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Research Article

Follow-up study of clinical and chest CT scans in confirmed COVID-19 patients

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Abstract

Objective: To analyze the CT imaging results of patients with COVID-19 who previously received several follow-up visits and to explain the changes in pulmonary inflammation.
Methods: Cases of 15 patients with COVID-19 were retrospectively analyzed: their epidemiology, clinical history, laboratory tests, and multiple CT chest scans obtained during the disease period were studied.
Results: The CT scans of the 15 patients showed different results. Four patients had no abnormal findings in their chest CT scans. The first scan of 1 patient revealed right lower lobe inflammation, while the lesion had been completely absorbed in follow-up. Two patients showed bilateral pulmonary inflammation in the first scan which had been absorbed by follow-up but the last examination showed extensive fibrosis. Two patients had no abnormalities in their first CT scans, while pulmonary inflammation was found in the second scan and this had not been completely absorbed by the last follow-up. One patient had pulmonary interstitial lesions with no evidence of National Cochlear Implant Programme (NCIP) on the first and second CT scans. NCIP was found at the third scan, and pulmonary inflammation was not completely absorbed at the last follow-up. Three patients were in the early stage of inflammation at the first scan, and the lesions were absorbed and repaired at the last follow-up. However, the lesions were not completely absorbed. One patient was in the advanced stage at the first scan, and the last follow-up pulmonary lesions were not completely absorbed. The first CT scan of 1 patient revealed large ground-glass opacity in the lungs involving the inner and middle bands. After follow-up, the disease progressed, and this condition was consistent with severe manifestations.
Conclusion: The follow-up of chest CT can reflect the change process of NCIP and the treatment effect. The first CT scan of lung lesions has a certain predictive effect on the outcome and prognosis of patients.

Keywords: COVID-19; Epidemiology; Clinical history; Laboratory tests; Chest CT scan follow-up

1. Introduction

An outbreak of pneumonia with unknown etiology occurred in Wuhan, China in December 2019. The new coronavirus has been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) by the WHO. Human-to-human transmission of SARS-CoV2 is possible, and the disease in humans caused by the virus is called the coronavirus disease 2019 (COVID-19). The disease is typically confirmed by reverse-

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transcription polymerase chain reaction (RT-PCR), but some patients with possible COVID-19 may initially have negative RT-PCR results for COVID-19, a phenomenon which may be due to insufficient cellular material for the detection or improper extraction of nucleic acids from clinical materials. Chest CT scan can be used for the effective and convenient assessment of pulmonary parenchymal abnormalities. Thus, this procedure can solve some challenges associated with the clinical diagnosis of patients with suspected false-negative results, especially symptomatic patients with dyspnea and respiratory distress [1,2]. NCIP is a gradual process, and the follow-up review of chest CT scan examinations can result in the rapid determination of lung lesion status and evaluation of treatment effect. However, at present, most NCIP imaging reports are CT examinations during the first admission [3,4], and changes in lesions in follow-up CT imaging are rarely reported [5–7]. In this study, 15 patients with COVID-19 were reviewed, who received follow-up CT imaging test. The results were used in exploring the process of lung inflammation changes. This study can provide an insight into COVID-19. (see Table 1)

2. Materials and methods

Our institutional review board (IRB) waived written informed consents for this retrospective study. This study evaluated de-identified data and involved no potential risk to patients. To avert any potential breach of confidentiality, we ensured that the patients and researchers had no available connection.

Table 1
Demographic and clinical characteristics of 15 patients with 2019 novel coronavirus (2019-nCoV) pneumonia (n = 15).

Characteristic	Value
Sex	
Male	10
Female	5
Age (years)	
Mean	45.5
Median	39
Range	23–77
Exposure history	
Recent travel to Wuhan	13
Exposure to infected patients	2
Signs and symptoms	
Fever	10
Body temperature range (°C)	37–39
Slight phlegm	2
Myalgia or fatigue	2
Headache	2
Cough	8
Stuffy and runny nose	0
Mild dyspnea or chest pain	0
Muscle soreness	2
Diarrhea	1
Nausea	0
Sore throat	1
No obvious symptoms	2
Laboratory testing	
Peripheral blood leukocytes decreased	1
Peripheral blood leukocytes normal	14
Lymphocytes decreased	4
Neutrophils increased	4
Monocytes increased	7
C-reactive protein increased	8

2.1. General information

The general and clinical information and the CT scan results and follow-up data of the 15 patients with COVID-19 admitted between January 20 and March 5, 2020 were collected. All the patients were confirmed to be infected with SARS-CoV-2 based on the criteria in *Diagnosis and Treatment Program for Novel Coronavirus Infected Pneumonia* (*Trial Version 7*) [8]. The throat swab samples of the 15 patients (10 males and 5 females, aged 23–77 years) were tested by reverse-polymerase chain reaction (RT-PCR). The samples were positive for SARS-CoV2 nucleic acid. The detailed records of epidemiology, clinical findings, laboratory examination, and chest CT imaging data during the outbreak were collected. The interval between the disease and onset of the patient's clinical symptoms, the first chest CT examination, the number of CT scan follow-up examinations during the outbreak and the interval between each follow-up, and the analysis of chest CT findings on follow-up were all considered. Each patient in this study signed an informed consent form before the examination.

2.2. Epidemiological information

Thirteen patients had travelled to Wuhan and other parts of Hubei within 2 weeks before the onset of fever. Two patients had a fever and a history of exposure to patients with similar symptoms for 2 weeks.

2.3. Clinical symptoms

The 15 patients presented in different ways, 2 patients showed no evident clinical symptoms; 10 patients had fever, among which, 1 presented only fever and showed no other accompanying symptoms; 7 patients had a cough, among which, 5 experienced a dry cough, and the other 2 presented with productive cough with white sputum. One patient had a fever and diarrhea. Another patient had a fever, chills, fatigue, and dizziness. One patient had no fever but presented other symptoms such as sore throat and cough. One patient presented with cluster headache, whereas another patient experienced full-body weakness.

2.4. Laboratory examination

Laboratory studies showed that 14 cases had normal peripheral blood leukocytes, and 1 case showed decreased results. The percentage of lymphocytes decreased in 4 cases and the percentage of neutrophils increased in 4 cases. The test also found an increased percentage of monocytes in 7 cases and increased C-reactive protein in 8 cases.

2.5. Instruments and methods

Chest CT scan was performed using the Philips 64 rows of spiral CT and 64-section scanner (Anke Anatom 64 CT; Anke Medical, China). The scan parameters were as follows: tube voltage was 130 kV, automatic tube current and pitch 1.0 were utilized, and scanning layer thickness and layer distance were 1.25 mm and 0.625 mm, respectively. Image reconstruction was conducted using a high-resolution algorithm, matrix 512 × 512. The scanning range was from the chest entrance to the top. The pulmonary window position and window width were 600−450 HU and 1000−1500 HU, respectively. The partition window position and window width were 35−40 HU and 300−350 HU, respectively. The CT scan examinations of this group of cases were performed during the disease phase.

2.6. Image analysis

Image analysis was conducted by 2 highly experienced senior diagnostic radiologists using the blind method of independent reading. Where a difference of opinion occurred, consensus was reached through discussion. The CT scans were used in evaluating distribution, morphology, density, and other characteristics by using the lung window and in assessing the hilar, mediastinal lymphadenopathy, and pleura or pleural effusion by using the mediastinal window image. For the first chest CT scan, the physician combined the stages of pulmonary inflammation with previous history and classified the CT scan phase as early, advanced, severe, or recovery phase [9]. For subsequent follow-up examinations, the physician compared the results with the previous lesion. Where the lesion was similar to the previous lesion, it was considered to be at the same stage as the previous lesion. Where the scope of the lesion and density increased, the lesion was considered to be progressing. Where the extent of the lesion and density decreased and fibrous foci appeared, the lesion was considered to be absorbed and repaired. For the final follow-up CT examination, the physician assessed whether the lung inflammation was fully absorbed.

3. Results

3.1. First CT imaging findings

The results of the first chest CT scans of 6 patients were normal. One patient had pulmonary interstitial lesions with no NCIP. The results of the first chest CT scans of 6 other patients presented consolidated opacity, ground-glass opacity, small nodules, and lesions located under the pleural membrane. These findings belonged to the early stage characteristics of NCIP. The CT scan results of 2 patients showed ground-glass opacity with consolidated opacity. This result belonged to the advanced characteristics of NCIP.

3.2. Chest CT follow-up

The 15 patients each underwent between 2 and 6 chest CT follow-up examinations. 2, 5, 4, 2, and 2 patients received 2, 3, 4, 5, and 6 follow-up examinations, respectively. The period of the first to the last CT examinations of the 15 patients varied from 3 days to 33 days. Two of the patients showed no clinical symptoms, whereas 13 patients exhibited different clinical symptoms. The interval between the clinical symptoms and the first CT scan examination ranged from 1 day to 10 days. By analyzing the follow-up time, the lesions shown by the CT examination were in the early, advanced, and repair stages 2−8 days, 5−13 days, and 13 days after the symptoms appeared, respectively. The CT scan examination showed that the early lungs lesions can enter the CT progress phase from 2 days to 3 days. Furthermore, after 1 week of the progression phase, the lesions enter the repair phase. However, some patients take as long as 2 weeks before the lesions were absorbed or repaired. This phenomenon mainly depends on the area and density of the lung lesions. The follow-up CT scan results of the 2 patients with asymptomatic COVID-19 showed no abnormality (Fig. 1).

3.3. Dynamic observation of chest CT follow-up performance

The follow-up chest CT scan results of the 4 patients showed no abnormal changes. One patient had lower right lung lobe lesions on CT examination. This result occurred in the progression phase 10 days after the appearance of symptoms. After 17 days, the CT scan result showed that the areas and densities of the lesions had decreased and were in the recovery period. On day 27, the follow-up examination showed that the lesions were fully absorbed, and no abnormality was found on the chest CT scan (Fig. 2). The CT scan examination of 2 patients showed that the lesions under the bilateral lung pleural membrane were in the early stage 2 days after the appearance of symptoms. The follow-up CT scan examination after 5 days showed that the area and density of lesions increased and were in the progression phase. After 30 days, the CT scan examination showed that the lung inflammation was slightly absorbed but presented extensive fibrosis. After 37 days, the CT scan examination showed that the lesions were slightly absorbed (Fig. 3). The CT scan examination of 2 patients showed no abnormality on the second day after the appearance of symptoms. However, at day 5, the follow-up CT scan examination showed ground-glass opacities in the bilateral lungs in the early stage. On day 13, a follow-up CT noted that the disease range and density increased and were in the progression phase. The follow-up CT scan examination of 1 patient showed no significant change in the size of the lesions, but the density was slightly reduced. The disease was absorbed and repaired on day 15. The follow-up CT

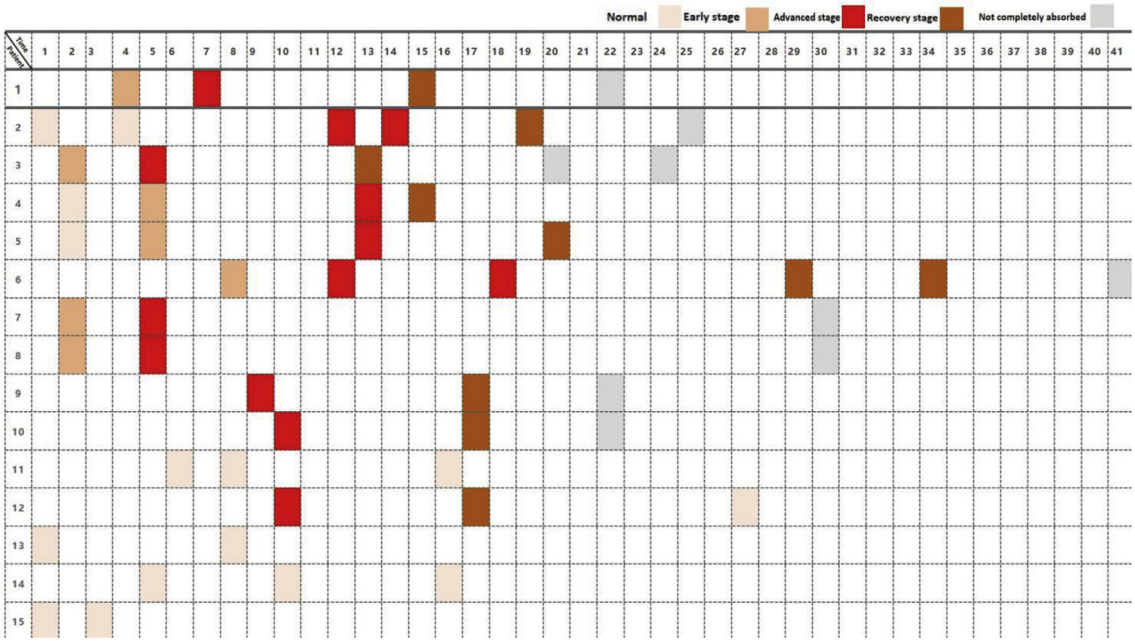
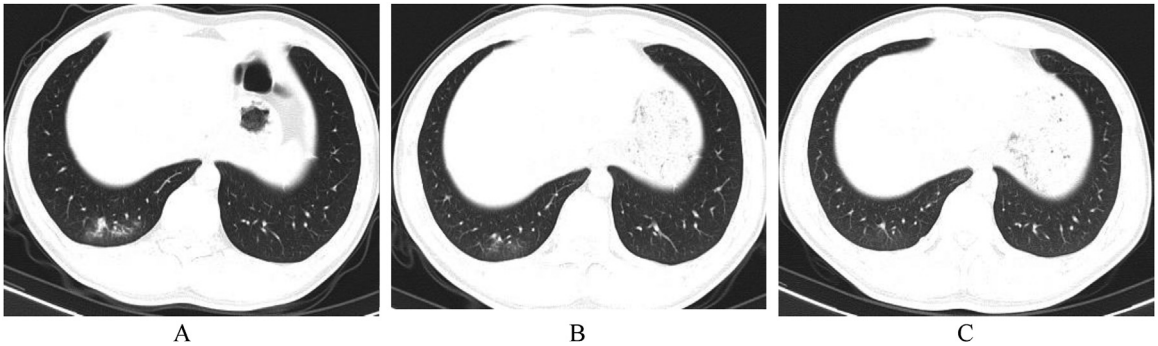


Fig. 1. Timeline from the onset of symptoms to CT scan test follow-up with COVID-19.

examination of another patient showed that the areas and densities of the lesions decreased and fibrotic lesions appeared which showed that the disease was in the repair phase. However, the lesions were not fully absorbed on day 20 (Fig. 4). The CT scan examination of 1 patient showed intrapulmonary lesions 1 day after the appearance of symptoms. However, any NCIP feature was not observed. On day 3, the follow-up CT scan examination still found no NCIP feature. On day 11, the follow-up CT scan examination showed lesions in the left upper lobe of the lung that were in the progression phase. On day 13, the CT scan examination showed bilateral upper lung lobe opacity, the density of the left upper lung lobe had increased, and the lesions were in the progression phase. On day 18, the follow-up results found that the density of lung opacity had slightly decreased, and the lesions had begun to repair. On day 24, the follow-up CT scan examination found decreased and incomplete absorbed lesion area that was in the repair phase (Fig. 5). The CT scan examination of a patient 8 days after the onset of symptoms showed a large ground-glass opacity in the lungs with a slightly thick lobular interval. This finding showed that the lesion was in the early stage. On day 11, the follow-up CT scan examination showed that the density was increased, and the range of the lesions was larger than before. This finding showed that the lesion was in the advanced stage. On day 14, the follow-up CT examination showed consolidation in the lesion, the scope further increased, and the lesion entered the critical stage. On day 19, the follow-up CT examination showed that a large patch of consolidation had appeared in the lesion, the scope was roughly the same as before and remained in the critical stage. On day 24, the follow-up CT examination showed that the range of patchy shadows and cable shadows in both lungs were smaller than before, and the lesions entered the repair phase. However, the lesions were not completely absorbed. The first CT scan examinations of 3 patients were in the early stage and progressed to the advanced stage after follow-up. Their final follow-up examination showed the lesions to already be in the repair stage. However, the lesions were not



A B C

Fig. 2. A 28-year-old male who had a fever for 10 days. CT scan examination was performed on February 3, 2020. Ground-glass opacity was observed in the lower lobe of right lung. A, thickening of the blood vessel shadow was observed; B, after 7 days, the CT scan examination showed that the area and density of lesions had decreased and was in the recovery period; C, on day 17, the follow-up examination showed that the lesions were fully absorbed, and chest CT scan examination showed no abnormality.

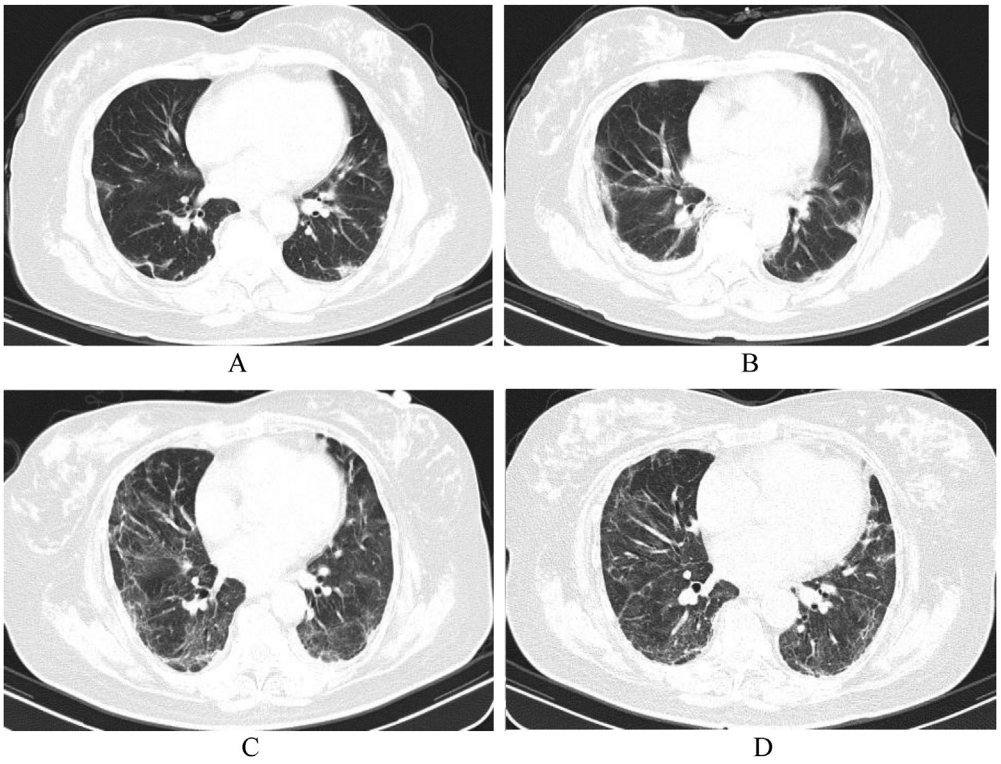


Fig. 3. A 60-year-old female had a fever for 2 days. A, CT scan examination was conducted on January 25, 2020. Numerous small pieces of real and rope shadows were observed under the bilateral lung pleural membrane; B, on day 3, a follow-up CT scan examination showed that the area and density of lesions increased; C, after 28 days, the CT scan examination showed that the lung inflammation was slightly absorbed but had extensive fibrosis; D, after 35 days, the CT scan showed that the lesions were slightly absorbed.

completely absorbed. One patient underwent CT scan examination 9 days after the onset of symptoms, and the first CT examination showed that the disease was in the progression phase. On day 17, the follow-up CT scan examination showed that the lesions were in the recovery period. However, on day 22, the follow-up CT scan examination showed that the lung lesions were still not fully absorbed.

4. Discussion

SARS-CoV2 is highly contagious and is mainly transmitted through respiratory droplets or close contact. It spreads through the upper respiratory tract and involves alveolar epithelial cells. According to the number of infected viruses and the body's immune status, patients exhibit different clinical presentations and symptoms after infection. Some can become asymptomatic carriers, whereas others can exhibit upper respiratory symptoms with or without pulmonary inflammation. Furthermore, some symptoms can even develop into severe or critical situations. In this paper, we included 15 patients, of which 2 were asymptomatic, 10 were common cases, 2 showed mild symptoms, and 1 was in critical condition.

SARS-COV 2 nucleic acid RT-PCR is the gold standard for the diagnosis of COVID-19. At present, the diagnostic criteria for the discharge of patients with COVID-19 is that 2 consecutive negative results from the nucleic acid test with improved patient clinical symptoms. Therefore, the nucleic acid test is only a standard for diagnosis of the disease and assessing discharge. Compared with the nucleic acid test, the chest CT has its unique and indispensable advantages in disease classification, staging, monitoring, and prognosis [10,11].

NCIP is a new infectious lung disease, the pathological mechanism of which remains unclear. According to the recent results of the limited autopsy and puncture histopathological research [8], infected lungs generally show different degrees of consolidation. Serous fluid, fibrin exudate, and transparent membrane are found microscopically in the alveolar cavity. Exuded cells are mainly monocytes and macrophages, and poly-nuclear giant cells are commonly found. The number of type II alveolar epithelial cells significantly increases, and a part of these cells are removed from the alveolar cavity. Viral inclusion bodies can be found in type II alveolar epithelial cells and macrophages. Alveolar septal vascular congestion and edema, mononuclear and lymphocytic cell infiltration and intravascular clear thrombosis are evident. Focal hemorrhage, necrosis, the mechanization of alveolar exudation, and pulmonary interstitial fibrosis can be observed. A portion of the epithelium of the bronchial mucosa is shed, and mucus and mucus plugs are formed in the cavity. Few alveoli are over-inflated with broken alveolar septum or the formation of cystic cavities. Under the electron microscope, coronavirus particles can be found in the cytoplasm of bronchial mucosal epithelium and type II alveolar epithelial cells.

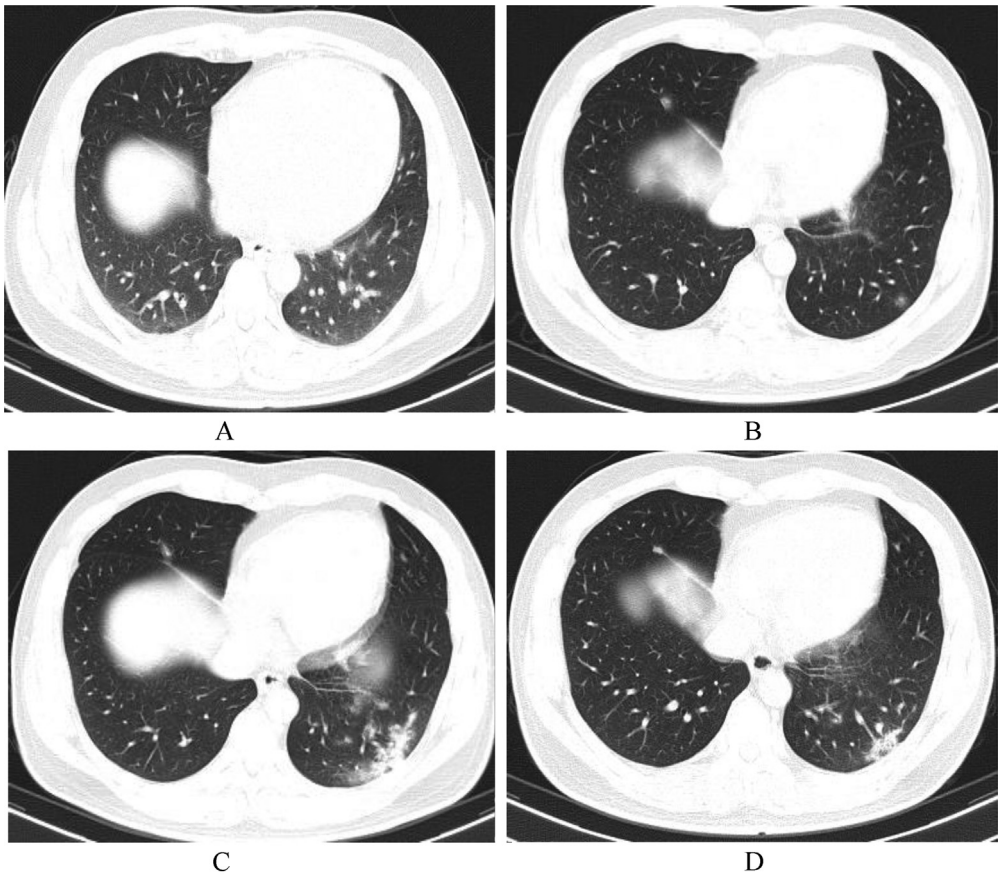


Fig. 4. A 35-year-old male who had fever for 2 days. A, CT scan examination was conducted on January 23, 2020. Chest CT scan examination showed no abnormality; B, after 3 days, the CT scan examination showed the mixed grinding glass conjunctivation in the mid-lobe of the right lung and lower lobe of the left lung; C, on day 11, a follow-up CT scan examination noted that the disease range and density increased and were in the progression phase; D, on day 18, a follow-up CT scan examination showed that the area and density of the lesions had decreased, fibrotic lesions appeared and were in the repair phase. However, the lesions remained not fully absorbed.

Immunohistochemistry shows that some alveolar epithelium and macrophages are positive for new coronavirus antigens.

NCIP is an evolving process [12,13], and the viruses are spread downward from the upper respiratory tract, infecting alveolar epithelial cells, resulting in the proliferation of alveolar epithelium and exudation in the alveolar cavity. A sheet-like ground-glass opacity with clear boundaries in the subpleural area of the lower lung can be observed on CT images. As the disease progresses, the alveolar septal vessels are congested and edematous. Mononuclear and lymphocyte cell infiltration thickens the lobular septum, which can be observed on CT images. With further disease development, the exudate in the alveolar cavity changes from serous fluid to fibrin, which increases lesion density. The formation of bronchial mucus plugs may cause local lung lobule atelectasis, which further increases lesion density. If the lesion is not managed immediately it will progress toward the inner-middle zone of the lung field. The lesions are diffusely distributed with ambiguous boundary. Small nodules and patchy foci merge into consolidation lesions, even with a wide range of consolidation. Segmental or lung atelectasis may occur if a mucus plug appears in the large bronchi. A few cases showed “white lung.” Bilateral pleural effusion can be observed. If the original changes of lung are relatively mild, and no alveolar septal rupture and no mucus plug formation are observed, the alveolar infiltration can be absorbed, and the lung can return to normal following clinical therapy. With severe original lung changes, alveolar lesions cannot be completely absorbed and then mechanize partially, and pulmonary interstitial is destroyed. This phenomenon causes the destruction of alveolar structure and pulmonary fibrosis. In severe cases, the lesion can fuse into the air containing space in the lung. CT images showed lung structural disorders and multiple fibrous foci.

CT follow-up showed that if COVID-19 patients underwent a CT scan within 2−8 days after the onset of symptoms, the CT images can demonstrate the early stage of lesions. Lung CT scans showed that the lung lesions were in the progressive stage within 5−13 days after the onset of symptom. After 13 days, the lung lesions entered the repair stage. The CT findings of lesions in early stage can develop into progressive stage within 2−3 days. The lesions entered the repair stage after approximately 1 week. However, the lesions of some patients

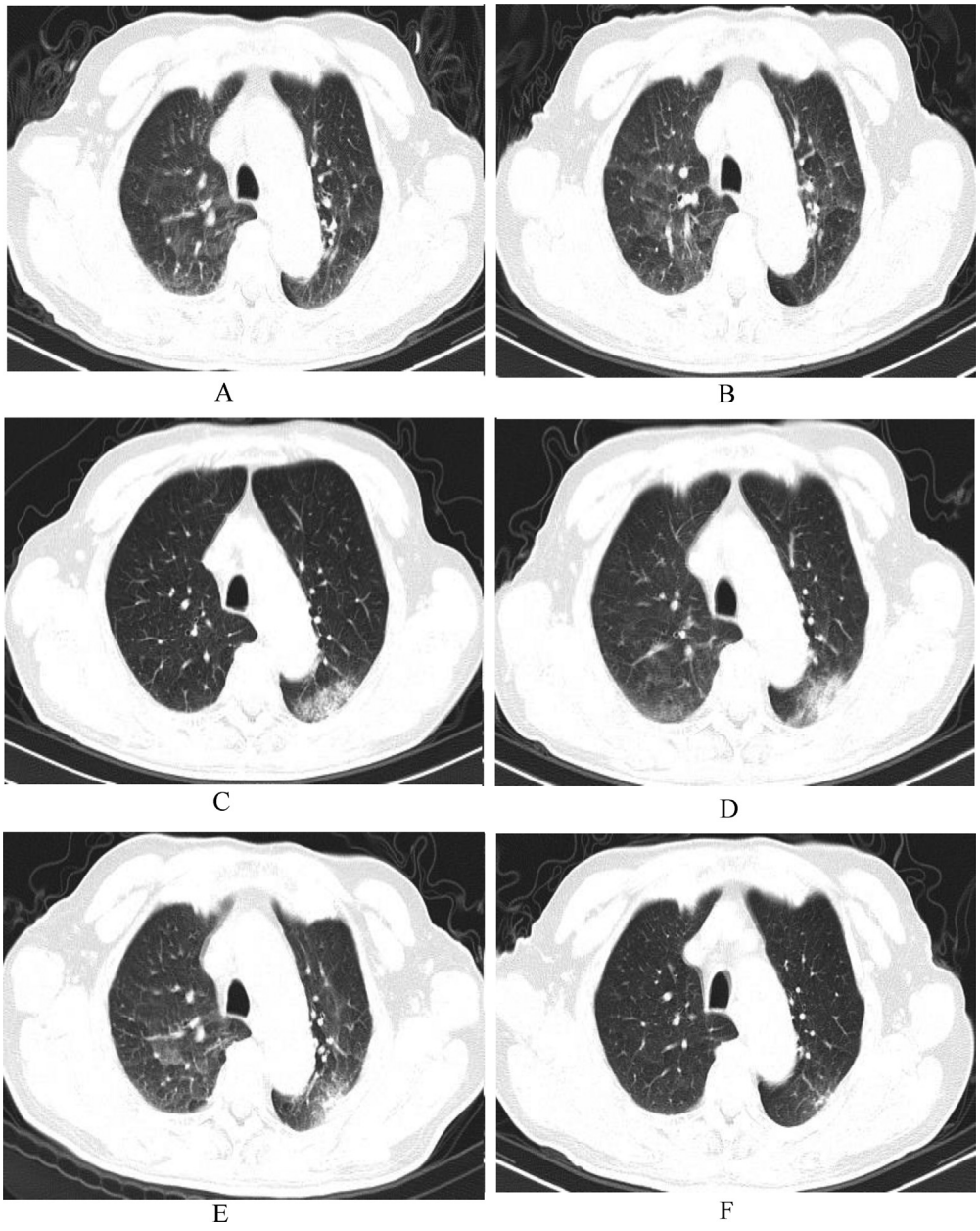


Fig. 5. A 77-year-old mad had a fever for 1 day. CT scan examination was performed on January 23, 2020. Intrapulmonary lesions were observed, but no NCIP feature was found; B, on day 3, the follow-up CT scan examination still found no NCIP feature; C, on day 11, the follow-up CT scan examination showed lesions in the left upper lobe of the lung; D, on day 13, the scan showed that the bilateral upper lobes of the lung had opacity, and the density of the left upper lobe of the lung had increased and lesions; E, on day 18, the follow-up examination showed that the density of lung opacity slightly decreased, and the lesions begun to repair; F, on day 24, the follow-up CT scan examination showed that the lesion area decreased but was not completely absorbed.

were not absorbed and repaired until 2 weeks after entering the progressive stage. The duration of the repair period depended on the extent and density of the lesions. The incidence rate of NCIP was lower in asymptomatic patients. Some young people with mild clinical symptoms and normal laboratory tests exhibited mild infections without pulmonary inflammation. Single ground-glass opacity was found in the first CT examination of the lung, and the lesions can be completely absorbed 2 weeks after follow-up. In relatively old patients, the first CT scan examination showed high consolidation density. The follow-up showed that the absorption of lesions was slow, and fibrosis might occur during the recovery stage. In patients with multiple ground-glass opacities in the early stage and consolidation mainly in the progressive stage, recovery period was prolonged, and fibrosis easily appeared in the lesion area, drawing nearby pleura with disordered bronchi and blood vessels. In patients with positive nucleic acid test, no pathological pulmonary findings were found on the first CT scan examination. However, this result did not necessarily indicate mild cases. Some patients showed pulmonary inflammation in the follow-up. Therefore, patients with a negative first CT scan examination must be reexamined at least 1 week after the

onset of symptoms. Most cases were mild in negative CT scan results.

Chest CT scan follow-up examination can reflect the change process of NCIP and assess the therapeutic effect. The status of lung lesions during the first chest CT scan examination exhibits a certain predictive effect on the outcome and prognosis of the patient. Given the small number of cases in the paper, the number and interval of CT scan follow-up examination were irregular and not unified. Given this, the conclusion is no adequately accurate. In the future, additional cases will be accumulated, and the experience will be summarized to further improve the understanding of the disease.

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Guarantor

The scientific guarantor of this publication is Guanxun Cheng.

Statistics and biometry

No complex statistical methods were used for this study.

Informed consent

Written informed consent was waived by the Institutional Review Board.

Ethical statement

Approval of the Institutional Review Board was obtained.

Methodology

- Retrospective.
- Observational.
- Single-center study.

Conflict of interest

The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

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