Radiological diagnosis of COVID-19: expert recommendation from the Chinese Society of Radiology (1st edition)

Chinese Society of Radiology, Chinese Medical Association
Corresponding author:
Guo Youmin, Department of Radiology, the Affiliated Hospital of Xi'an Jiaotong University, Xi'an 710061, China, Email: cjr.guoyoumin@vip.163.com;
Liu Shiyuan, Department of Radiology, Changzheng Hospital, Second Military Medical University, Shanghai 200003, China, Email:cjr.liushiyuan@vip.163.com

[Abstract] Since December 2019, patients with unexplained pneumonia have been found in Wuhan, Hubei Province. The pathogen has been confirmed by the World Health Organization and named 2019-Novel Coronavirus, the pneumonia caused by which is called Coronavirus Pneumonia Disease (COVID-19). Radiological diagnosis is an essential part of COVID-19 diagnosis and treatment. Leaded by Chinese Society of Radiology, the National Society Members and part of the Cardiothoracic Committee members and other experienced experts were organized to discuss and compile the"*Recommendation*", in order to further standardize the radiological diagnosis of COVID-19. It describes and summarizes the radiological examination process, imaging findings, imaging stages, imaging prognosis, as well as the clinical value of radiology in suspected case, clinically diagnosed case, follow-ups, and discharge evidence based on radiological findings. Also, the clinical characteristics and radiological features of children's COVID-19 are described. Overall, the Recommendation aims to guide the medical units at all levels for the radiological diagnostic manipulation.

Since December 2019, patients with unexplained pneumonia have been found in Wuhan, Hubei Province, which attracted great attentions from government at all levels and administrative departments of health. Disease control agencies, medical units and scientific research institutions were organized rapidly to carry out investigations, surveys, intensive medical cares and bench-side as well as bedside researches. The pathogen was identified as a novel coronavirus, and the pneumonia caused by the pathogen infection was named coronavirus pneumonia disease. Later on, the World Health Organization (WHO) confirmed the Chinese claims, and named the virus 2019-novel Coronal virus (2019-nCoV), and the official classification of the International Committee on Taxonomy of Viruses (ICTV) was Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The official name of the disease caused by the virus has announced by the WHO as COVID-19[1-8].

Radiological examination and diagnosis is one of the crucial parts in the diagnosis and treatment of COVID-19. In order to further improve and standardize the diagnosis of COVID-19, and ensure medical quality and safety, leaded by Chinese Society of Radiology, its National Society Members and part of the Cardiothoracic Committee members as well as other experienced Chinese experts were organized to discuss and compile this *Radiological diagnosis of novel coronavirus pneumonia: expert recommendation from the Chinese Society*

of Radiology (First edition). The Recommendation aims to guide the radiological diagnostic work of medical units at all levels.

This recommendation was drafted based on the following documents: *Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is Suspected. Interim guidance* [5], *Infection prevention and control during health care for when novel coronavirus (nCoV) infectionis suspected. Interim guidance* [6], *Diagnosis and Treatment Protocols of COVID-19 Infection (6th edition)* [7], *Technical guidelines for novel coronavirus infection prevention and control in medical institutions (First Edition)* [8]. It also collected practical experiences of radiological diagnosis of COVID-19 in Wuhan and other domestic hospitals.

1 Overview of COVID-19

1.1 Etiological characteristics

The 2019-nCoV is a member of the β-coronavirus family with envelope. Its particle is generally spherical or oval, expect sometimes show its pleomorphism. Diameter varies from about 60 to 140 nm. Its genetic characteristics are significantly different from those of Severe Acute Respiratory Syndrome related Coronavirus (SARSr-CoV) and Middle East Respiratory Syndrome related Coronavirus (MERSr-CoV). Current studies show its over 85% homology with SARS-like coronavirus (bat-SL-CoVZC45) in bat [7]. 2019-nCoV can be observed in human respiratory epithelial cells at about 96 hours after isolation and culture in vitro, while it takes about 6 days to isolate and culture in Vero E6 and Huh-7 cell lines.

The understanding of the physicochemical properties of coronaviruses mostly comes from the studies of SARSr-CoV and MERSr-CoV. The virus is sensitive to heat. Virus inactivation can be achieved by keeping at 56℃ for 30 minutes, 75% ethanol, chlorine-containing disinfectant, hydrogen peroxide disinfectant, chloroform and other lipid solvents. However, chlorhexidine cannot effectively inactivate the virus.

1.2 Epidemiological characteristics

1.2.1 Source of infection

Human beings with the COVID-19 are the main source of infection. Human beings with asymptomatic infection may also be a source of infection.

1.2.2 Route of transmission

Respiratory droplets and close contact transmission are two main routes of transmission. Aerosol is a potential route of transmission in the event of exposure to high aerosol concentration for a long time in a relatively closed environment.

1.2.3 Susceptible population

Human beings are generally susceptible.

1.3 Clinical characteristics

1.3.1 Clinical manifestations

Based on the current epidemiological data, the incubation period may last for 1 to 14 days, up to 24 days, mostly 3 to 7 days. The most common manifestations were fever, dry cough, and fatigue, and less common symptoms were nasal obstruction, rhinorrhea, sore throat, myalgia and diarrhea. Severe cases were more likely to developed dyspnea and / or hypoxemia a week after the onset of symptoms and severe cases may rapidly progress to

acute respiratory distress syndrome, septic shock, intractable metabolic acidosis and coagulation dysfunction. Notably, critically ill patients could develop be low or mild fever, or even n do not experience fever during the course.

Mild patients only presented with low fever, mild fatigue, and even no signs of pneumonia.

As for the current cases, most patients had a good prognosis, with only a few were in critical condition. Elderly patients and patients with underlying comorbidities may have a poorer prognosis. Symptoms of children were relatively mild.

1.3.2 Laboratory test

In the early stage of the onset, patients had normal or decreased white blood cell count and lymphocytopenia. Some patients had elevated liver enzymes, lactate dehydrogenase (LDH), creatase and myoglobin. Increased troponin was seen in some severe cases. Most patients had normal levels of procalcitonin but increased C-reactive protein (CRP) and erythrocyte sedimentation rate on admission. In severe cases, D-dimer level was higher and lymphocytes of peripheral blood progressively decreased. Heavy type and critical type patients often had elevated inflammatory factors. Novel coronavirus nucleic acids can be detected in nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, and feces. In order to improve the positive rate of nucleic acid detection, sputum is recommended, and lower respiratory tract secretions is recommended for patients with tracheal intubation. The specimens should be sent for test as soon as possible after the collection.

2 Radiology Examination of COVID-19

2.1 Radiology examination procedure

Radiology examination plays an important role in the diagnosis and treatment of COVID-19. The recommended procedure is listed as follows (Figure 1)

2.2 DR

For DR examination, the missed diagnosis rate of COVID-19 is high. At the initial stage, DR images usually appears normal. So, it is not recommended to use DR on admission. As the disease progresses, later representative findings include patchy opacification or multifocal consolidation. Severe cases can appear as "white lung" with severe hypoxemia.

2.3 CT

For radiological examination of COVID-19, the first choice is CT scan. The slice thickness should be less than 5 mm, and images are reconstructed with 1.0 ~ 1.5mm in thickness. By this way, radiologist can observe lesions on transverse, sagittal and coronal planes, which is beneficial for early detection and evaluation of COVID-19.

3 Radiology findings of COVID-19

3.1 X-ray findings

The chest X-ray film usually appears normal at the initial stage. The common type patients with positive nucleic acid test mostly manifest as localized patchy or multi-segmental patchy opacification in the outer zone and sub-pleura space of bilateral lungs (Figure 2). In severe cases, multifocal consolidation can be found in bilateral lung fields, and can merged into large consolidation, with small pleural effusion (Figure 3). When lesion aggravation continued, later

images could show as diffuse consolidation, which we call it the "white lung" (Figure 4), accompanied by a small amount of pleural effusion.

3.2 Chest CT findings

3.2.1 Common CT findings

There are no abnormal findings on CT in the early stage of some moderate type of patients. With the progression of disease, abnormal CT findings could appear, showing patchy ground-glass opacity (GGO) or focal peri-bronchovasular GGO. The common CT findings include multiple patchy GGO or consolidation with peri-bronchovascular and subpleural distribution, thickening of small vessels and" crazy paving "sign.

For the progressive stage of COVID-19, many CT findings coexist, including GGO, consolidation, nodule and even fibrosis, predominantly in the peripheral, subpleural and basal of lung. The air bronchogram sign and thickening of bronchial wall are common in consolidation. Distortion of lung architecture and thickening of adjacent pleura or fissures may be seen in fibrosis. Small amount of pleural effusion can occur, while lymphadenopathy is rare.

3.2.2 CT staging system

At present, there is lack of systematic comparison study between imaging findings and clinical case-control data. There is no big data research about the imaging stage and grading of COVID-19. Based on the current clinical practice, the COVID-19 is temporarily divided into four stages: early stage, progressive stage, severe stage and resolved stage according to the extent of pneumonia.

3.2.2.1 Early stage

It shows single or multiple GGO, nodule (Fig. 5, 6), small patchy GGO (Fig. 7, 8) or large patchy GGO (Fig. 9, 10). The majority of GGO shows ill-defined interface, while some with well-defined interface. The lesions are located predominately in the middle and lower lung lobes with subpleural (Fig. 5, 6), peri-fissure (Fig.7, 8), or peri-bronchovascular distribution. The thickening of bronchial wall (Fig. 11), thickening of small vessels, air bronchogram sign (Fig. 9) and the thickening of adjacent interlobular pleura are common (Fig. 12).

Some large patchy GGO with subsegmental distribution and increased small vessels, seems like the fine grid shadow or "crazy paving " sign (Fig. 13). Some GGO shows "reversed halo" sign (Fig. 14).

3.2.2.2 Progressive stage

Multiple new lesions similar to those in the early stage appeared. Most of the original lesions would enlarge, with the presence of consolidation varying sizes and density. Nodular, halo sign and air bronchogram sign in the consolidation could be seen. Fusion or partial absorption of the original GGOs or consolidation could be seen. The scope and shape of lesions often changed after the fusion, which might not distribute along the bronchovascular bundle completely.

3.2.2.3 Severe stage

With further progression of the disease, diffuse consolidation with increased density would occur. The bronchiectasis and air bronchogram sign appeared. Patchy GGOs were shown in non-consolidated regions. "White lung" appeared when most of the lungs involved (Figure 20). Thickened interlobular and bilateral pleura were commonly seen with small amount of pleural effusion, which appeared as free or locally encapsulated. The minority of the patients

with basic diseases or aged showed extension, distortion and densification of the lesions as the disease progressed. The "white lung" might appear when severely advanced.

3.2.2.4 Resolved stage

After effective treatment, the vast majority of COVID-19 patients tend to be stable and improved, showing that the range of lesions diminished, the density gradually decreased, the number of lesions reduced. The GGOs can be fully absorbed (figure 21, 22). In some cases, the lesions can evolve into fibrous cord in a relatively short period (figure 23~26). But whether fibrosis is the characteristic of disease reversal needs further information accumulation.

To be noted, the staging based on CT findings is not completely corresponding to the disease severity (i.e., mild, severe, critical and improved). A further gradually correction based on large-sample studies is required.

In view of the fact that the evolution of COVID-19 are not clear at present. A previous longitudinal CT study of SARS [10] demonstrated that the consolidation could disappear or reduce to GGOs, while GGOs could persist or even develop to interlobular septal thickening, fibrosis and bronchiectasis. Thus, large-sample and multicenter researches are needed in order to explore disease evolution process and regularity from the perspective of radiology.

4 The role of radiology in the diagnosis of COVID-19

As one of the main diagnosis methods of COVID-19, radiology has the value of lesions detection, diagnosis, classification, and follow-up, and to facilitate clinical evaluation, treatment, and management. However, it should be mentioned that radiological diagnosis is not the confirmed diagnosis, and the reference standard for the diagnosis of the COVID-19 is the positive 2019-nCoV nucleic acid test.

According to observations in clinical practice, the patients with COVID-19 displayed the following: ① Novel coronavirus nucleic acid tests were positive, but the initial radiological examinations were negative, or the abnormalities were found in re-examinations (Figures 27, 28); ② The patients were asymptomatic but with exposure history. The chest CT scans revealed lesions in the lungs, and infections were confirmed by positive novel coronavirus nucleic acid tests subsequently; ③ The infected patients had exposure history and obvious lesions in the lungs. The novel coronavirus nucleic acid tests were negative for the first few times but turned positive in the end (Figures 29, 30).

Owing to the present clinical scenario, abnormalities observed in radiological examinations should be carefully compared with the clinical characteristics of other related diseases such as influenza and mycoplasma infections. Additionally, novel coronavirus nucleic acid tests should be performed a couple of times even if the initial test results were negative.

Meanwhile, there is no definite rationale for the radiological follow-up to confirmed COVID-19 cases. Based on previous observations, and integrating clinical experiences from Wuhan, we recommend the following: ① For newly diagnosed patients with typical clinical manifestations, positive novel coronavirus nucleic acid test and negative initial chest CT, it is recommended to repeat the chest CT in 3~5 days; ② For clinically diagnosed cases with atypical clinical manifestations and typical radiological manifestations, it is recommended to repeat the chest CT in 5~7 days to observe the progression of the lesions along with novel coronavirus nucleic acid tests; ③ For non-severe confirmed patients, it is recommended to

repeat the chest CT in 5~7 days to observe the progression of the lesions. Radiation doses should be closely monitored for patients with frequent CT examinations. For severe patients, bedside radiographs can be used to observe the progression of the lesions, the frequency should be based on clinical needs.

5 The radiological recommendation for discharge

After effective treatment of COVID-19, on the premise of clinical cure, the radiological recommendation for discharge is the following: ① The lung lesions were reduced obviously or disappeared totally; ② Only little residue fibrosis; ③No new lesions。

6 Clinical characteristics and radiological findings of children with COVID-19

The epidemiological characteristics is family clustering, especially in children, which is the second generation of COVID-19 infection, even involving newborns. The positive rate of nuclear acid test of COVID-19 from throat swabs was lower in children than that in adult. The method of anal test was more sensitive, especially neonate.

The CT appearances of COVID-19 was varied and non-specific. The most common appearances were GGO and consolidation. It made the diagnosis difficult that less lesions in lung and mild symptoms in patients. For suspected cases, CT examination shows abnormal manifestations in the lungs, which can assist early treatment and intervention, But the definite diagnosis should combine with the epidemiology and nuclear acid test of COVID-19.

7 Radiological differential diagnosis

COVID-19 should be differentiated from other virus pneumonia (such as influenza virus, avian influenza virus and SARSr-CoV et al.), mycoplasma pneumonia and bacterial pneumonia. In general, (1) the top three pathogenic bacteria in children with community-acquired pneumonia(CAP) are mycoplasma pneumoniae, bacteria, and respiratory syncytial virus [11]. (2) viral infections account for 15.0%-34.9% of adult CAP, with influenza virus taking the first place. Other viruses include parainfluenza virus, rhinovirus, adenovirus, human metapneumovirus, and respiratory syncytial virus [12]. 5.8%-65.7% of patients with positive virus test may be co-infected with bacterial or atypical pathogen infections [13-15]. (3) COVID-19 should also be distinguished from non-infective diseases, such as vasculitis, acute pulmonary interstitial pneumonia, connective tissue-related lung disease, cryptogenic organizing pneumonia and so on.

COVID-19 differs greatly in epidemiological history from the diseases mentioned above. At the current specific period which is also the season of high incidence of influenza, if there are imaging manifestations such as exudation, consolidation, and nodules in the lung, it is necessary to exclude ordinary influenza, mycoplasma and bacteria. Meanwhile, according to the latest guideline of *Diagnosis and Treatment Protocols of COVID-19 Infection (6th edition)* [7], a descriptive radiological diagnosis is needed based on the epidemiological history and clinical characteristics, and the final diagnosis requires to be confirmed by nucleic acid tests.

In conclusion, further explorations and collections of data are needed to identify the evolution process and rule of COVID-19. We pay a tribute to all the medical staff who are fighting COVID-19. Together, we can fight the epidemic!

Counselors:

Jin Zhengyu, Liu Shiyuan, Xu Ke, Chen Min, Lu Guangming, Cheng Jingliang, Liang Changhong, Hong Nan

Chief Editors:

Shi Heshui, Yu Jie, Zheng Chuansheng, Jin Chenwang, Shen Cong

Revisers: Xia Liming, Zhu Wenzhen, Zha Yunfei, Li Hongjun, Xu Haibo, Zhang Xiaochun, Shao Jianbo, Shi Yuxin, Wu Jianlin, Chen Qihang, Song Wei, Hu Chunhong, Xiao Yi, Wang Jian, Luo Liangping, Zhao Shihua, Zhang Zhiyong, Yang Li, Wu Ning, Yang Zhigang, Zhang Minming, Zhang Lina, Ye Zhaoxiang, Han Dan, Jiang Huijie, Zhang Xiaoqin, Ye Jianding, Yu Hong, Zheng Minwen

Expert group:

Ma Lin, Wang Zhenchang, Xian Junfang, Yuan Huishu, Zhao Xinming, Zhang Hui, Yu Chunshui, Li Songbai, Zhang Huimao, Yan Fuhua, Wang Peijun, Ju Shenghong, Jia Wenxiao, Li Kuncheng, Li Xin, Shen Wen, Zhang Xuening, Geng Zuojun, Liu Aishi, Liu Ailian, Liu Zhaoyu, Peng Weijun, Zeng Mengsu, Cheng Yingsheng, Li Cheng, Shi Haibin, Yuan Jianhua, Yu Yongqiang, Cao Dairong, Zeng Xianjun, Ma Xiangxing, Sun Gang, Wang Bin, Wang Meiyun, Liu Yulin, Shan Hong, Jiang Xinqing, Li Ziping, Long Liling, Luo Tianyou, Zhang Weiguo, Gong Qiyong, Zhou Shi, Yin Wu, Yin Hong, Guo Shunlin, Zhang Yonghai, Zhu Li, Song Faliang

Translators:

Huadan Xue, Longjiang Zhang, Zaiyi Liu, Li Fan, Bing Zhang, Dong Li, Xiaoling Zhang, Xingui Peng, Chunmei Li, Yinfeng Qian, Xiaoyi Duan, Lina Zhang, Jing Zhang, Su Lv, Shuang Xia, Miao Chang

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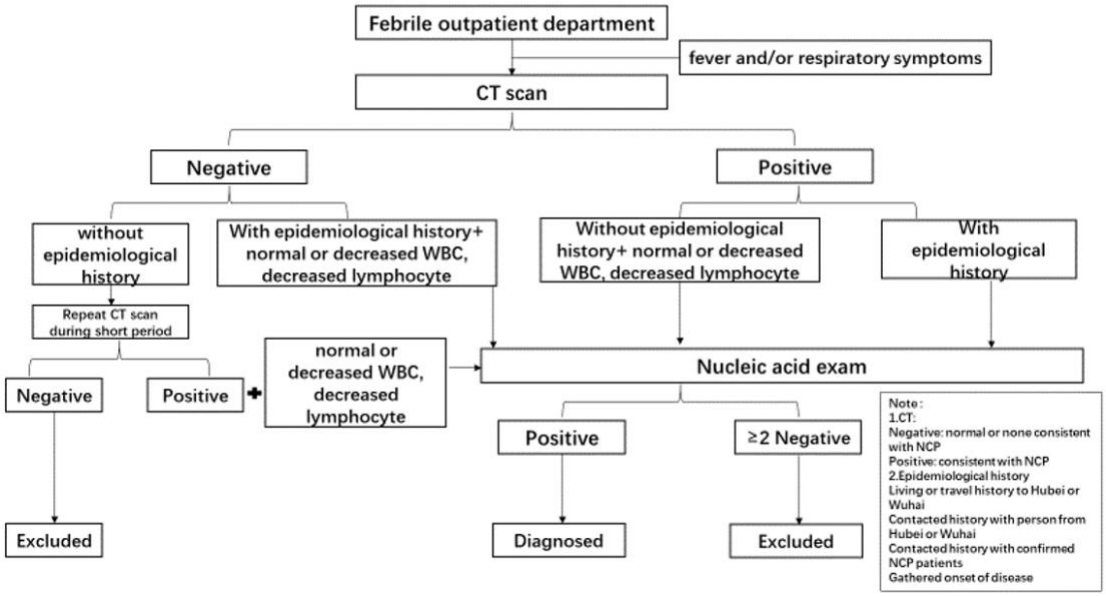

Figure 1 Screening process for COVID-19 in febrile outpatient department.

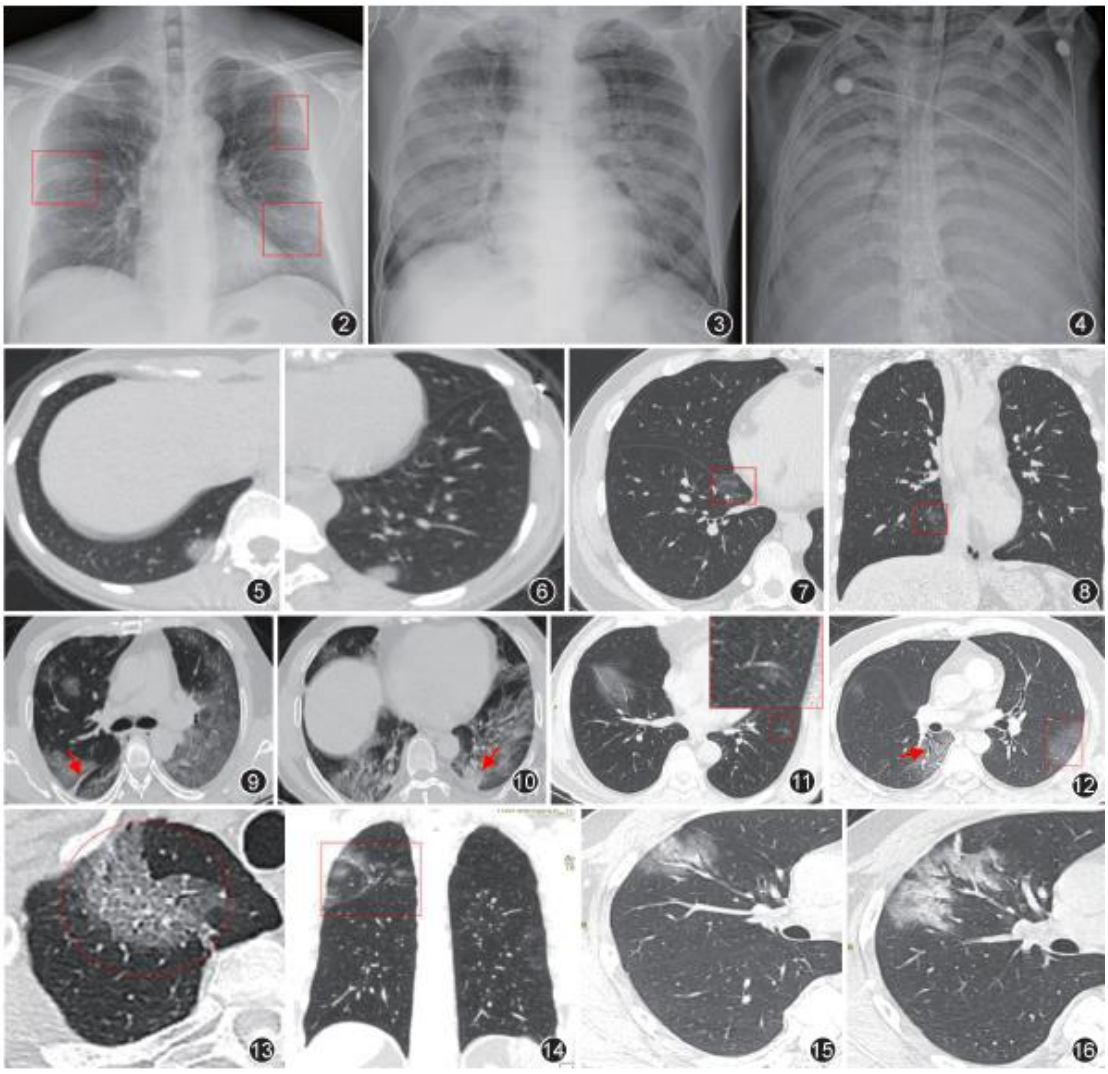

Figure 2 Male, 43 years old. The plain chest X-ray film showed scattered patchy opacification in the right middle lung and the upper and lower left lung, with unclear boundary.

Figure 3 Male, 69 years old. The plain chest radiograph showed a large area of ground glass opacification in both lungs, especially in the right lung lobe with lung marking thickened and partial horizontal interlobar pleural thickened. The obtuse right costal diaphragm angle suggested a small amount of pleural effusion.

Figure 4 Male, 44 years old. The plain chest radiograph showed diffuse consolidation, appeared as "the white lung", and the air bronchi sign was found near hilum.

Figure 5,6 Male, 32 years old. No fever. The lung window setting of Chest CT shows small subpleural nodules in the posterior basal segment of both right lower lobe (Figure.5) and the left lower lobe (Figure.6) with halo signs.

Figure 7,8 Male, 38 years old. Axial (Figure.7) and coronal (Figure.8) chest CT images shows small patchy GGO (red box) in the medial basal segment of the right lower lobe.

Figure 9,10 Male, 50 years old. The lung window setting of Chest CT shows bilateral large and patchy GGO, mostly distributed in the middle and outer zone and subpleural of the lung. Right oblique fissure is thickening (Figure. 9), the consolidation is visible in the posterior basal segment of left lower lobe (Figure. 10)

Figure 11 Male, 51 years old. The lung window setting of Chest CT shows large and patchy GGO with increased small vessels, air bronchogram and bronchial wall thickening. Small patchy GGO (boxes) around the small vessels is seen in the left lower lobe.

Figure 12 Male, 55 years old. The lung window setting of Chest CT shows GGO in the left upper and lower lobes, and the slight thickening of oblique fissure (in the red frame). Columnar thickening of the bronchial wall within the subsegmental GGO (↑), local subpleural consolidation with interlobular septal thickening and displacement is seen in the dorsal segment of the right lower lobe.

Figure 13 Male, 49 years old. The lung window setting of Chest CT shows subpleural patchy GGO in the right upper lobe with increased small vessels, appearing as " crazy paving" sign. The air bronchogram is seen in the lesion.

Figure 14 Male, 38 years old. The lung window setting of Chest CT shows subpleural "reversed halo" sign in the right upper lobe and multiple small patches GGO.

Figure 15,16 Male, 44 years old. The plain CT scan of the lung window of baseline (Fig.15) and 4 days later (Fig.16). The lesion in the anterior segment of the right upper lobe became larger and locally denser as progressed, with air bronchogram sign and bronchovascular bundles thickening.

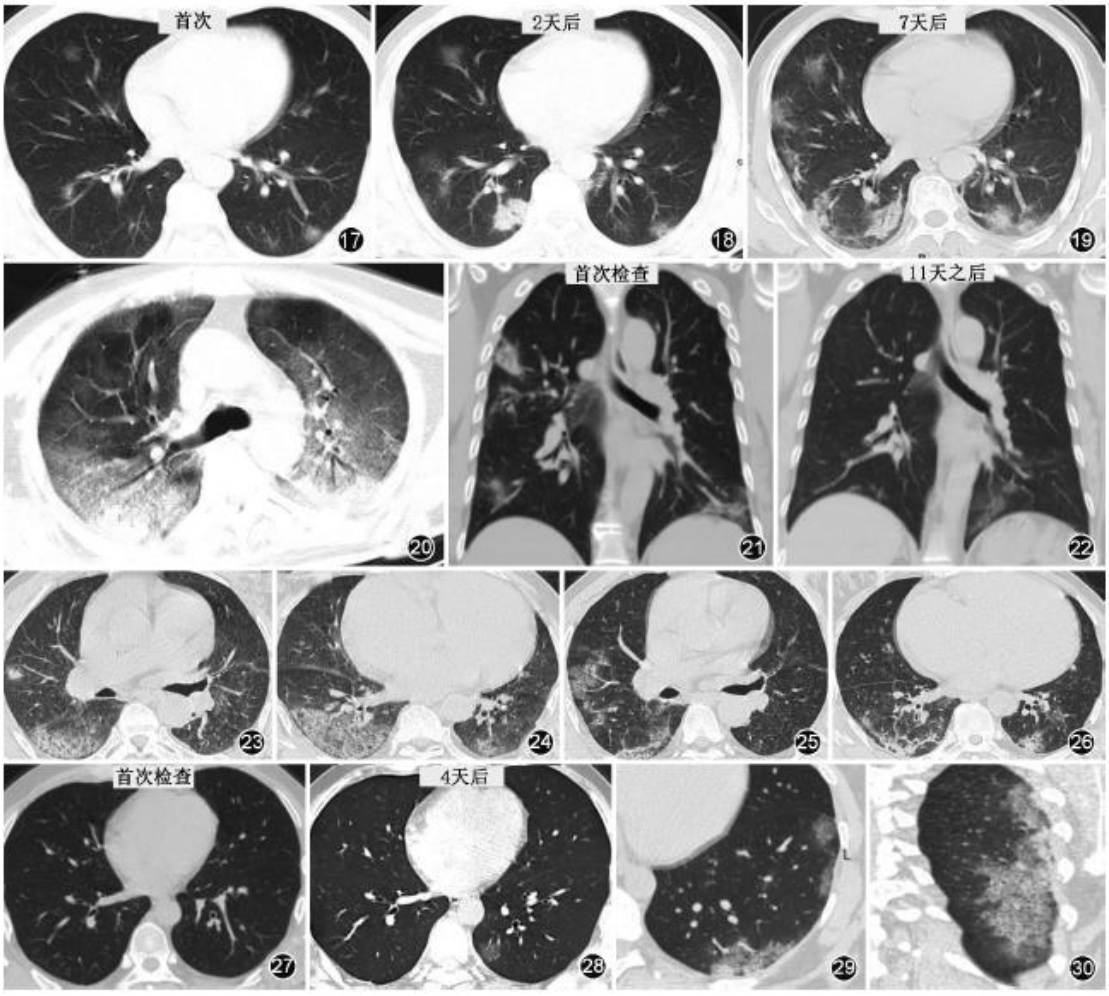

Figure 17~19 Male, 46 years old. The baseline CT image (Fig.17) showed multiple thin GGOs in both lungs and nodular with halo sign, mainly distributed sub-pleura. After 2 days (Fig.18) and 7 days (Fig.19), plain CT images showed the enlargement of the original lesions and appearance of new lesions. Air bronchogram sign in the consolidation of the right lower lung was shown.

Figure 20 Male, 60 years old. CT scan of the lung window showed multiple reticular GGOs were shown in most of the lungs, most obviously in the dorsal zones with part consolidation, which appeared as the "white lung". Air bronchogram signs was seen.

Figure 21,22 Male, 48 years old. The baseline CT image (Fig.21) showed multiple patchy GGOs and consolidations. After 11 days treatment (Fig.22), follow-up CT images showed the lesions were absorbed, and only some fibrous cords were in the inferior lobe of left lung.

Figure 23~26 Male, 60 years old. The baseline CT image (Fig.23,24) showed patchy GGOs in bilateral lungs, and nodules with halo sign in right lung. The first nucleic acid test was negative. After 5 days (Fig.25,26), follow-up CT images showed most previous GGOs were disappeared, while new GGOs with increased vessels and pleural thickness develop. Pulmonary fibrosis and bronchiectasis could be seen in inferior lobes of bilateral lungs.

Figure 27, 28 Male, 44 years old. The baseline CT image (Fig.27) showed no abnormal findings. After 4 days (Fig.28), follow-up CT images showed the GGO in the posterior segment of the left lower lung.

Figure 29, 30 Female, 34 years old. Her mother was with COVID-19. The first and second nucleic acid test was negative, while the third was positive. The first CT images showed patchy GGOs with "crazy paving" sign and increased small vessels.