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The Longitudinal Changes in the Chest CT in Novel Coronavirus Disease Pneumonia Patients

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Abstract

Purpose: Chest Computed Tomographic (CT) scans play an important part in diagnosing and treating novel Coronavirus Disease (COVID-19). However, studies on the long-time changes in chest CT are scarce. The present work aimed to assess those longitudinal alterations in COVID-19 from the chest CT images.

Methods: COVID-19 cases were recruited into this work in a retrospective manner between January 30th, 2020 and March 20th, 2020, in the COVID-19 designated hospital, Chaoyang district, Beijing. Novel coronavirus nucleic acid test detected by RT-PCR was essential for diagnosis. For the discharged cases, two follow-up visits were performed at an interval of 2 weeks. The associations of chest CT characteristics and clinical factors with progression were examined.

Results: Altogether, 16 confirmed COVID-19 cases (including 9 male and 7 female cases) were assessed, with the age ranging from 26 to 68 years. All patients had at least one clinical symptom. These symptoms include fever (15/16, 93.75%), sputum (10/16, 62.5%), fatigue (8/16, 50%), diarrhea (5/16, 31.25%), dyspnea (4/16, 25%), cough (2/16, 12.5%), chest pain (1/16, 6.25%), and vomiting (1/16, 6.25%). Pulmonary opacifications were observed in chest CT in almost all patients (15/16, 93.75%). There was one patient with normal imaging of CT. The lesions were unilateral pulmonary in three cases (one in right lower while two in right middle lobes) and bilateral pulmonary in 12 cases, observed in both lower lobes. The chest CT features included ground-glass opacities (15/15, 100%), consolidation (14/15, 93.33%), reticular pattern (12/15, 80%), subpleural linear opacity (11/15, 73.33%), bronchial dilatation (5/15, 33.33%), adjacent pleura thickening (4/15, 26.67%), and centrilobular nodular (3/15, 20%). All patients received antiviral (Arbidol Hydrochloride), antibacterial therapy (moxifloxacin), and traditional Chinese medicine. All patients were cured and discharged after symptoms were decreased, and the nucleic acid test for novel coronavirus was negative in at least two tests. Most of the lesions presented by the chest CT imaging were absorbed. However, nucleic acid test results of sputum and stool in two patients were consistently positive, even though the chest CT imaging lesions had been completely absorbed or showed fibrous cords. For cases who had negative results in two nucleic acid tests performed between 24 h, they were finally discharged home. For the discharged cases, the length of stay ranged from 11 to 45 (average, 24 ± 12) days and were followed up for four weeks (once every two weeks). The mean interval between the initial symptoms to last chest CT examination ranged from 31 to 61 (average, 48 ± 9) days. Each case received 4 ± 1 CT scans on average (range, 3 to 6). No abnormal changes in chest CT were observed in one patient from admission to the end of follow-up. In 15 patients with imaging manifestations, chest CT was regularly reviewed during the observation period. Finally, seven patients had completely absorbed lung lesions, two patients presented as light ground glass shadow, one presented as line spline shadow, and five were accompanied by both light ground glass and line spline shadows.

Conclusion: Chest CT may be adopted to help diagnose and treat COVID-19, but not to determine whether the patient is contagious or requires isolation. After long-term observation, regardless of the initial imaging findings, most pulmonary lesions could be well absorbed.

Keywords: 2019 novel coronavirus pneumonia; Infection; Imaging features; Computed tomography; Ground-glass opacity

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Introduction

The first novel Coronavirus Disease (COVID-19) case was reported in December 2019 in China. At present, COVID-19 has gradually accelerated at an exponential rate globally and becomes the

global pandemic. Typically, the Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) belongs to *Betacoronavirus* of the coronavirus family. It contains an outer membrane, round, or elliptical with a diameter of 60 nm ~ 140 nm. COVID-19 is a respiratory infection spreading easily among people, with asymptomatic infected persons also being a source of infection. In addition to clinical symptoms and imaging findings, Ribonucleic Acid (RNA) of SARS-CoV-2 was positive through nucleic acid testing, including PCR and the viral genetic sequence was extensive homology with the known novel coronavirus. Subpleural Ground-Glass Opacity (GGO), reticular pattern, patchy consolidation, subpleural linear, pleural effusion, and pleural thickening in unilateral or bilateral pulmonary, single or multiple lobes were characteristic imaging findings for COVID-19 [1-3].

At present, there is no relevant report on the relationship between nucleic acid test results and imaging changes in COVID-19 patients, as well as the long-term imaging changes and outcomes. This study showed the long-term imaging changes and their clinical relationship in 16 COVID-19 cases.

Methods

Patients

This work was approved by the Ethics Committee of Beijing Chuiyangliu Hospital (No.2020-011KY). And this study also was conducted following the Helsinki Declaration.

Study participants and design

All patients who were identified with COVID-19 through Real-Time PCR (RT-PCR) tests of nasopharyngeal swab, stool or sputum were recruited from January 30th, 2020 to March 20th, 2020 from the designated hospital for COVID-19 treatment in Chaoyang District, Beijing. The clinical data, which included gender, age, symptoms, exposure history, comorbidities, and laboratory tests, were analyzed.

Clinical data

This study examined the clinical symptoms, demographic characteristics, and laboratory tests in a retrospective manner.

CT data

Each case received baseline chest High Resolution Computed Tomography (HRCT) scan at the hospital. The patients were asked to lie on their backs, raise their arms, and hold breath, so as to keep lung inflation. Chest CT scans were performed to evaluate the progression of the disease after treatment, with the slice thickness and total scanning time of 1.25 mm and 2 s, respectively. And the last chest CT examinations were required four weeks after discharge as recovered well.

Imaging data analysis

Each chest CT image was examined by 2 experienced chest radiologists who had 20 to 25 years of experience. On every image, the lesion characteristics, such as distribution features, affected lobe number, lesion distribution in lobe, as well as lesion types. GGO referred to a hazy radiopacity region, which was clear below the vascular and bronchial margins. Consolidation referred to a region with obscure vascular and bronchial margins. Reticular pattern referred to a region with GGO-related thickening of interlobular septal.

Each case with normal temperature for 3 days, significantly improved symptoms, significantly absorbed exudation of acute lung lesions, negative results in 2 consecutive nasopharyngeal swabs, sputum, and stool specimens at an interval of 24 h, was treated and discharged home. If the lesions were almost completely absorbed in the chest CT examination in the second week after discharge, the chest CT examination would not be conducted in the fourth week. Otherwise, it should be performed again in the fourth week.

The mean value (SD) was used to represent continuous measurements. The measurement data were presented as mean + SD (minimum-maximum), whereas enumeration data were presented in the manner of total. The outliers were also assessed. SPSS26.0 was adopted in all statistical analyses.

Results

This work recruited altogether 16 confirmed COVID-19 cases in Chaoyang district who were discharged home from January 30th, 2020 to March 20th, 2020. Each case was confirmed for COVID-19 through nasopharyngeal swabs, sputum nucleic acid, and stool nucleic acid tests. The 16 patients included 9 male and 7 female patients, with the average age of 44 ± 13 (range, 26 to 68) years. The symptoms were fever (15/16, 93.75%), sputum (10/16, 62.5%), fatigue (8/16, 50%), diarrhea (5/16, 31.25%), dyspnea (4/16, 25%), cough (2/16, 12.5%), chest pain (1/16, 6.25%), and vomiting (1/16, 6.25%). Among these 16 patients, one had hypertension, and the other had diabetes (Table 1).

The duration between the first symptom and the first chest CT imaging examination was 7 ± 3 days (range: 2 to 15 days). Among the 16 patients, 15 had abnormal chest CT imaging features. There was one patient negative in chest CT imaging. The lesions were unilateral pulmonary in three cases (one in right lower and two in right middle lobes) and bilateral pulmonary in 12 cases, observed in both lower lobes. The chest CT features included ground-glass opacities (15/15, 100%), consolidation (14/15, 93.33%), reticular pattern (12/15, 80%), subpleural linear opacity (11/15, 73.33%), bronchial dilatation (5/15, 33.33%), adjacent pleura thickening (4/15, 26.67%), and centrilobular nodular (3/15, 20%) (Table 2).

All patients were treated with Arbidol Hydrochloride, moxifloxacin, and traditional Chinese medicine. The changes in vital signs were monitored during hospitalization, and nucleic acid tests of nasopharyngeal swabs, sputum, and stool and chest CT were regularly reviewed. The symptoms of all patients gradually alleviated during the treatment. For the 13 cases, their chest CT images were gradually absorbed, and images of two patients were temporarily aggravated

Table 1: Baseline characteristics of patients.

All patients	n = 16
Age(y)	44 ± 13 (26~68)
Gender	
Male	9
Female	7
Initial symptoms	
Fever(n)	15 (93.75%)
Sputum(n)	10 (62.5%)
Fatigue(n)	8 (50%)
Diarrhea(n)	5 (31.25%)
Dyspnea(n)	4 (25%)
Cough(n)	2 (12.5%)
Chest pain(n)	1 (6.25%)
Vomit(n)	1 (6.25%)

Table 2: Imaging features on chest CT images of patients (n=15).

Abnormal CT imaging features (n=15)	N
No. of unilateral pulmonary	3
Right middle lobe	2
Right lower lobe	1
No. of bilateral pulmonary	12
Pattern of opacities	
Ground-glass opacities	15 (100%)
Consolidation	14 (93.33%)
Reticular pattern	12 (80%)
Subpleural linear opacity	11 (73.33%)
Bronchial dilatation	5 (33.33%)
Adjacent pleura thickening	4 (26.67%)
Centrilobular nodular	3 (20%)
The period between the onset of initial symptoms and the first scan (d)	7 ±3 (2~15)
The period between the onset of initial symptoms and the last scan (d)	48 ±9 (31~61)
The interval between the first CT scan and the last scan(d)	41 ±9 (26~58)
Numbers of scans (n)	4 ±1 (3~6)
The hospitalized period (d)	24 ±12 (11~25)

in the first week of admission, but eventually, all the patients' lesions were gradually absorbed. The patient, negative in chest CT imaging, did not have a consistent abnormality.

After regular treatment, when a patient had normal temperature for over 3 days, symptom disappearance, the inflammatory lesions of chest CT were significantly absorbed, and the nucleic acid test was twice negative at 24 h interval, the patient could be discharged. All patients were discharged after hospitalization of 24 ± 12 days (range: 11~45 days).

Each case received a 4-week follow-up period with the blood oxygen, blood routine, C-reactive protein, blood biochemical examination, and nasopharyngeal nucleic acid tests performed on the 14th and 28th day after discharge. A routine chest CT scan was performed on day 14 after discharge. If the chest CT lesions were completely absorbed, chest CT scan was not performed on day 28 after discharge. If the chest CT on the 14th day after discharge showed ground-glass or cable shadow, the chest CT was again performed on the 28th day after discharge. The duration from first to last chest CT scans was 41 ± 9 days (range: 26 to 58 days). The number of chest CT scans times was 4 ± 1 (range: 3 to 6) (Table 2, Figures 1-3).

Discussion

SARS-CoV-2, a kind of beta-coronavirus, is one of the coronavirus family members. It has an outer membrane, round or elliptical, with a diameter of 60 nm ~ 140 nm [1,4,5]. COVID-19 is a newly discovered global respiratory infectious disease, mainly manifested as viral pneumonia, which spreads easily among people. The infected cases with no symptoms have posed the possible risk of infection [6]. The primary symptoms are fever, fatigue, cough, and dyspnea. The respiratory symptoms such as the dry pharynx, stuffy, and runny nose are not obvious. Patients with mild symptoms often have no obvious positive signs on physical examination. Severe patients may have the appearance of lung rales, a decrease of respiratory sounds, dullness detected upon lung percussion, and elevated or reduced tactile chatter [7-9]. Several patchy GGOs may be observed in chest CT images, consolidation shadows, mesh signs, and subpleural linear shadows. These images are observed in the peripheral and subpleural areas of single or double lungs [10-13]. In addition to clinical symptoms as well as imaging findings, RNA of SARS-CoV-2 was found as positive through nucleic acid testing, including real-time PCR, and the genetic sequence of the virus showed high homology to novel coronavirus that has been recognized [14-16].

On chest CT images, COVID-19 mainly manifested as bilateral lung involvement, while the unilateral was rare, and most of the lesions were peripheral to the inferior lobe of both lungs or subpleural [17-21]. All the patients in this group received chest CT examination 2 to 15 days after the onset of symptoms, with 15 patients presenting with different degrees of pulmonary imaging manifestations. Most cases showed bilateral lung (12/15, 80%), and the unilateral lesions were in the right lung (3/15, 20%). All 12 patients with bilateral lung disease had both lower lobe lesions, consistent with the literature

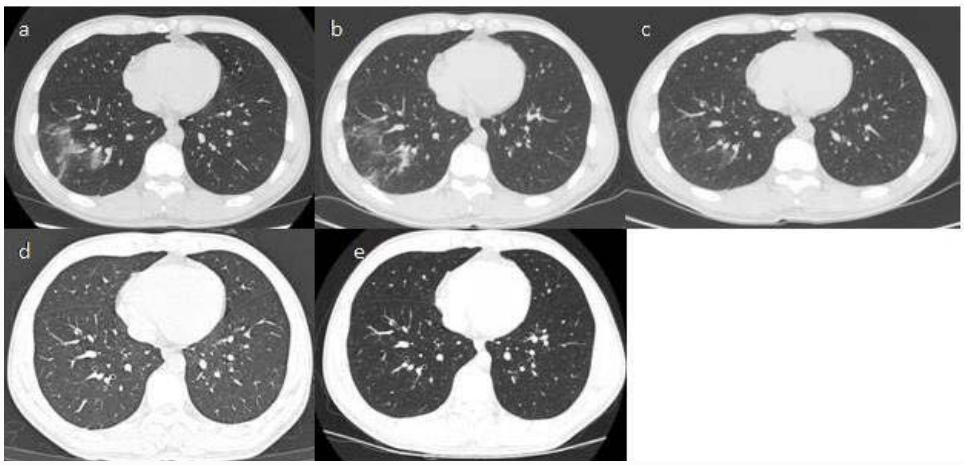

Figure 1: Chest CT images in the 32-year-old man.
1a show that there are ground-glass opacities and consolidation in the right lung.
1b, 1c show that the extent and density of lesions have significantly decreased.
1d show that ground-glass opacities and consolidation have completely absorbed in the right lung.
1e show that CT scan shows no difference, three weeks later.

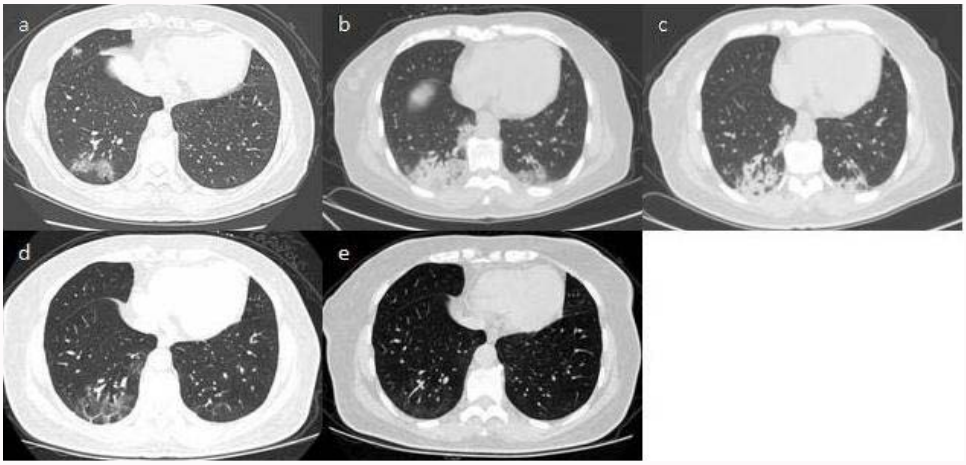

Figure 2: Chest CT images of the 57-year-old woman.
2a show that there are ground-glass opacities, consolidation, or both in bilateral lungs.
2b show that the extent and density of lesions have significantly aggravated.
2c, 2d show that multiple patchy ground-glass opacities and consolidation in bilateral lungs have differently absorbed.
2e shows that the residual light ground glass and wire spline shadow in the right lung, two weeks later.

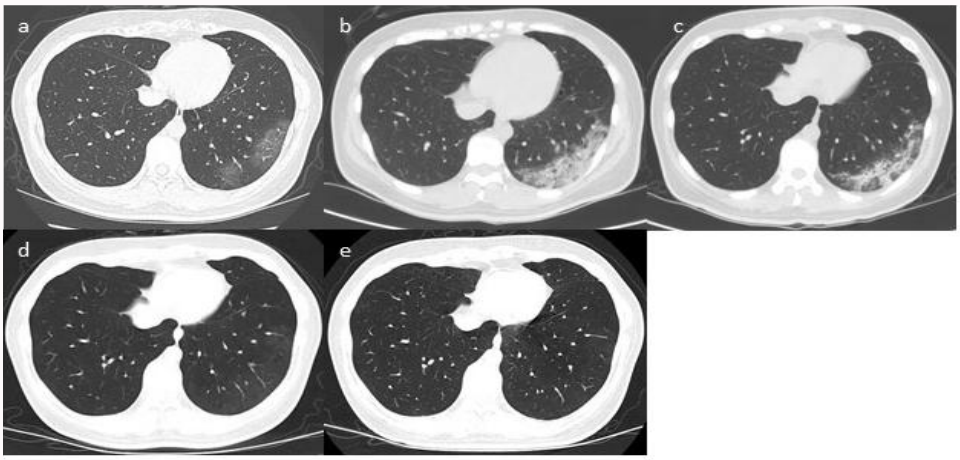

Figure 3: Chest CT images of the 31-year-old woman.
3a show that there are ground-glass opacities in the left lungs.
3b, 3c show that the extent and density of lesions have significantly aggravated.
3d show that CT scan shows the residual light ground glass and wire spline shadow in the left lung.
3e show that ground-glass opacities have completed absorbed in the left lung, two weeks later.

reports. Besides, there were 10 cases with lesions in left upper lobe, 6 in right middle lobes while 9 in right upper lobe. In the three unilateral lesions cases, two were confined to the middle lobe of the right lung, and one was confined to the lower lobe of the right lung. We found that those lesions of 15 patients did not further appear in other pulmonary lobes during the treatment. Considering the possibility of the activity of the virus gradually decreasing after drug therapy, the lesion can remain confined to the primary lesion of the pulmonary lobule without further spread. A female patient was infected with novel coronavirus as her husband was COVID-19 positive. The case suffered from fatigue and cough for ten days. A pharyngeal swab test indicated the admission of the patient to the hospital with the positive nucleic acid. No abnormal chest CT findings were observed in the patient. After regular therapy, the patient's symptoms disappeared. The nucleic acid tested negative twice consecutively at 24 h interval, and the patient was discharged from the hospital. Since there was no change consistently in the chest CT, the patient was considered as a mild patient.

GGO in pulmonary lobule is the dominant imaging finding for COVID-19, combined with patchy consolidation, grid-like changes, and parallel filaments of visceral pleura. Central lobular nodules and pleural effusion are rare [22-24]. In this study, the chest CT images showed ground glass change (15/15), consolidation shadow (14/15), messy change (12/15), subpleural cable shadow (11/15), localized interlobular pleural thickening (4/15), and a small number of central lobular nodules (3/15). The manifestations of the lesions were consistent with the literature reports. However, partial localized pleural thickening was observed in this group of patients, considered to be related to the local pleural effusion stimulated by inflammation. There were three patients with central lobular nodules, considered to be related to the large range of lesions.

Chest CT images and dynamic alterations of COVID-19 can be used for estimation of the evolution of the disease [25-29]. Through

this study, it is confirmed that imaging detection can understand the situation of patients and help to monitor the progress of the disease. During the treatment, chest CT images of three patients indicated further aggravation of lesions in a short period, presenting gradual consolidation and widening range. But the patient's symptoms gradually abated, without the aggravation, which may be related to the patient's young age and good physical compensation. Eventually, the lesions of all patients gradually became pale and absorbed. Also, 14 patients were discharged from the hospital with negative sputum and fecal nucleic acid. The nucleic acid test results of sputum and stool in two patients were not consistent with imaging changes, which was noteworthy. Although the imaging lesions of the chest had been completely absorbed or changed into fibrous cords, sputum, and stool nucleic acid tests were always positive. In one case, the chest CT lesion had been completely absorbed, but the sputum and stool were always positive. Finally, the patient was discharged from the hospital two days later with negative nucleic acid twice consecutively. The other one was accompanied by light frosted glass shadow and cable strip shadow when he was discharged from the hospital with negative sputum and stool nucleic acid. So, changes in chest CT imaging do not predict the results of nucleic acid testing, and it does not represent changes in imaging. It may be related to the degree and speed of elimination of viral nucleic acid from the body. Therefore, changes in chest CT and nucleic acid detection should be complementary. In such cases, nucleic acids in sputum and stool should be monitored repeatedly.

At present, there is no international report on long-term imaging observation of COVID-19, and only some reports on long-term follow-up of pulmonary imaging of SARS [30,31]. This group of patients has the longest observation time of COVID-19 patients, with an average of 48 ± 9 days (range: 31 to 61 days). The interval between the first chest CT scan and the last chest CT scan was 41 ± 9 days (range: 26 to 58 days). Through long-term observation, most of the lung shadows on chest CT images were well absorbed. The patient recovered and left the hospital with some faint shadows of lung residue. During the follow-up, the lung shadow of seven patients (46.67%) was completely absorbed, five (33.33%) had a residual light ground glass and wire spline shadow, two (13.33%) had a residual light ground-glass, and one patient (6.67%) had residual wire spline shadow. For nine patients with incomplete absorption, the observation time can be further extended for the confirmation.

Although, we found some interesting results. Due to the limitations of conditions and time, the number of cases in our study was limited and the follow-up time was not enough long. But these results can be verified in the future by further increasing the number of cases and extending the follow-up time.

Chest CT may be applied to help diagnose and treat COVID-19, but not to determine whether the patient is contagious or requires isolation. After long-term observation, most pulmonary lesions could be well absorbed regardless of the initial imaging findings.

Main Points

1. During the treatment, chest CT plays a very important role and may be adopted to help diagnose and treat COVID-19.

2. According to our findings, chest CT can not to be determine whether the patient is contagious or requires isolation.

3. After long-term observation, regardless of the initial imaging findings, most pulmonary lesions could be well absorbed.

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