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COVID-19 Dynamic Computed Tomography (CT) Performance and Observation of Some Laboratory Indicators

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AE 1 **Xiangsen Jiang***

CE 1 **Zudong Yin***

D 2 **Tao Wang**

B 2 **Nailiang Zhai**

C 2 **Feng Lu**

BD 3 **Chunhua Zhan**

AF 4 **Qizheng Han**

AF 5 **Changjiang Feng**

1 Department of Radiology, Shandong Provincial Third Hospital, Cheeloo College of Medicine, Shandong University, Jinan, Shandong, P.R. China

2 Department of Respiratory and Critical Care Medicine, Binzhou Medical University Hospital, Binzhou, Shandong, P.R. China

3 Department of Infection Control, Xishui County People's Hospital, Huanggang, Hubei, P.R. China

4 Department of Respiratory and Critical Care Medicine, Shandong Provincial ENT Hospital, Shandong Provincial ENT Hospital Affiliated to Shandong University, Jinan, Shandong, P.R. China

5 Department of Traditional Chinese Medicine, Xishui County People's Hospital, Huanggang, Hubei, P.R. China

* Xiangsen Jiang and Zudong Yin contributed equally to this article

Corresponding Authors:

Qizheng Han, e-mail: hanqizheng321@163.com, Changjiang Feng, e-mail: fcj2567@163.com

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Background:

Chest CT has an essential role in the detection and evaluation of novel coronary pneumonia (COVID-19) and has been regarded as a critical supplement for RT-PCR. This study explored the dynamic CT manifestations of COVID-19 at different times and the value of some laboratory indicators for clinical guidance.

Material/Methods:

This retrospective review included 44 patients who were infected with COVID-19. The dynamic chest CT and laboratory findings were obtained from electronic medical records. The intervals between onset and CT scans and the dynamic changes of the lesions were recorded. The above data were reviewed, sorted, and analyzed by using SPSS 21.0 software.

Results:

From the time of onset, the dynamic image of the lungs became more complete. Fibrous cord shadow absorption in the lungs were observed. Experimental indicators, biochemical indicators of lymphocytes, and protein series were decreased to varying degrees, while erythrocyte sedimentation, fibrinogen, and D-dimer were increased to varying degrees.

Conclusions:

The dynamic changes of CT images of lungs of COVID-19 patients, combined with the clinical manifestations and laboratory indicators of patients, can help guide clinical diagnosis and treatment.

MeSH Keywords:

COVID-19 • Tomography Scanners, X-Ray Computed • Tomography, X-Ray Computed

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Background

Novel coronavirus pneumonia refers to pneumonia caused by 2019 Novel Coronavirus (2019-nCoV) infection. On February 11, 2020, the World Health Organization (WHO) named the disease caused by the novel coronavirus infection as COVID-19. On February 22, 2020, the National Health Commission announced that the English name of the novel coronavirus pneumonia was COVID-19 [1]. Because COVID-19 is highly contagious, and the population is generally susceptible, early diagnosis and early isolation and treatment are of great significance for disease prognosis and epidemic control. At present, COVID-19 virus nucleic acid positivity or viral gene sequencing positivity is an important basis for diagnosis. However, chest CT, as the most commonly used imaging examination for respiratory diseases, has an irreplaceable role in the detection and evaluation of COVID-19 [2]. This study dynamically observed the imaging characteristics of patients who were infected with COVID-19 from the onset of clinical symptoms until recovery. We also assessed some laboratory indexes of patients to provide a reference for the clinical diagnosis and management of COVID-19.

Material and Methods

General information

Clinical records of inpatients and severe patients in the third pneumonia ward in Xishui County People's Hospital of Huanggang City, which was taken over by Shandong Medical Team of Hubei Province, were retrospectively reviewed from January 25, 2020 to March 10, 2020. Including age, gender, clinical history, laboratory test results, and chest CT imaging data. Patients were diagnosed according to the diagnostic criteria of the "New Coronavirus Pneumonia Diagnosis and Treatment Plan (Trial Version 6)". A total of 44 patients – 27 males (61.4%) and 17 females (38.6%) – with complete CT imaging data were included.

Research methods

Chest CT scans were conducted using Anke ANATOM 32-row spiral CT scanners. Patients wore masks during the entire examination. Protective measures were taken for the scanning technicians as required. After patients were placed in a supine position with arms raised and advanced head, continuous spiral scanning was performed from the lung apex to lung bottom during a single breath-holding of the patient. The tube voltage was 120 kV with automatic tube current modulation or 160 Ma, the layer thickness was 7 mm, and section thickness was 1 mm for reconstructions.

Patient age, gender, epidemiological history, and clinical symptoms (e.g., fever, cough, chest tightness, and fatigue) were recorded by reviewing the medical records. The interval between the onset of symptoms and first CT scans was calculated. The images were reviewed independently by an experienced radiologist and a clinician, and the results of the lesion site, number, shape, density, border, pleural effusion, and hilar and mediastinal lymph nodes on each CT examination were recorded. Disagreements during the evaluation were resolved by discussion and consensus. We also assessed and recorded some laboratory indicators of patients, including white blood cells, lymphocytes, lymphocyte ratio, erythrocyte sedimentation, C-reactive protein, prealbumin, total protein, albumin, globulin, fibrinogen, and D-dimer.

Statistical analysis

Retrieved data were recorded into Microsoft® Excel for Mac (version 16.30) and analyzed. SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Count data were assessed using the chi-square test, and $P < 0.05$ was considered statistically significant.

Results

A total of 44 patients – 27 males (61.4%) and 17 females (38.6%) – diagnosed with COVID-19 were included, with an average age of 50.8 (27–75) years. There were 40 patients (89.5%) who had a history of living, traveling, or being in close contact with confirmed COVID-19 patients, 2 patients (5.3%) personally denied contact history, 2 patients (5.3%) had unknown contact history, 2 patients had a previous history of hypertension and diabetes, and 2 patients had a previous history of hypertension. Fever (86.4%) and cough (79.5%) were the main symptoms, and other symptoms were chest tightness (25.0%), fatigue (15.9%), and diarrhea (5.3%). The basic manifestations and dynamic changes of the time course between the onset of clinical symptoms and CT scan are displayed in Table 1 and Figure 1, respectively. The lesions were scattered in both lungs, in multiple peripheral areas of the lung field, and on the dorsal side.

At 1–6 days after onset, scattered and multiple lesions were observed in both lungs in 33 patients (75.0%); 3 patients had 4 lung lobes involved; 3 patients had 3 lobes involved, 3 had 2 lobes involved, and only 2 had involvement of a single lobe. In the early stage (1–3 days), 21 (100%) patients presented with patchy wedge-shaped, fan-shaped, round, or irregular ground-glass lesions, some of which had the long axis parallel to the adjacent pleura (Figure 2). Three patients (14.3%) presented with sub-solidified ground-glass-like shadows with uneven density, and 11 (52.4%) showed reticular interlobular

Table 1. Dynamic changes of chest CT scans of COVID-19 patients at different times of onset.

Onset of clinical symptoms and CT interval	Number of cases n	Progression of lesion n (%)	Absorption of lesion improved n (%)
1~3 d	21	0	0
4~6 d	22	9 (40.9)	0
7~9 d	36	20 (55.6)	7 (19.4)
10~12 d	28	13 (46.4)	14 (50.0)
13~15 d	36	5 (13.9)	31 (86.1)
16~18 d	32	1 (3.1)	31 (96.9)
≥19 d	36	0	36 (100.0)
χ^2		60.52	138.15
<i>P</i>		<0.001	<0.001

septal thickening. At 4–6 days, 9 patients (40.9%) had disease progression, which was characterized by increased ground-glass shadows, enlargement, increased density, patchy consolidation and sub-consolidation, partial fusion, and reticular interlobular septal thickening, and the remaining 13 were patients who received the first CT examination. In 20 patients (55.6%) lesions had progressed at 7–9 days, and the lesions were absorbed in 7 patients (19.4%), showing shrinking and reduced lesions, reduced lesion density, blurred edges, and fibrous cord shadow. There were 13 patients (46.4%) with disease progression from 10 to 12 days, and lesions were absorbed in 14 patients (50.0%). The lesions were progressed in 5 patients (13.9%) and absorbed in 31 patients (86.1%) from 13 to 15 days. One patient (3.1%) had disease progression on the 17th day, and 31 had better absorption from 16 to 18 days. In the ≥19-day CT re-examination, 36 cases of lesions had further shrinkage, reduction, and density became lighter, but the absorption of lesions was slower than in the earlier stage, among which 4 cases were slightly absorbed, and the re-examination showed that fibrous cord-like shadows disappeared in 2 cases (Figure 3). Small amount of pleural effusion was detected in 1 case and no enlarged lymph nodes were noticed in the hilar mediastinum.

Laboratory observation indicators showed the following: white blood cell count was increased in 2 cases (4.5%), within normal range in 23 cases (52.3%), and decreased in 19 cases (43.2%), 17 cases (38.6%) had decreased lymphocyte count, and 29 cases had decreased lymphocyte ratio (65.9%), 31 cases (70.5%) had increased ESR, 40 cases (90.9%) had increased C-reactive protein, 36 cases (81.8%) had decreased prealbumin, 39 cases (88.6%) had decreased total protein, albumin was decreased in 16 cases (36.4%), globulin was decreased in 33 cases (75.0%), fibrinogen was increased in 35 cases (79.5%), and D-dimer was increased in 24 cases (54.5%).

Statistical analysis of patients' CT images showed that the progression and absorption of lesions were significantly different at different time periods ($P<0.05$). The CT scans showed that the disease progressed from the clinical symptoms to 7–9 days, and the lesions began to be absorbed at 13–15 days.

Discussion

As a highly contagious disease, COVID-19 is mainly transmitted via droplets and contact. In a relatively closed environment, COVID-19 can be transmitted through aerosol for a long time, and patients in the incubation period and asymptomatic virus carriers are also infectious [2,3]. The incubation period is generally 1–14 days, and most show symptoms 3–7 days after infection. There are very few cases in which the incubation period exceeds 14 days, and the longest can reach 24 days [4]. Fever, cough, and fatigue are the main clinical manifestations of COVID-19 in the early stage. A few patients present with other symptoms such as nasal congestion, runny nose, sore throat, myalgia, and diarrhea. The clinical manifestations of the 44 patients in this group, in which 38 had fever (86.4%) and 35 had cough (79.5%), are in line with other studies. At present, the diagnostic criteria are mainly based on real-time fluorescent RT-PCR of respiratory specimens or blood specimens to detect novel coronavirus nucleic acid-positive or viral gene sequencing, which are highly homologous with known novel coronaviruses. Although the detection of novel coronavirus in respiratory specimens by RT-PCR can generally obtain results within 4–6 hours [5], various factors can ultimately affect the accuracy of nucleic acid detection results, and false-negative results can occur. Recently, a study compared the sensitivity of RT-PCR and CT in COVID-19 detection among 1014 patients, and found that 59% had positive RT-PCR results, while 88% had positive chest CT scans, suggesting that the sensitivity of

Figure 1. CT findings in a 44-year-old male patient who had a dry cough and intermittent fever for 10 days. **(A)** Six days after the onset of symptoms, CT examination showed patchy ground-glass-like density shadow in the left lower lobe and circular ground-glass-like density shadow in the right lower lobe. **(B)** On day 13, the range of ground-glass-like shadows of the lower lobe of both lungs increased with increased density, and some consolidations occurred. Irregular ground-glass-like density shadows appeared in the lower lobe of the right lung and the upper lingual segment of the left lung. **(C–F)** On days 17, 20, 24, and 31, the range of lesions gradually decreased with decreased density, and a few fibrous cord shadows appeared.

Figure 2. (A, B) CT findings in a 63-year-old male patient who had a history of close contact in the epidemic area and presented with fever for 9 days. Six days after the onset of symptoms, patchy wedge-shaped, fan-shaped, round or irregular ground-glass lesions were scattered in the peripheral area of the lung field and dorsal aspect of 2 lungs.

CT was 97% based on positive RT-PCR results in detection of COVID-19 [6]. Researchers recently found that in use of CT and nucleic acid detection in the diagnosis of COVID-19, there are more factors that cause false-negative results during nucleic acid detection [7]. Therefore, chest CT is an important supplementary tool for RT-PCR in the diagnosis of COVID-19 and has irreplaceable significance.

Chest HRCT is currently the imaging method used for screening COVID-19. COVID-19 can be divided into 4 stages according to CT scans of the lungs, the evolution of the lesions, and the imaging performance in overlap of different stages [8–12]. In the early stage (commonly within 1 week of onset), single or multiple lesions were mostly noticed in the periphery of the lungs or under the pleura. With progression of disease, the GGO density gradually increased, and thickened small blood vessel shadows or local lobular septum thickening were seen. There are multiple lesions in advanced stage, which are manifested by increased GGO, partial fusion, or accompanied by consolidation, gradually increasing density, and bilateral asymmetric subpleural distribution. For the severe stage (critical illness), which is equivalent to the terminal stage of the disease, bilateral lung lesions showed diffuse and extensive further progression, and some of them present as “white lung”. The lesions developed rapidly, becoming solid, and, combined with GGO, bronchial inflation signs can be seen, which can increase by more than 50% in 48 hours. During the transition period, the density of the lesions decreased, shrank, or were absorbed, and fibrous cord-like shadows were seen in some cases.

The 44 patients observed in this study received timely and effective treatment without severe deterioration or death. However, during the entire diagnosis and treatment process,

the patient’s chest CT results changed dynamically with evolution of the disease. There have been reports of dynamic changes of CT manifestations in China [13,14]. Because there is often a certain time interval between the onset of symptoms and hospitalization, unlike previous observations, the time of appearance of a patients’ first symptoms was defined by carefully consulting the relevant case data in our study. The basic manifestations and dynamic changes of clinical symptoms and different CT scan intervals were observed and analyzed for the first time. This study showed that the early manifestations of the disease were mainly GGO, which represents acute tissue damage. With the development of the disease, GGO can be increased, enlarged, and partially fused, and a few lesions can also be directly absorbed, which is basically consistent with the most common conclusion of previous studies [13], that GGO is found 2–5 days after admission. With the further development of the disease, GGO gradually decreased, consolidation lesions gradually increased, and the density of most lesions gradually increased unevenly.

In the course of disease improvement, consolidation was gradually absorbed, density decreased unevenly, scope was reduced, and edge was unclear. Some lesions may have fibrous cord shadow, which can appear from the beginning of absorption, and shows a gradually increasing trend. With the continuous review of CT, absorption decreased. We observed that the fibrous cord shadow was gradually reduced and the edge gradually became clearer or even completely disappeared. In 2 patients, the cord shadow partially disappeared after 19 days. This may be related to the exudative component of the lesion, which can be further observed in subsequent follow-up reviews. During the dynamic observation of the outcome of the disease, we found that the disease progressed significantly at

Figure 3. CT changes in a 60-year-old male patient who had a history of close contact in the epidemic area and presented with cough and low fever for 7 days. (A, B) 14 days after the onset of symptoms, fibrous cord-like shadows and a little ground-glass like shadows in the lower lobe of the right lung. (C, D) 37 days after the onset of symptoms, CT re-examination showed that the fibrous cord-like shadow has been basically absorbed in the right lower lobe.

4–9 days, was most significant at 7–9 days (55.6%), then disease progressed slowly at 10–12 days and the absorption of the lesions become apparent, and the absorption of the lesions was obvious at 13–15 days (86.1%). These results differ from a previous study [13] reporting that patients with lung lesions progressed most obviously at days 6–9 of admission, and the absorption was more obvious at 10–14 days. This may be because our data were based on the onset time. If the time from symptom onset to hospital admission is excluded, the above conclusions are basically consistent.

As in previous studies, we assessed decreased white blood cell and lymphocyte counts, as well as increased C-reactive protein, erythrocyte sedimentation rate, fibrinogen, and D-dimer [2,15]. C-reactive protein and erythrocyte sedimentation rate elevation often appeared in the early and middle stages of COVID-19

disease progression. The imaging manifestations were mainly ground-glass-like high-density shadows and consolidation shadows. C-reactive protein and erythrocyte sedimentation rate returned to normal range in the terminal stage in some patients, perhaps due to the rapid increase of CRP and the acceleration of ESR when human tissue being inflamed and infected in the early and middle stages. However, in the late stage, inflammation and infection were gradually controlled, and the absorption and density of lung lesions were decreased. A recent study indicated remarkably higher ESR and CRP levels in COVID-19 patients than in healthy controls [16]. Ma et al. [17] showed that the CT score was proportional to the onset time and CRP according to the CT performance score, which was also consistent with our results. A decrease in the lymphocyte ratio was also observed in this group of data. Previous studies [17] used a semi-quantitative description of chest CT involvement,

and showed a negative correlation between CT score and lymphocyte count. In the present study, the relationship between lymphocyte count and imaging performance was not further observed, and will be further improved in subsequent studies. Results of prealbumin, total protein, albumin, and globulin indicated that most patients experienced a decrease in albumin during the onset of disease. Only part of the patients' albumin recovered to the normal range at the later stage of absorption. So far, no relevant report has been found on this topic. The possible causes are: vascular endothelial damage and capillary leakage caused by virus infection; or anorexia resulting in reduced nutrition intake, the catabolism of the body greater than the anabolism, resulting in the negative nitrogen balance of the body; or respiratory symptoms such as cough, expectoration, and other systemic diseases like low fever resulting in increased consumption. The specific causes need to be further explored.

The present study is the first to use the time of appearance of clinical symptoms and the interval between each CT scan as observation nodes. At the same time, some fibrous cord

shadows could be absorbed, and the ratio of lymphocytes and protein series in laboratory examinations were reduced to varying degrees. The limitations of this study are that the sample size was small, and the mechanism for the absorption of fibrous cord-like shadows and the abnormality of some laboratory indicators have not been further analyzed. There are many factors that affect the imaging performance and laboratory tests, such as drugs used and underlying diseases, which will be further addressed in future studies.

Conclusions

Lung CT scans can fully display the distribution, morphology, and density changes and dynamic changes of outcomes of patients with COVID-19 during the process of the disease. Clinical manifestations combined with laboratory indicators of patients can help guide early clinical diagnosis, early isolation, and early treatment of COVID-19 and can be regarded as a basis for evaluating the therapeutic effect of comprehensive clinical treatment.

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