient with COVID-19 showed left lower lobe nodule shadow with peripheral halo sign. Wu et al. (22) also reported a patient with a fever for two days. Multiple nodules with halo sign in both lungs were found on CT for the first time. Re-examination of CT on the 8th and 11th day showed that the nodule density decreased and gradually changed to ground-glass opacity. We believe that the early appearance of nodules with halo sign may be one of the earliest imaging findings in some patients with COVID-19 pneumonia. Yang et al. (30) study on the CT manifestations of 8 cluster cases of imported COVID-19 found that the chest CT images of these patients were various, but absorbed quickly, suggesting that the clinical symptoms and CT manifestations of overseas imported cases are more concealed and complex, so it is necessary to be vigilant and avoid misdiagnosis.

It has been reported in the literature (6, 23) that small ground-glass nodules or ground-glass shadow may appear in chest CT in patients with COVID-19 without clinical symptoms. In this study, an asymptomatic patient was found, and a nodular shadow of the left lower lobe was found on chest CT, which was consistent with the literature. Therefore, our study displays that lung manifestations can be earlier than clinical symptoms, and the chest CT plays an important role in early detection, timely prevention, and control in these patients with COVID-19.

A few COVID-19 patients with positive nucleic acid tests showed no obvious abnormality in early CT (6, 7, 9, 10). In this group, one patient with fever and other clinical symptoms had normal CT examination, and CT showed ground-glass opacity in both lungs 2 days later, which indicated that the lung manifestation could be later than the clinical symptoms. In two COVID-19 patients reported by Tian et al. (27), no abnormality was found in CT examination before the operation. Still, postoperative pathology showed edema, protein exudation, only a small amount of inflammatory cell infiltration, focal multinucleated giant cell formation, and ground-glass shadow in CT, which was similar to that in this case. On the basis of these considerations, we think that inflammatory reaction has been found in this part of COVID-19 patients, but chest CT has not been shown yet.

It is worth mentioning that there are two important limitations to the study. Firstly, due to the short course of the disease with COVID-19 pneumonia, continuous variations of chest CT during its entire course have not been completely followed and recorded for all patients. Much

more importantly, there is not adequate pathologic data on these patients for comparative research to be implemented.

In conclusion, the clinical characteristics of 2019-nCoV pneumonia are similar to those of common viral pneumonia. The chest CT findings of early COVID-19 showed characteristic features, with nodular shadow or ground-glass opacity along the subpleural or/and along with the bronchovascular bundle. The chest CT images may be helpful for the early detection of novel coronavirus pneumonia.

Footnotes

Authors' Contribution: Study concept and design: Xianwu Xia, Liang Sheng, Jihong Feng and Jianmin Shen; acquisition of data: Guobing Zhang, Li Ding; analysis and interpretation of data: Xianwu Xia, Liang Sheng, Tiejun Yang; drafting of the manuscript: Xianwu Xia, Jihong Feng; critical revision of the manuscript for important intellectual content: Xianwu Xia, Jihong Feng, Jianmin Shen; statistical analysis: Xianwu Xia, Jihong Feng.

Conflict of Interests: The authors have no conflict of interest.

Ethical Approval: The Ethics Committee of the Municipal Hospital Affiliated to Medical School of Taizhou University waived the need for informed consent for this retrospective study.

Funding/Support: This work was supported by projects from the key disciplines of medicine in Taizhou (2019-2022), the National Natural Science Foundation of China (81560407) and Natural Science Foundation of Zhejiang Province (Y20H160211).

Informed Consent: Since this was a retrospective study and MRI images were obtained for diagnostic reasons before the beginning of the study and not for research purposes, informed consent was waived by the Institutional Ethics Committee. No harm (neither to the fetus nor to the mother) or extra charges was made to the subjects during the reviewing MR images.

References

- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;**395**(10223):497-506. doi: [10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5). [PubMed: [31986264](https://pubmed.ncbi.nlm.nih.gov/31986264/)]. [PubMed Central: [PMC7159299](https://pubmed.ncbi.nlm.nih.gov/PMC7159299/)].
- Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. 2020;**395**(10223):514-23. doi: [10.1016/S0140-6736\(20\)30154-9](https://doi.org/10.1016/S0140-6736(20)30154-9). [PubMed: [31986261](https://pubmed.ncbi.nlm.nih.gov/31986261/)]. [PubMed Central: [PMC7159286](https://pubmed.ncbi.nlm.nih.gov/PMC7159286/)].
- Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med*. 2020;**382**(13):1199-207. doi: [10.1056/NEJMoa2001316](https://doi.org/10.1056/NEJMoa2001316). [PubMed: [31995857](https://pubmed.ncbi.nlm.nih.gov/31995857/)]. [PubMed Central: [PMC7121484](https://pubmed.ncbi.nlm.nih.gov/PMC7121484/)].
- General Office of National Health Commission. *Notice on the issuance of a programme for the diagnosis and treatment of novel coronavirus (2019-nCoV) infected pneumonia (trial sixth edition)*. 2020. Available from: <http://www.nhc.gov.cn/xcs/zhengcwj/202002/8334a8326dd94d329df351d7da8aefc2.shtml>.
- Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. *Radiology*. 2020;200432. doi: [10.1148/radiol.2020200432](https://doi.org/10.1148/radiol.2020200432). [PubMed: [32073353](https://pubmed.ncbi.nlm.nih.gov/32073353/)].
- Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). *Radiology*. 2020;**295**(1):202-7. doi: [10.1148/radiol.2020200230](https://doi.org/10.1148/radiol.2020200230). [PubMed: [32017661](https://pubmed.ncbi.nlm.nih.gov/32017661/)].
- Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. *Radiology*. 2020;200370. doi: [10.1148/radiol.2020200370](https://doi.org/10.1148/radiol.2020200370). [PubMed: [32053470](https://pubmed.ncbi.nlm.nih.gov/32053470/)].
- Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging 2019 Novel Coronavirus (2019-nCoV) Pneumonia. *Radiology*. 2020;**295**(1):210-7. doi: [10.1148/radiol.2020200274](https://doi.org/10.1148/radiol.2020200274). [PubMed: [32027573](https://pubmed.ncbi.nlm.nih.gov/32027573/)].
- Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection. *Radiology*. 2020;200463. doi: [10.1148/radiol.2020200463](https://doi.org/10.1148/radiol.2020200463). [PubMed: [32077789](https://pubmed.ncbi.nlm.nih.gov/32077789/)].
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020. doi: [10.1056/NEJMoa2002032](https://doi.org/10.1056/NEJMoa2002032). [PubMed: [32109013](https://pubmed.ncbi.nlm.nih.gov/32109013/)]. [PubMed Central: [PMC7092819](https://pubmed.ncbi.nlm.nih.gov/PMC7092819/)].
- Hansell DM, Bankier AA, MacMahon H, McLoud TC, Muller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. *Radiology*. 2008;**246**(3):697-722. doi: [10.1148/radiol.2462070712](https://doi.org/10.1148/radiol.2462070712). [PubMed: [18195376](https://pubmed.ncbi.nlm.nih.gov/18195376/)].
- Wu X, Dong D, Ma D. Thin-Section Computed Tomography Manifestations During Convalescence and Long-Term Follow-Up of Patients with Severe Acute Respiratory Syndrome (SARS). *Med Sci Monit*. 2016;**22**:2793-9. doi: [10.12659/msm.896985](https://doi.org/10.12659/msm.896985). [PubMed: [27501327](https://pubmed.ncbi.nlm.nih.gov/27501327/)]. [PubMed Central: [PMC4982531](https://pubmed.ncbi.nlm.nih.gov/PMC4982531/)].
- Yang Y, Yang M, Shen C, Wang F, Yuan J, Li J, et al. Evaluating the accuracy of different respiratory specimens in the laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. *medRxiv*. 2020. doi: [10.1101/2020.02.11.20021493](https://doi.org/10.1101/2020.02.11.20021493).
- Huang P, Liu T, Huang L, Liu H, Lei M, Xu W, et al. Use of Chest CT in Combination with Negative RT-PCR Assay for the 2019 Novel Coronavirus but High Clinical Suspicion. *Radiology*. 2020;**295**(1):22-3. doi: [10.1148/radiol.2020200330](https://doi.org/10.1148/radiol.2020200330). [PubMed: [32049600](https://pubmed.ncbi.nlm.nih.gov/32049600/)].
- Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. *Radiology*. 2020;200343. doi: [10.1148/radiol.2020200343](https://doi.org/10.1148/radiol.2020200343). [PubMed: [32049601](https://pubmed.ncbi.nlm.nih.gov/32049601/)].
- Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology*. 2020;200642. doi: [10.1148/radiol.2020200642](https://doi.org/10.1148/radiol.2020200642). [PubMed: [32101510](https://pubmed.ncbi.nlm.nih.gov/32101510/)].
- Munster VJ, Koopmans M, van Doremalen N, van Riel D, de Wit E. A Novel Coronavirus Emerging in China - Key Questions for Impact Assessment. *N Engl J Med*. 2020;**382**(8):692-4. doi: [10.1056/NEJMp2000929](https://doi.org/10.1056/NEJMp2000929). [PubMed: [31978293](https://pubmed.ncbi.nlm.nih.gov/31978293/)].
- Lee N, Hui D, Wu A, Chan P, Cameron P, Joynt GM, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med*. 2003;**348**(20):1986-94. doi: [10.1056/NEJMoa030685](https://doi.org/10.1056/NEJMoa030685). [PubMed: [12682352](https://pubmed.ncbi.nlm.nih.gov/12682352/)].
- Assiri A, Al-Tawfiq JA, Al-Rabeeh AA, Al-Rabiah FA, Al-Hajjar S, Al-Barrak A, et al. Epidemiological, demographic, and clinical characteristics of 47 cases of Middle East respiratory syndrome coronavirus disease

- from Saudi Arabia: a descriptive study. *Lancet Infect Dis.* 2013;**13**(9):752-61. doi: [10.1016/S1473-3099\(13\)70204-4](https://doi.org/10.1016/S1473-3099(13)70204-4). [PubMed: [23891402](https://pubmed.ncbi.nlm.nih.gov/23891402/)].
20. Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, et al. First Case of 2019 Novel Coronavirus in the United States. *N Engl J Med.* 2020;**382**(10):929-36. doi: [10.1056/NEJMoa2001191](https://doi.org/10.1056/NEJMoa2001191). [PubMed: [32004427](https://pubmed.ncbi.nlm.nih.gov/32004427/)]. [PubMed Central: [PMC7092802](https://pubmed.ncbi.nlm.nih.gov/PMC7092802/)].
 21. Li X, Zeng X, Liu B, Yu Y. COVID-19 Infection Presenting with CT Halo Sign. *Radiology: Cardiothoracic Imaging.* 2020;**2**(1). e200026. doi: [10.1148/ryct.2020200026](https://doi.org/10.1148/ryct.2020200026).
 22. Wu Y, Xie Y, Wang X. Longitudinal CT Findings in COVID-19 Pneumonia: Case Presenting Organizing Pneumonia Pattern. *Radiology: Cardiothoracic Imaging.* 2020;**2**(1). e200031. doi: [10.1148/ryct.2020200031](https://doi.org/10.1148/ryct.2020200031).
 23. Jiang N, Zheng C, Fan Y, Han X, Chen Y, Cheng Q, et al. CT appearance of new coronavirus pneumonia in subclinical period and short-term changes. *Chin J Radiol.* 2020;**54**. doi: [10.3760/cma.j.cn112149-20200306-00333](https://doi.org/10.3760/cma.j.cn112149-20200306-00333).
 24. Liu H, Zhang D, Yang Y, Long B, Yin L, Zhao M, et al. Analysis of early chest high resolution CT images of novel coronavirus pneumonia. *Chin J Radiol.* 2020;**54**. doi: [10.3760/cma.j.issn.1005-1201.2020.0007](https://doi.org/10.3760/cma.j.issn.1005-1201.2020.0007).
 25. Lu X, Gong W, Wang L, Li L, Xie B, Peng Z, et al. Clinical features and high resolution CT imaging findings of preliminary diagnosis novel coronavirus pneumonia. *Chin J Radiol.* 2020;**54**. doi: [10.3760/cma.j.issn.1005-1201.2020.0006](https://doi.org/10.3760/cma.j.issn.1005-1201.2020.0006).
 26. Yan R, Zhang Y, Guo Y, Xia L, Zhou Q. Structure of dimeric full-length human ACE2 in complex with B0AT1. *bioRxiv.* 2020. doi: [10.1101/2020.02.19.956946](https://doi.org/10.1101/2020.02.19.956946).
 27. Tian S, Hu W, Niu L, Liu H, Xu H, Xiao S. Pulmonary Pathology of Early Phase SARS-COV-2 Pneumonia. *Preprints.* 2020. doi: [10.20944/preprints202002.0220.v1](https://doi.org/10.20944/preprints202002.0220.v1).
 28. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med.* 2020;**8**(4):420-2. doi: [10.1016/S2213-2600\(20\)30076-X](https://doi.org/10.1016/S2213-2600(20)30076-X). [PubMed: [32085846](https://pubmed.ncbi.nlm.nih.gov/32085846/)]. [PubMed Central: [PMC7164771](https://pubmed.ncbi.nlm.nih.gov/PMC7164771/)].
 29. Ooi GC, Khong PL, Muller NL, Yiu WC, Zhou LJ, Ho JC, et al. Severe acute respiratory syndrome: temporal lung changes at thin-section CT in 30 patients. *Radiology.* 2004;**230**(3):836-44. doi: [10.1148/radiol.2303030853](https://doi.org/10.1148/radiol.2303030853). [PubMed: [14990845](https://pubmed.ncbi.nlm.nih.gov/14990845/)].
 30. Yang WB, Weng QY, Xiao YR, Lin J, Zhang YP, Ji JS. CT features and clinical characteristics of 8 cluster cases of imported COVID-19. *Chin J Radiol.* 2020;**54**. doi: [10.3760/cma.j.cn112149-20200306-00333](https://doi.org/10.3760/cma.j.cn112149-20200306-00333).