CT Imaging Features of Patients Infected with 2019 Novel Coronavirus

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Overview of COVID-19

Coronavirus disease 2019 (COVID-19) is an acute, infectious pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection after full genetic testing [1, 2]. Coronaviruses are enveloped segmental positive RNA viruses belonging to the Coronaviridae family and the Nidovirales order. Coronaviruses are widespread among humans and other mammals, and can cause severe respiratory, intestinal, liver, and nervous system diseases [3]. SARS-CoV-2 belongs to the genus coronavirus, and its genetic characteristics are significantly different from severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) and are more similar to bat SARS-like coronaviruses (bat-SL-CoV ZC45 and bat-SL-CoV ZXC21) [4–6]. The confirmed human-to-human transmission of SARS-CoV-2 [7–10] makes it a highly infectious virus, resulting in the ongoing global pandemic. People are generally susceptible, normally with an incubation period of 1–14 days [8], but the case fatality rate is higher in the elderly and people with underlying diseases [11, 12]. Respiratory droplets and contact transmission are the main routes of infection [13]. The virus can also be spread by aerosols, especially in a relatively closed environment. Furthermore, recent research has suggested that the virus can be spread through feces and urine [14, 15]. Patients infected with SARS-CoV-2 usually have a history of epidemiological exposure, and a small number of patients show signs of throat congestion and tonsil swelling when infected. COVID-19 patients mainly present symptoms of lower respiratory tract infection, such as dry cough, fever, dyspnea, sputum production, etc. Besides, there is the possibility of accompanying symptoms of fatigue, myalgia or arthralgia, headache and chills [16–18]. In severe cases, SARS-CoV-2 can cause acute respiratory distress syndrome (ARDS) and sepsis. Asymptomatic infected people might also become the source of infection.

The importance of computed tomography imaging in the diagnosis of COVID-19

Currently, the diagnosis of COVID-19 mainly consists of a hematological examination, nucleic acid testing, and medical imaging (X-ray and computed tomography [CT] scan). A clinical blood test can be used for COVID-19 identification; indicators includes routine blood tests, liver and kidney function, and electrolyte assessments. For most patients in the early stage of COVID-19, the number of peripheral blood leukocytes will be normal or will decrease, but the number of

Abstract
Novel coronavirus pneumonia is an acute, infectious pneumonia caused by a novel coronavirus infection. Computed tomographic (CT) imaging is one of the main methods to screen and diagnose patients with this disease. Here, the importance and clinical value of chest CT examination in the diagnosis of COVID-19 is expounded, and the pulmonary CT findings of COVID-19 patients in different stages are briefly summarized, thus providing a reference document for the CT diagnosis of COVID-19 patients.

Keywords
lymphocytes will decrease [16, 19]. The liver enzymes, myoglobin, and myozyme, will increase in some patients [16]. Inflammatory response indicators, such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), increase in most patients, but procalcitonin levels remain normal [20, 21]. For severe patients, the D-dimer typically increases, and the number of peripheral blood lymphocytes decreases progressively [22, 23]. However, as some other diseases can also induce a similar testing result, the blood test is unlikely a reliable standalone tool to confirm COVID-19 infection [24].

Generally, the standard method of COVID-19 confirmation is real-time reverse transcription polymerase chain reaction (RT-PCR) after obtaining nucleic acid samples from the respiratory tracts of subjects [25]. Nonetheless, in the actual anti-epidemic process, there are problems such as the insufficient number of basic nucleic acid detection kits, long detection time, and the existence of false negatives [26]. Although RT-PCR has become increasingly available a year into the epidemic, it is still helpful to ascertain the radiological characteristics of the COVID-19 patients.

Along with laboratory testing, imaging examination is another important method in the diagnosis of COVID-19, especially for patients with false-negative RT-PCR results or with limited access to RT-PCR examinations [27, 28]. Chest X-ray is a two-dimensional projection technology based on overlapping images, so its density resolution is not as good as that of a chest CT examination. For example, overlying heart or rib images might obscure the pulmonary pathology, and the rate of missed diagnosis of pulmonary lesions is relatively high [29–35]. By contrast, chest CT imaging, as a cross-sectional three-dimensional imaging technique without overlapping structure interference [36, 37], can provide a very clear display of the early, slight inflammatory changes in the lung. Irrespective, for the imaging of lung stroma or lung parenchyma, its specificity, detection rate, sensitivity, and negative or positive predictive values are all better than using X-rays. In addition, its fast-reporting speed and strong feasibility [38] also make it a vital player in COVID-19 diagnosis.

The clinical value of CT imaging in diagnosis can be summarized as follows. First, to identify the presence or absence of lesions in the lung. Second, to clarify the range, degree, and stage of the disease [39, 40], as well as to assist in clinical classification, disease progression monitoring, and post-treatment efficacy evaluation [41, 42]. Third, to predict the outcome of this disease in combination with clinical and laboratory indicators with the assistance of radiomics and deep learning [43, 44]. Finally, to distinguish COVID-19 from other lung diseases, especially other coronavirus diseases, such as SARS and MERS [45].

Different diseases might sometimes exhibit exactly the same scan features using chest CT imaging. Therefore, chest CT imaging cannot substitute for nucleic acid detection to confirm COVID-19. Nevertheless, CT imaging is a powerful supplementary means to spot suspected cases and to track close contacts, especially in epidemic areas where nucleic acid testing is not applicable, and a large number of suspected cases fail to be confirmed.

### CT imaging diagnosis of COVID-19 at various stages

COVID-19 can be divided into early stage, progressive stage, severe stage, and recovery stage according to the scope and type of lesions. The CT scanning images of each period are distinct [39, 46]. However, there is no time standard for CT staging; it mainly depends on the CT reexamination during the disease course of a specific patient.

#### Early stage

In the early stage of COVID-19, CT imaging shows unilateral or bilateral lungs with localized inflammatory infiltrates, usually with the irregular, patchy, round-like, sub-segmental, or segmental ground-glass opacity (GGO) [47], associated with vascular engorgement, thickening [48], and traveling within the lesion [39]. It can also show a variety of manifestations, such as ground-glass shadow, consolidation shadow, nodule shadow, interlobular septal thickening, and interstitial change [48]. GGO is often seen in the early stage of COVID-19, and it is a kind of vascular-perfusion abnormality [49]. GGO is mostly manifested as a light cloudy shape, and the vascular texture and margins are often clearly visible [50, 51]. At this time, the pathological changes are dominated by exudate and inflammatory cell infiltration, and the alveoli are filled with exudate [52].

In terms of the distribution of lesions, they often invade cortical lung tissue at the very beginning, which can be visually summarized as the route of “rural encirclement of cities”. The peripheral subpleural involvement of intrapulmonary inflammation is more common in the early course of the disease, which might be related to pathological mechanisms that initially involve the terminal bronchioles and the pulmonary parenchyma around the respiratory bronchioles, and then the whole pulmonary lobules [53]. The morphology of the lesions in the early stage is mainly in three forms: solitary and round lesions (Figure 1A, B), single-lobed and large-sized lesions, or multi-lobed and multi-focal (Figure 1C). In a few cases, the transmucouscence of part of the lung parenchyma increases, and there is a mosaic-like change with the surrounding dense shadow. This might be due to an inflammatory response involving the bronchioles, which stimulates vasoconstriction and causes air retention in the distal alveoli. Special CT features seen during the early stage of COVID-19 include multiple flaxy ground glass shadows with a grid-like internal texture [54]. It is noteworthy that the thin ground glass density shadow and micro-nodular shadow, usually appearing in the early stage, can be easily overlooked. A small number of COVID-19 patients present negative CT findings in the early course of the disease but show positively upon reexamination [55], which indicates that chest CT imaging lacks complete sensitivity, especially in the early stage of the infection and incubation period [56]. It is more likely to have a precursor phase of viral infection, presenting symptoms before the appearance of imaging findings by CT examination. Special attention should be given to asymptomatic patients [57], who might...
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Progressive stage

The consolidation of lung tissue is an indicator of disease progression [61, 62]. The CT characteristic findings of COVID-19 in the progressive stage are as follows: 1) the lesions extend in number and scope involving multiple pulmonary lobes (Figure 2A), and some lesions are consolidated (Figure 2B); 2) ground glass shadow coexists with consolidation shadow or striated shadow (in irregular, patchy, round-like, and anti-butterfly shape, scattered or diffused patches even fusing into large patches with increased density [39]); 3) sometimes crazy-paving signs appears [47, 51] (Figure 2C), accompanied by interlobular septal thickening and bronchopneumonia signs [39]. Additionally, there is the possibility of a reversed halo sign and pulmonary nodules with a halo sign, but this is rare [63, 64].

During the progressive stage, the pathological changes can be dramatic upon reexamination, even within a short period. As the effusion of the liquid phase inside the alveolar of the pneumonitis is caused by the virus in the early stage and for the proteins inside the fluid, the leukocytes, there are less epithelial cells, showing a relatively transparent liquid membrane. Accordingly, a lower density and an unclear boundary are presented. The original ground glass shadows or solid shadows can be fused or partially absorbed during this time, and the lesion scope and morphology often change after fusion, which is not completely distributed along with the bronchial vascular bundle. However, as the disease progresses, when combined with the bacterial infection, ever more exudate content is generated. As a result, the density of the alveolar gradually increases, and the density difference between alveolar of pneumonitis and blood vessels becomes smaller, displaying a large consolidation.

Severe stage

During the course of the disease, the lesions gradually spread to occupy two-thirds or even the whole of the lung, which can be accompanied by pleural reaction and interlobar pleural thickening. The lesions on CT imaging present as diffuse lesions of double lungs [66], GGO combined with consolidation and paving stone signs, are often accompanied by a fiber cable shadow (Figure 3A). A “white lung” would present when the diffuse lesions are further developed [51, 62]. During this time, a consolidation shadow is the main feature, accompanied by a ground glass shadow (Figure 3B). This might also be accompanied by pleural adhesion. Also, pleural effusion is more common in severe and critical COVID-19 patients. Pulmonary bronchogram (Figure 3C), lung parenchyma extensive exudation, lung structure distortion, subsegmental atelectasis, and other possible...
manifestations might also be seen [67]. More importantly, the pleural parallel sign can be viewed as the most valuable characteristic [68].

During the severe stage of COVID-19, the lesions of patients progress rapidly, and can increase by more than 50% within 48 h. This results in the rapid deterioration of patients’ conditions, aggravation of breathing difficulties, and high mortality. After analyzing 1023 deaths among COVID-19 patients up to February 11, 2020, in China, Wu et al. [69] concluded that the case fatality rate for critical cases is 49%, and that for cases with the underlying disease this rate is even higher. Among those who died, 10.5% had cardiovascular disease, 7.3% had diabetes, 6.3% had chronic respiratory disease, 6.0% had hypertension, and 5.6% had cancer.

Recovery stage

During the convalescent stage, the range of lesions and the density in the lungs of COVID-19 patients decrease [55], and the consolidation shadow gradually changes to ground glass density shadow (Figure 4A). Ultimately, the lesions will appear as small fiber stripe shadows [72] (Figure 4B) or completely disappear (Figure 4C), and the pleural effusion will be fully absorbed [7].

The start time of lesion absorption varies from person to person, and there is no obvious specificity. In most cases, the symptoms begin to ease at ~1 week after the onset of pneumonia, while the CT images begin to normalize later. The return to the negativity of the CT imaging and nucleic acid detection results might be unsynchronized, and can occur in either order [60]. Intrapulmonary lesions might be completely absorbed, but might also be organized, in which situation the time of recovery for severe cases is delayed. Some cases can change from normal type or from the state of remission of symptoms (nucleic acid test to negative) to severe disease (nucleic acid test to positive) in about 10 days [73].

In addition to the characteristic CT findings of each stage of COVID-19 introduced separately above, the relationship between the frequency of CT abnormality and infection time course has been studied by Bernheim et al. [75]. These authors found that with disease development, CT manifestations become more diverse, including more consolidation and the aggravation of bilateral lobe involvement. The process of lesion development of COVID-19 can be compared to “a piece of candy melting”: as the disease progresses, the initial consolidation area begins to absorb, the density decreases, and gradually becomes a ground glass density shadow, just like a piece of candy melting.

Not all patients are lucky enough to go through these four stages, ending with recovery. Because of autoimmunity and active treatment, most patients get better quickly, and the scope and density of the lesions are reduced before

Figure 4  CT images of COVID-19 patients in the recovery stage. (A) The image shows GGOs gradually changed from mass consolidation shadow, though the lesion is still relatively large. (Reproduced with permission [71], Copyright 2020 Elsevier Ltd.) (B) The image from a 47-year-old woman shows minimal residual GGOs and parenchymal bands, with linear opacities being observed. (Reproduced with permission [65], Copyright 2020 Radiological Society of North America.) (C) The image from a 46-year-old woman shows GGOs are mostly resolved. (Reproduced with permission [74], Copyright 2020 Radiological Society of North America.)
developing into severe disease, followed by gradual recovery. Meanwhile, some patients experience early, progressive, and severe stages, gradually improve, and eventually recover or enter a chronic phase. However, the therapeutic effect of a small number of patients is worse. Combined with other pathogens infection, the lesions extend rapidly, which eventually causes death.

The specification of CT imaging in the diagnosis of COVID-19

Specific attention should be paid to the operation specifications of CT in practical applications. First, all CT equipment should be equipped with the necessary protection, including a lead rubber gonadal protective apron, a lead rubber neck sleeve, a lead rubber hat and so on. Second, the accompany examiners should not stay in the machine room in non-specialized circumstances, and they should wear lead protective clothing during the CT test. Third, the legitimacy judgment of X-ray examination for women of child-bearing age, pregnant women, and infants should be strictly strengthened [76]. Generally, it is critical to do the best job protecting the gonads and other organs in the examination of infants and adolescents. Pregnant women should not accept a CT examination of the lower abdomen if not in urgent necessary. Beyond that, CT examination for COVID-19 patients should be applied to people who have had contact history, display symptoms or can show pathogenic evidence, rather than the whole population including numerous asymptomatic subjects without contact history [56].

Moreover, virus transmission during the CT procedure also poses a threat to the people being examined and the imaging technician [56]. Hence, during the application of CT imaging for COVID-19 identification, a series of adjustments have to be implemented. For example, staggering the use of dedicated CT scanners in fever clinics to avoid cross-infection, strictly disinfecting rooms before and after each examination, arranging examinations time ahead of schedule to minimize contact among people in the waiting areas, as well as strengthening radiographers perception of the associated risk [77].

Conclusions

In summary, there are various methods in terms of the diagnosis of COVID-19, CT imaging is a powerful supplementary means, especially in spotting suspected cases and tracking close contacts in a timely fashion.

Chest CT imaging of COVID-19 patients mainly shows ground-glass, density shadows, and cotton-mass and reticular nodules, distributed across both lungs. The subpleural distribution of the lower lungs is dominant, which is more prominent than that of the middle and upper lobes. In the early stage of the disease, there are single or multiple patchy, subsegmental, or segmental ground glass shadows, and interstitial changes, mainly involving the external lung and interstitial lung, which can also be accompanied by interlobular septa thickening. In most cases, air bronchiole can be seen; then, it develops into multiple ground glass shadows and infiltration shadows. Frequently, ground glass shadows, consolidation shadows and strip shadows can coexist at this stage. In some severe cases, diffuse lesions of both lungs can be found, and lung consolidation might be accompanied by a pleural reaction.

Although chest CT imaging has many advantages and plays an important role in COVID-19 diagnosis, it should not be employed excessively and should be used with special caution because of the potential harm from the associated radiation. In addition, as the CT manifestations of some other diseases are similar to that of COVID-19, a comprehensive diagnosis should be used to confirm the result, thereby reducing the risk of misdiagnosis. Combining the patient’s epidemiological history, clinical symptoms, and laboratory examinations, and correctly recognizing the chest CT imaging manifestations can help to accurately diagnose SARS-CoV-2 infection.

Conflict of interest

The authors declare no competing financial interest.

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References


