Clinical and Imaging features in COVID-19 Patients: Analysis of Data from Patients in Non-pandemic areas

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Research article

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Abstract

Purpose To describe the imaging characteristics in COVID-19 Patients from non-pandemic regions to improve understanding of the disease.

Methods We reviewed chest CT scans of 30 COVID-19 patients from three hospitals in Sichuan province, China.

Results Typical CT manifestations include the involvement of multiple lobes, mostly in the peripheral zone of the lungs, and subpleural distribution. GGO, crazy paving or mixed GGO and consolidation is the most common signs. Few patients can present small amount of pleural effusion. It is worth noting that none of the lung cavities, tree buds, and lymphadenopathy appeared. The follow-up imaging findings of some patients showed progress when the initial CT score reached 7.

Conclusion The CT scan still play an important role in screening the COVID-19, most of the images present positive signs, mainly subpleural, multiple GGO. CT might can predict the severity or whether the patient will progress to severe illness. A small number of patients may be missed if they are based on CT findings alone, which should be closely combined with the patient's epidemiological history and nucleic acid test.

Background

Since December 8, 2019, a series of unexplained pneumonia cases appeared in Wuhan, Hubei Province, China, with clinical manifestations and chest radiography similar to viral pneumonia[1]. On January 7, 2020, the Chinese Center for Disease Control and Prevention (CDC) identified a new type of coronavirus from oropharyngeal swab specimen samples of the above patients, and it was subsequently named by the WHO as 2019-nCoV [2] and then subsequently renamed as SARS-CoV-2. Since the outbreak of 2019-nCoV in Wuhan, China, the COVID-19 has escalated and SARS-CoV-2 has spread rapidly to most of the countries in the world. Up to March 8, 2020, there are more than 100000 confirmed cases around the world. As the 2019-nCoV is highly contagious and the transmission dynamics is still not fully understood. There have been some reports about the clinical features of the COVID-19 patients, the initial report from Wuhan showed that patients usually present with lower respiratory tract illness like fever, dry cough, and some severe patient may present dyspnea[3]. But with the spread of the virus, some studies from patients outside Hubei suggest that the severity of the disease outside Hubei seems to be lower than the pandemic areas. One of the biggest challenges now is how to screen and diagnose early. CT scan is a very important diagnostic method for lung diseases, and has been used in the diagnosis of COVID-19. However, there are few related studies. Up until now the chest radiological changes in COVID-19 patients has not been fully characterized except some case reports and the report from Shi[4].but the enrolled patients were from Wuhan area, in view of the lack of understanding of the disease and the lack of resources in the early stages of the disease, it may lead to selection bias. So the use of CT as a screening tool for suspected or mild patient is still not well understood, without a therapeutic vaccine or specific

antiviral drugs, early recognition is essential for the management of COVID-19. In this study, we try to describe CT imaging features of 30 Patients, to help clinicians better understand the significance of imaging, and to screen out the COVID-19 earlier.

Method

Research design

This study is a multi-center retrospective study. There were 30 confirmed patients admitted to the three hospitals from Jan 27, 2020 to Feb 11, 2020 who were diagnosed with COVID-19. All cases were diagnosed with 2019-nCoV pneumonia according to the WHO provisional guidelines[2]. positive of the SARS-CoV-2 nucleic acid test (The following primers and probe targeted to the envelope gene of SARS-CoV-2 were used: forward primer 5′TCAGAATGCCAATCTCCCCAAC3′; reverse primer 5′AAAGGTCCACCCGATACATTGA3′; probe 5′CY5CTAGTTACACTAGCCATCCTTACTGC3′BHQ1), and have been excluded from influenza A and B, respiratory syncytial virus, adenovirus, rhinovirus, etc. All CT scans were using one of the following scanners: UCT528 40-row 40-slice spiral CT (United Imaging, shanghai, china) ,Siemens 16-row CT (Emotion; Germany) and Siemens 64-row (SOMATOM Perspective),and the following parameters were used: tube voltage 130kv,tube current 30mAs ,tube voltage 120 kV. tube current was regulated by an automatic exposure control system. Images were reconstructed with a slice thickness of 1·5 mm or 1 mm and an interval of 1·5 mm or 1 mm, respectively. All scans were performed on the day of the patient's consultation with a CT examination, and were performed in the supine position at the time of the end of inhalation. All enrolled patients have an epidemiological history. The study was approved by the medical ethics committees of Sichuan Provincial People's Hospital, and informed consent from the patient or legal representative was obtained.

Research methods

We collected and analyzed demographics, clinical manifestations, laboratory test which were shown in Table 1.

Image interpretation

Images from all cases were collected and seen at Sichuan Provincial People's Hospital, and were analysed by two radiologists (H. P [a thoracic radiologist with 28 years'experience] and S. P[a radiology attending doctor with 7 years' experience in interpreting chest CT images]). All Digital Imaging and Communications in Medicine (DICOM) images from the CT studies were analyzed without access to clinical or laboratory findings. The evaluators independently and freely assessed the CT features using both axial CT images and multiplanar reconstruction images. CT imaging features recorded from our cohort were summarized in Table 2.

Each segment of the lung is examined to determine whether there are Ground Glass Opacities (GGO), Consolidation, Mix GGO and Consolidation, reticular shadows, and the affected lung segment, range,

location of the lesion, whether there was pleural effusion, and lymphadenopathy. We use semi-quantitative score system to evaluate the area of the lesion. The specific scoring rule is: the entire lung is divided into 5 lung lobes according to anatomy, and one lung lobe is 1 point, which accumulates in turn, with a maximum of 5 points[3]. The range of lesions in each lung lobe is scored on a scale of 0-4 points (0 points, no lesions; 1 point, 0-25%; 2 points, 25-50%; 3 points, 50-75%; 4 points, > 75%). Lesion progression score (0 points, no change; 1 point, a slight increase of 0-25%; 2 points, a moderate increase of 25-50%; 3 points, a significant increase> 50%). If the lesion is located outside one third of the lung, it is positioned as a peripheral lesion; otherwise, it is positioned as a central lesion. 21 patients underwent rescan of CT.

Result

28 patients travel history in the epidemic area，2 patients had the history of contact with confirmed patients. As of Feb 25, 2020, 8 patients were undergoing treatment, and 22 patients have a good recovery and discharged. The interval time from the onset of symptoms to the first CT scan was 1-16 days, the median average was (4 days). Most of the patient present fever, dry cough, Myalgia or fatigue. 47% of patients experienced varying degrees of decline in lymphocyte counts.

Of all patients, only one patient had a negative CT image. The most common CT manifestations were GGO, followed by mix GGO and consolidation (Figure 1). A few patients present pleural effusion. Consolidation (10/30), mix GGO and consolidation (14/30), fibrous stripes (7/30), solid nodules (1/30), solid nodules with halo signs (9/30), Reversed halo pattern (2/30), crazy paving (14/30), bronchial wall thickening (7/30), traction bronchiectasis (1/30) as showed in Table 2.

From the perspective of the distribution of the lesions, multi-lobe and segment involvement was predominant, with the lower lobe of the two lungs being the most commonly affected place (Figure 2). 21 of the 30 patients (70%) involved the left lower lobe, and 16 affected the left upper lobe (53%), 17 cases involved the right upper lobe (57%), 9 cases involved the right middle lobe (30%), and 21 cases involved the right lower lobe (70%). Of the 30 patients, only one lung segment was affected in 8 patients (8/30), and the remaining patients (22/30) were affected by two or more lung segments. The whole lung was involved in 9 patients (9/30). Each patient had an average of 3 segmental involvement. Lesion distribution: inner middle band (1/30), subpleural distribution (29/30); the lower lung involvement (28/30) is shown in Table 2.

Lesion severity: The average score of lung involvement severity in 30 patients was 3.5 points (range 0-8, standard deviation 2.3). There were 2 cases of interlobular pleural effusion (2/30) (a small amount of right effusion). Lymphadenopathy, cavities, and “tree in buds” sign were not found in all patients.

During the study period, 21 patients underwent a CT rescan, and the median average time between first chest CT and follow-up was 4.5 days (1-8 days). Of these, 10 patients underwent twice CT follow-ups and 5 patients underwent three times CT follow-up, five patients performed four times CT follow-ups, and one patient performed five CT follow-ups. There were 4 cases present mild exacerbation in CT image during

the follow-up, the imaging findings were consistent with clinical symptoms, the patient experienced significant dyspnea and decreased oxygen saturation. 12 cases present continuous improvement, and 5 cases present no significant change (Table 2). One patient had small amount of pleural effusion on the initial CT examination, and disappeared after the second CT examination. One patient had five times of CT examinations. The first CT scan showed solid nodules with halo signs in both lungs. During the second scan, the solid nodules became mixed GGO and consolidation. or GGO, the range increased, and right pleural effusion appeared. The third scan did not change much, the fourth scan showed the infected lesions increased slightly, and the pleural effusion also increased. The fifth scan, pulmonary infection became better, pleural effusion disappeared and the patient discharged with good prognosis (Figure 3). One lung cancer patient underwent a second scan after the initial CT examination, from the thickening of the bronchial wall at the first time to the presence of mixed GGO and consolidation in both lungs at the second time, and the GGO in the left upper lung increased, and the remaining lesions became lighter and smaller at the third time scan (Figure 4).

Discussion

It seems that the SARS-CoV-2 is a cross-species virus of animal origin that can infect humans. SARS-CoV-2 can attack human respiratory epithelial cells through the viral S protein with angiotensin-converting enzyme 2 receptor on human cell[5]. The most common viruses that can infect the human respiratory tract are influenza A and B, parainfluenza viruses, coronavirus, respiratory syncytial virus, and adenoviruses[6, 7].These viruses usually cause local respiratory tract infection. But these years, the SARS and MERS viruses from the coronavirus family have repeatedly caused large-scale epidemics and higher morbidity which become a threat to global public health. SARS and MERS viruses can cause many abnormal manifestations after infecting the human body, such as blood routine (decreased lymphocyte count), elevated body temperature, and decreased oxygenation. So, our cases were still mainly manifested by symptoms of infected lower respiratory tract such as fever, cough and dyspnea. These pathophysiology changes also cause abnormal imaging manifestations, which had been reported before[8, 9].

Among all CT imaging features in our research, GGO is the most common sign (96%). This is consistent with the previous CT performance of patients suffered SARS or MERS. According to the latest autopsy pathology report from Wang Fusheng et al the histological lesion was caused by bilateral alveolar injury with fibrous mucus exudation[10]. GGO is usually considered to be a manifestation of exudation. This is consistent with autopsy pathology. In our case, some patients present crazy paving (Figure 1c)□ and consolidation is also a common manifestation. The pathological results of LIU suggest that a large amount of viscous secretions can be seen from the alveoli on the cut surface[11]. Another CT feature is that the lesions have a multi-lobe distribution and usually at the outer band distribution. SARS-CoV-2 is mainly transmitted through droplets and aerosols. These particles with a diameter of several microns can smoothly enter the distal end of the respiratory tract and colonize[2]. It may be the reason that the lesions were usually in the outer zone and the multi-lobed distribution. This is also consistent with the pathological results[11]. At the same time, we noticed that in our research there were two cases showed a

small amount of pleural effusion (rare, localized, unilateral, all accompanied by inflammatory lesions near the effusion), which is similar to the previous report[4, 12, 13]. It is suggested that the pleural effusion is caused by direct damage to the lung tissue and rarely breaks through the pleural barrier by SARS-CoV-2. However, these two patients with pleural effusion have lower CT scores, and pleural effusions may have no relationship with CT scores. It is also coincided with the autopsy report[10] [11]. Therefore, if the patient present lot amount of pleural effusion it is less likely that he got infected by SARS-CoV-2. We also conducted a follow-up of some of these patients. During an average follow-up time of 4.5 days, the CT score of about 14/21 patients had significantly improved. However, there were of 4/21 patients had a progressive increase in CT image (three of them present dyspnea, decreased oxygen saturation). The remaining 3/21 patients had no significant change in the CT score. This result suggests that most patients have stable or improved conditions within one week after the consultation who can have good prognosis, but some patients may still have the possibility to progress to severe condition, physicians should pay close attention to these kinds of patients. In our research, we can see that in the patients whose CT score reached 7 points, and there might be a greater chance of progressing to severe illness. These patients also present more severe reductions in lymphocytes and increased C-reactive protein.

We also have some interesting findings. An enrolled lung cancer patient only present bronchial wall thickening at the initial CT scan, followed by 5 days of rescan of CT with multiple GGO and mixed GGO and consolidation. And we have another patient present fever, cough, and had an epidemiological history, the nucleic acid test was positive after admission and lymphocytes decreased, however, the initial and second time of CT scan were negative. The patient's fever symptom disappeared in about a week, discharged after 2 weeks, which suggesting that few patients can present positive of the nucleic acid test but negative in the CT scan.

The limitation of this study is the relatively small sample size. If the sample size increases, there may be more findings. We will continue to explore this topic in further studies. The patients we studied came from non-pandemic area. In addition, compared with previous reports, it seems that the overall CT score is not too high. This is worthy of more research to confirm. Our study and research from Li [14]both show that the patients from outside the pandemic area are less likely to progress to severe illness. We are not sure whether it is related to the gradual weakening of virulence during breeding the next generation of SARS-CoV-2, or it may also be related with adequate of medical resources and comprehensive response measures that different from Hubei province during the early stage of outbreak. Nevertheless, our research has enriched the clinical and imaging knowledge of COVID-19 and bring some help for physicians.

Conclusion

First, the CT scan still play an important role in screening the COVID-19, most of the image present positive signs. The CT manifestations are mainly subpleural, multiple GGO. Second, CT might can predict the severity or whether he will progress to severe illness. Third, a small number of patients may be missed

if they are based on CT findings alone, which should be closely combined with the patient's epidemiological history and nucleic acid test. We are continuing to expand the sample size and perform deeper analysis of CT images to try to find a better method for the diagnosis of COVID-19.

Abbreviations

CT：Computed Tomography

COVID-19：Corona Virus Disease 2019

SARS-CoV-2：Severe Acute Respiratory Syndrome Corona Virus 2 GGO： 2019-nCoV： 2019-Novel Coronavirus

GGO：Ground Glass Opacities

CDC：Centers for Disease Control and Prevention

WHO：World Health Organization

DICOM：Digital Imaging and Communications in Medicine

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Tables

Table 1 Demographic and baseline characteristics of COVID-19 patients

Characteristics	All patients (n=30)
Age, years	42.6(14.4)
>50	8 (27%)
≤50	22 (73%)
Sex	
Male	12 (40%)
Female	18 (60%)
Epidemiological history to Hubei Province	21 (70%)
Symptoms	
Fever	19 (63%)
Cough	18 (60%)
Myalgia or fatigue	12 (40%)
Sputum	10 (33%)
Dizziness	3 (10%)
Diarrhea	3 (10%)
Dyspnea	2 (7%)
Chest tightness	2 (7%)
Respiratory rate >24 bpm	2 (7%)
Familiar cluster cases	13 (43%)
Laboratory results	
Leukocyte count, ×10 /L	5.39(2.45)
<10	29 (97%)
≥10	1 (3%)
Lymphocyte count, ×10 /L	1.20(0.54)
<1.0	14 (47%)
≥1.0	16 (53%)
Neutrophil count, ×10 /L	4.02(2.21)
C-reactive protein, mg/L	16.86(25.90)
Platelet count, ×10 /L	188(63)
<100	2 (7%)
≥100	28 (93%)
Procalcitonin (ng/mL)	
<0.1	22 (89%)
≥0.1	3 (11%)
Comorbidities	
Hypertension	2 (7%)
Arthrolithiasis	1 (3%)
Diabetes	1 (3%)
Fracture	1 (3%)

Table 2 Initial CT features ,distribution and Lung Severity Score in 30 Patients

CT Findings	Number	%
GGO	29/30	96%
Crazy paving	14/30	47%
Mix GGO and Consolidation	14/30	47%
Consolidation	10/30	33%
Reversed halo pattern	2/30	37%
Solid nodules with halo signs	9/30	30%
Fibrous stripes	7/30	23%
Bronchial wall thickening	7/30	23%
Solid nodules	1/30	3%
Traction bronchiectasis	1/30	3%
Pleural effusion	1/30	3%
Lymphadenopathy	0/30	0%
Location		
Sub-pleural	29/30	96%
Left Lower Lobe	21/30	70%
Right Lower Lobe	21/30	70%
Right Upper Lobe	17/30	57%
Left Upper Lobe	16/30	53%
Right Middle Lobe	9/30	30%
Medial lobe of lung	1/30	3%
Lobe affected	**Number**	**%**
0	1	3%
1	7	23%
2	4	13%
3	4	13%
4	5	17%
5	9	30%
Total Lung Severity Score		
Total	106	
Mean	3.53	
Range	0-8	

Figures

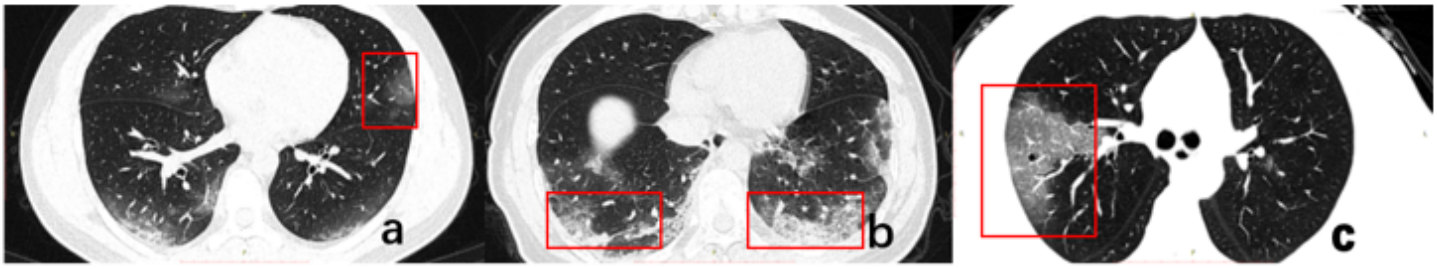

Figure 1. Typical CT features and case report of COVID-19 patient. **(a)** GGO **(b)** Mix GGO and consolidation **(c)** Crazy paving.

Figure 1

[See figure]

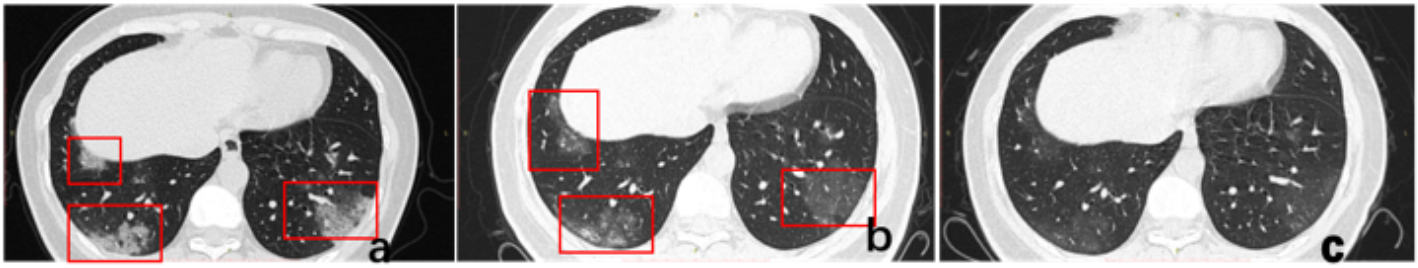

Figure 2. A middle age male with epidemiological history, presenting with cough and fever in fever clinic **(a)** Initial CT Axial thin-section non-contrast present multiple GGOs in the subpleural in the lower lobe of both lungs **(b)** Four days follow-up CT image present fewer peripheral ground-glass lesion **(c)** Ten days follow-up CT image present significant improvement.

Figure 2

[See figure]

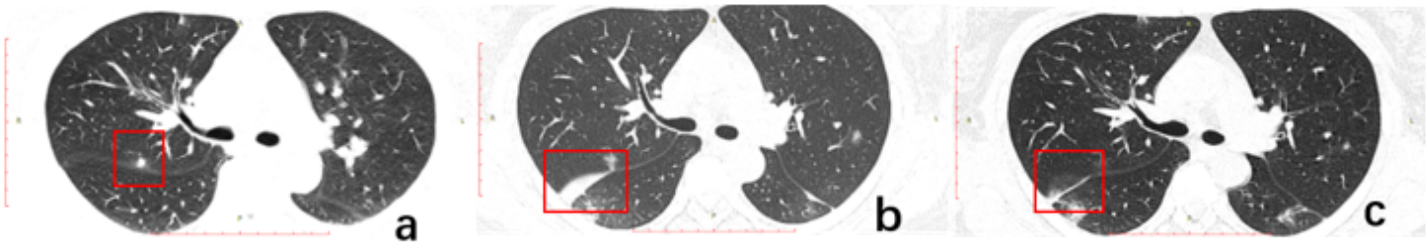

Figure 3. A middle age male with epidemiological history, presenting with cough in fever clinic **(a)** One days Axial thin-section non-contrast CT scan present Subpleural nodule with halo sign **(b)** Four days follow-up CT image present pleural effusion in the right interlobe **(c)** Eight days follow-up CT image present pleural effusion absorption

Figure 3

[See figure]

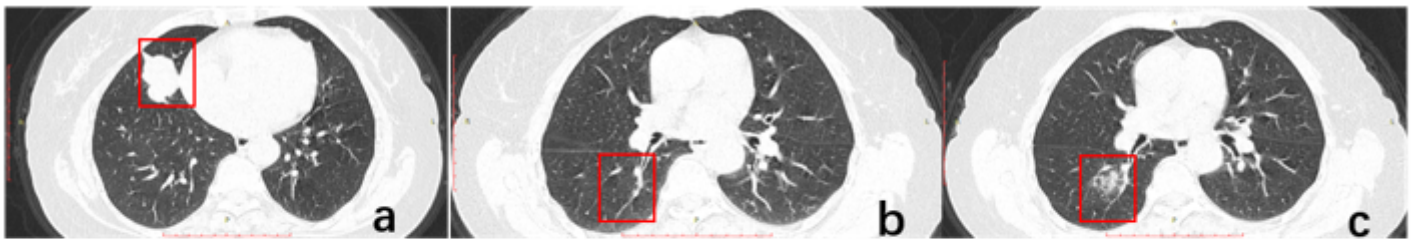

Figure 4. An old age female lung cancer patient with epidemiological history, presenting with myalgia and a dry cough in fever clinic **(a)** Initial CT present tumor in middle lobe of right lung ; **(b)** Initial CT present thickening of branch wall in the right lower lobe; **(c)** Five days follow-up CT image present new GGO appears for the first time at the same level.

Figure 4

[See figure]

Supplementary Files

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