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**Review Article,**

## **An Update of Clinical Characteristics and Chest CT Findings of Coronavirus Disease 2019 (COVID- 19)**

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### **Abstract:**

Novel coronavirus disease (COVID- 19) is a highly infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-cov-2). This novel virus is mainly transmitted through respiratory droplets and close personal contact, causing recent global public health emergency. COVID- 19 high-risk groups include elderly and immunocompromised patients, patients with preexisting comorbidities such as cardiovascular disease, hypertension, diabetes, respiratory disease, and oncological complications. Chest computed tomography (CT), especially high- resolution CT (HRCT) plays an important role in the early diagnosis, staging and monitoring of patients with COVID- 19 pneumonia. The clinical characteristics and chest CT findings of COVID- 19 are reviewed, including the time course of lung changes on chest CT during recovery and correlation of chest CT and reverse-transcription polymerase chain reaction (RT-PCR) testing in COVID- 19.

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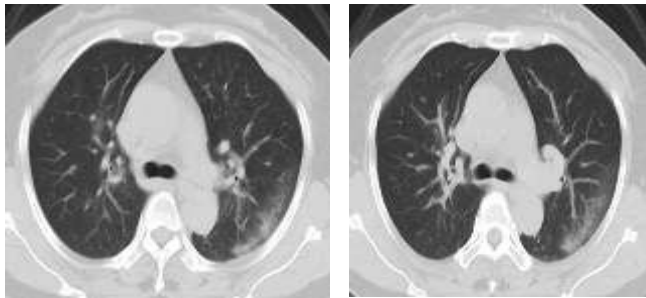
**Key words:** COVID- 19; coronavirus; chest CT; HRCT; RT-PCR.

### **Introduction:**

Coronavirus disease (COVID- 19) is an emerging infection caused by a novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. This novel virus is mainly transmitted through respiratory droplets generated when an infected person coughs or sneezes. Since December 2019, an increasing number of COVID- 19 cases emerged in Wuhan, Hubei Province, China, and subsequently, an outbreak of COVID- 19 swept the globe [2, 3]. World Health Organization (WHO) has declared this outbreak as a 'global public health emergency' on January 30, 2020. Until September 1, 2020, WHO reported total number of confirmed COVID- 19 cases 25,334,339 with 848,084 patient deaths globally? The primary CT characteristic of COVID- 19 is multiple small subpleural ground glass opacities (GGO) that grew larger with crazy-paving pattern

and consolidation [4]. Recent studies showed that the typical chest CT findings of COVID- 19 pneumonia demonstrated clear destruction of the pulmonary parenchyma including interstitial inflammation and extensive consolidation [5, 6]. COVID- 19 has unique biological properties, clinical characteristics and chest CT findings, though considerable progress has been made on the clinical management. Real-time reverse-transcription polymerase chain reaction (RT-PCR) of viral nucleic acid is regarded as the reference standard in the diagnosis of COVID- 19; however, recent research addressed the importance of Chest computed tomography (CT), especially high-resolution CT (HRCT) in the early diagnosis of COVID- 19 with false negative RT-PCR results, and reported the sensitivity of CT as 98% compared to RT-PCR sensitivity of 71% [7-9]. Chest CT scan is also helpful in the staging and

monitoring of patients with COVID- 19 pneumonia. In this review, we analyzed the clinical characteristics and chest CT findings of COVID-19, including the time course of lung changes on chest CT during recovery and correlation of chest CT and reverse-transcription polymerase chain reaction (RT-PCR) testing in COVID- 19.



**Figure 1.** Early phase showing single small subpleural ground glass opacity (GGO) in the upper lobe of left lung.

### Discussion:

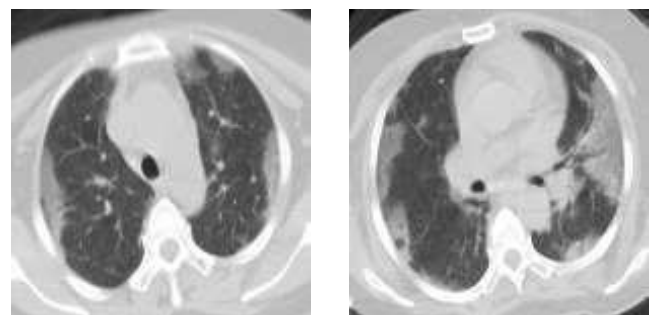
The current outbreak of coronavirus disease (COVID- 19) is highly contagious, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID- 19 is mainly transmitted through close contact from person-to-person in respiratory droplets generated when an infected person coughs or sneezes or talks. Some recent studies have suggested that some people without symptoms may be able to spread virus. SARS-CoV-2 is a novel virus of zoonotic origin that causes inflammation in the respiratory system. It has an incubation period of 1-14 days, usually ranging from 3 to 7 days [10]. On the basis of different clinical and imaging manifestations, the patients could be clinically classified into mild, moderate, severe, and critical cases [11-13]. The most common symptoms of patients are fever (98.6%), fatigue (69.6%), dry cough, and diarrhea. Patients with mild disease may present with clinical symptoms of an upper respiratory tract infection such as dry cough, nasal congestion, sore throat, mild fever, headache, muscle pain, and malaise. The majority of COVID- 19 cases are mild in severity with no pneumonia on imaging; however, patients can quickly deteriorate into severe or critical cases. Patients with moderate disease may present with clinical symptoms such as fever, cough, shortness of breath, tachypnea, and manifestations of pneumonia on imaging. Patients with severe disease present with one or more of the following conditions: (1) shortness of breath with a respiratory rate  $\geq 30$ /minute, (2) finger oxygen saturation  $\leq 93\%$  in the resting state

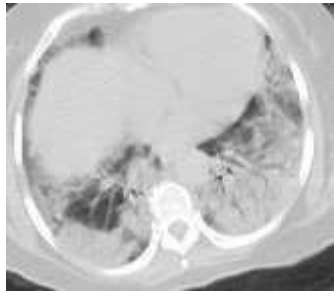
( $\text{SpO}_2 \leq 93\%$ ); (3) arterial partial pressure of oxygen/fraction of inspiration of oxygen  $\leq 300\text{mmHg}$  ( $\text{PaO}_2/\text{FiO}_2 \leq 300\text{mmHg}$ ); and (4) lesion pregression of greater than 50% within 24 to 48 hours on the chest imaging. Critical disease features include respiratory failure requiring mechanical ventilation, septic shock, and multiple organ dysfunctions. Patients with preexisting comorbidities have a higher case fatality rate. These comorbidities include cardiovascular disease (10.5%), hypertension (6%), diabetes (7.3%), respiratory disease (6.5%), and oncological complications (5.6%) [13]. Patients without comorbidities have a lower case fatality rate (0.9%) [13].

SARS-CoV-2 was reported to utilize angiotensin-converting enzyme-2 (ACE2) as the cell receptor into humans [14], and firstly causing pulmonary interstitial damages and subsequent with parenchymal changes. Chest CT scan plays an important role in the early diagnosis of COVID-19. To avoid misdiagnosis of early ground glass opacity (GGO) with plain chest radiography, high-resolution CT (HRCT) scan of chest allows objective evaluation of the lung lesions, enabling to better understand the pathogenesis of the disease [15, 16]. The most common CT findings include ground glass opacities (86%), consolidation (29%), crazy paving (19%), bilateral disease distribution (76%), and peripheral disease distribution (33%) [17]. The primary CT characteristic of COVID- 19 is multiple small subpleural ground glass opacities (GGO) that grew larger with crazy-paving pattern and consolidation [4]. In a study by Pan Y et al. [18], CT findings are categorized into four phases: early phase, progressive phase, severe phase, and dissipative phase. In the early phase, single or multiple small patchy shadows and interstitial changes emerge, and show a distribution along the sub-pleural areas or bronchi. In the progressive phase, the lesions increase significantly and enlarge, developing into multiple GGOs as well as infiltrating consolidation in both lungs. In the severe phase, massive pulmonary consolidations and lesions appearing bilaterally with diffuse infiltration of both lungs, manifesting as 'white lungs' are seen. In the dissipative phase, the GGOs and pulmonary consolidations are gradually absorbed, and the lesions began to change into cord-like high-density shadows, indicative of fibrosis. Zhou et al. [19], analyzed the CT findings in early stage and progressive stage of COVID- 19 and reported GGO (61.3%), followed by GGO

with consolidation (35.5%), rounded opacity (25.8%), a crazy-paving pattern (25.8%), and an air bronchogram (22.6%). Atypical CT manifestations of COVID- 19 include halo sign [20], reversed halo sign or atoll sign [21, 22], fibrosis [18], bronchial wall thickening [23], pleural changes such as pleural thickening or pleural effusion [24], vascular enlargement [7], mediastinal lymphadenopathy [24], pericardial effusion [23]. Elderly and immunocompromised patients are more likely to have extensive lung lobe involvement, interstitial changes, and pleural thickening [25]. COVID- 19 pneumonia manifest non-specific and diverse chest CT findings with a different time course and disease severity. Recognition and understanding the spectrum of CT features is helpful for the diagnosis, staging and monitoring of patients. Laboratory findings specific to COVID- 19 include elevated prothrombin time (PT), D-dimer, lactate dehydrogenase (LDH), alanine aminotransferase (ALT), C-reactive protein (CRP), and creatine kinase (CK) [13]. Lymphocytopenia and a marked reduction in CD4 and CD8 lymphocytes noted in the early stages of the disease [13, 26]. SARS-CoV-2 might damage liver, heart and kidney; showing elevated ALT, CK, myoglobin, troponin, serum creatinine or blood urea nitrogen [2, 3, 27]. Huang C et al [3]. proposed that patients in the intensive care unit (ICU) might suffer severe cytokine storms with higher levels of interleukin (IL) 2, IL-7, IL-10, granulocyte colony-stimulating factor (GCSF), interferon gamma-induced protein 10 (IP10), monocyte chemotactic protein 1 (MCP1), macrophage inflammatory protein alpha (MIP1A), and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). In critical patients, amylase and D-dimer levels are significantly raised [3,12]. Levels of CRP correlate directly with disease severity and progression. Real-time reverse-transcription polymerase chain reaction (RT-PCR) of viral nucleic acid is regarded as the reference standard in the diagnosis of COVID- 19; however, with limitations of sample collection, transportation, and kit performance, the total positive rate of RT-PCR for throat swab samples has been reported to be about 30% to 60% at initial presentation [28]. Recent research addressed the importance of Chest computed tomography (CT), especially high- resolution CT (HRCT) in the early diagnosis of COVID- 19 with false negative RT-PCR results, and reported the sensitivity of CT as 98% compared to RT-PCR sensitivity of 71% [7-9]. Xu et al. [29] reported CT

findings of 3 patients with COVID- 19 pneumonia with negative RT-PCR test. There is no specific anti-viral treatment or vaccine currently available that has been proven to be effective for COVID- 19. Treatment includes symptomatic care and oxygen therapy. Patients with mild illness require early supportive management such as nutritional supplements, external cooling, oxygen therapy, acetaminophen, and anti-bacterial therapy [13]. Critical patients require high flow oxygen, extracorporeal membrane oxygenation (ECMO), glucocorticoid therapy, and convalescent plasma [13]. Patients with respiratory failure may require high-flow nasal oxygen, or non-invasive ventilation, intubation, or mechanical ventilation [12]. Management of septic shock requires hemodynamic support with vasopressors administration. Therapeutically, aerosol administration of  $\alpha$ -interferon, chloroquine phosphate, lopinavir/ ritonavir, and ribavirin/ abidor have been suggested [12, 13]. Combinations of three or more anti-viral drugs are not suggested. Ongoing clinical studies suggest that remdesivir (GS5734) can be used for prophylaxis and therapy [12]. Furthermore, a fusion inhibitor targeting the HR1 domain of spike protein is reported to have the potential to treat COVID- 19. Preventive measures include frequent hand washing with soap and water or alcohol-based hand rub, avoid touching eyes, nose and mouth, cover nose and mouth when coughing and sneezing with tissue or flexed elbow, avoid crowded places, avoid close contact with anyone with cold or flu-like symptoms. Healthcare personnel must use personal protective equipment such as N95 mask, eye protection, gloves, and gowns. COVID-19 prevention strategies for radiologists include equipment and manpower, infection control practices, and team segregation.





**Figure 2.** Progressive phase→severe phase, showing multiple small subpleural ground glass opacities (GGO) as well as infiltrating consolidations in both lungs.

### Conclusions:

Integrated with clinical history, Chest CT scan (HRCT) plays a vital role in the early diagnosis of COVID- 19, especially in the epidemic area with false negative RT-PCR. Early diagnosis of COVID- 19 is a key consideration for disease control and treatment to improve patient outcomes. Chest CT scan is also helpful in the staging and monitoring of patients with COVID- 19 pneumonia. The primary CT characteristic of COVID- 19 is multiple small subpleural ground glass opacities (GGO) that grew larger with crazy-paving pattern and consolidation.

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