CHAPTER 15

THE IMAGING AND RADIOLOGICAL DIAGNOSIS METHOD IN PATIENT WITH COVID-19

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INTRODUCTION

Infection originated by the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), since December 2019, give rise to a global pandemic in the first few months of 2020 that currently affects almost every country in the world. Coronavirus disease 2019 (COVID-19) infection and the clinical spectrum of the disease vary, ranging from asymptomatic infection or mild upper respiratory disease to respiratory failure and, in some cases, severe viral pneumonia with death. Major clinical signs include fever, cough, shortness of breath, fatigue, and shortness of breath. In the study, first published in January 2020, chest imaging results of COVID-19 reported involvement in the form of ground glass opacities (GGO) in the bilateral lungs of most hospitalized patients. However, these results are not specific, as they

may occur with other diseases such as viral pneumonia, atypical bacterial pneumonia, drug toxicity, eosinophilic pneumonia, or cryptogenic organizing pneumonia. It has been reported that 20% of COVID-19 pneumonia cases and 41% of hospitalized patients are complicated as acute respiratory distress syndrome (ARDS).

Covid-19 is a new infectious disease that spreads very quickly and causes inflammation in the respiratory system. Chest imaging is important for diagnosing lesions and evaluating the extent of lesions. It also helps to accurately observe changes in patient follow-up. CT has been reported as an important tool to help diagnose and manage patients with COVID-19

IMAGING RESULTS

Chest radiograph

Chest radiography is the first imaging method used in patients with suspected COVID-19 infection. It is advantageous that it can be used in low transmission risk and follow-up even though its sensitivity is low compared to CT. Results on chest radiographs are often normal in the early stages of COVID-19 pneumonia and mild cases. Lung results may also become apparent on posteroanterior (PA) chest radiographs on approximately the 10th day. Ground-glass densities observed in CT may be overlooked in retrocardiac and diaphragm locations on PA chest radiography. Widespread patchy radiopacities, which can be seen as opaque lungs on chest radiography, can be observed in severe disease or critical disease stages. Accompanying pleural effusion and consolidation can be seen on chest radiographs in severe patients. Wong et al. reported abnormal initial chest radiography results in 69% of PCR positive patients and 80% of hospitalized patients. Bandıralı et al. found a 58.8% rate of chest radiographs with abnormal results in PCR-positive patients who did not need to be hospitalized. Pakray et al. found abnormal chest radiography results in 89.6% of PCR positive patients. PA chest radiography is recommended in pregnant or pediatric patients and in the follow-up of hospitalized patients even though the diagnostic sensitivity of chest radiography is low in COVID-19 patients.

Computed Tomography

Computed Tomography (CT) plays an important role in the diagnosis of COVID-19 and the imaging of its possible complications. Chest CT sensitivity

was reported as 98% in the diagnosis of COVID-19. CT may be normal in the early stages of the disease process. The most common results detected in CT are ground-glass densities and consolidations. Crazy paving, interlobular septal thickening, bronchiectasis, and halo results are less frequent. Pleural or pericardial effusions, mediastinal lymphadenopathy, and pulmonary nodules are rarely observed compared to other results.

Ground-glass densities

Ground-glass densities are the most common result in CT images of COVID-19 patients. The prevalence of ground-glass densities was found to be between 34-91% in studies with a high number of patients. The definition of ground-glass densities is a hazy, increased lung attenuation area by preserving bronchial and vascular borders (**Figure 1**).

It shows peripheral localization and multilobed involvement close to the pleural surface, including fissures. Chest CT often involves the middle/lower lobes and posterior section. Pure ground-glass densities can be seen in 0-4 days after the onset of symptoms.Consolidations may accompany ground-glass densities, and the number of ground-glass areas may increase in the days
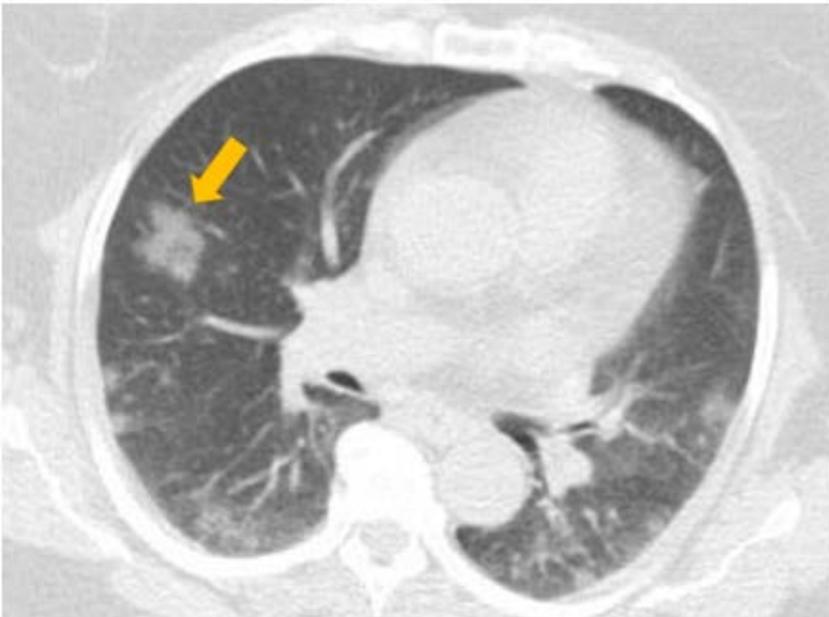
Figure 1. Ground-glass density in a 48-year-old female with COVID-19 patient presenting with fever and cough. Axial CT scan shows bilateral groundglass density (yellow arrow) in the middle and lower lobes.

ahead (days 6-13). It has been reported that focal ground-glass area accompanying fibrotic band or subsegmental atelectasis can be seen while ground-glass densities contract during the recovery period of the disease.

Consolidation

In chest imaging, COVID-19 patients had progressive opacities and consolidation during the course of the disease. Various chest CT results were present in 10-70% of COVID-19 cases proven by the RT-PCR test and consolidation was reported as 51.5%. The most common chest CT results are bilaterally distributed ground-glass density/consolidation (without subpleural preservation) in peripheral areas.

Air bronchograms are usually present within these areas as consolidation areas grow. As the disease progresses, fibrous exudate will increase in the alveolar space, air bronchograms and bronchial enlargement, secondary to this, diffuse consolidation of varying intensity in the lungs is observed on chest CT (**Figure 2**). With some curvilinear opacities compatible with fibrosis in the lungs, the gradual dissolution of the ground glass density and the formation of consolidation are seen during the dissipation phase.

It was reported that the number of absolute lung findings increased from the onset of symptoms in a study of 51 patients. Ground glass density and consolidation in the lungs are the main findings on the CT image. Con-
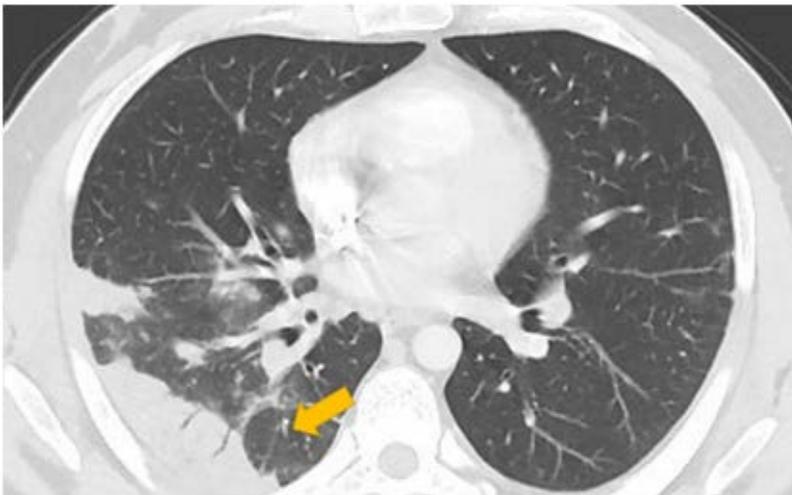

Figure 2. A 52yearold male coronavirus disease 2019 patient presenting with fever and cough for 10 days. Axial CT scan shows a groundglass density with consolidation of the right lower lobe (yellow arrow).

solidated lesions, including consolidated ground-glass opacities, and isolated consolidation correlated slightly positively with the time between the onset of symptoms and CT. In a prospective analysis of 41 patients, 98% of patients admitted to the intensive care unit (ICU) showed bilateral lung involvement on chest CT images. Imaging abnormalities in the form of multiple lobular and subsegmental consolidation areas, the most common result on chest CT, were generally higher in those with ICU patients. Lesions are associated with developmental time compared to previous studies: mainly GGO in the early stage (0-4 days), increased crazy paving pattern in the progression stage (5-8 days), consolidation in the peak stage (9-13 days), and consolidation dissolution in the dissipative stage ($\geq$14 days).

Crazy Paving Pattern

Interlobular septal thickening and prominent intralobular lines may show overlapping with ground-glass density . (**Figure 3**). This imaging finding is called the crazy paving pattern.

The crazy paving pattern in chest CT has been described with increased ground-glass densities (5-8 days after onset of symptoms) in the progressive phase, which is roughly one of the four stages of COVID-19. As previously reported, chest CT of patients with Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) may show crazy paving pat-
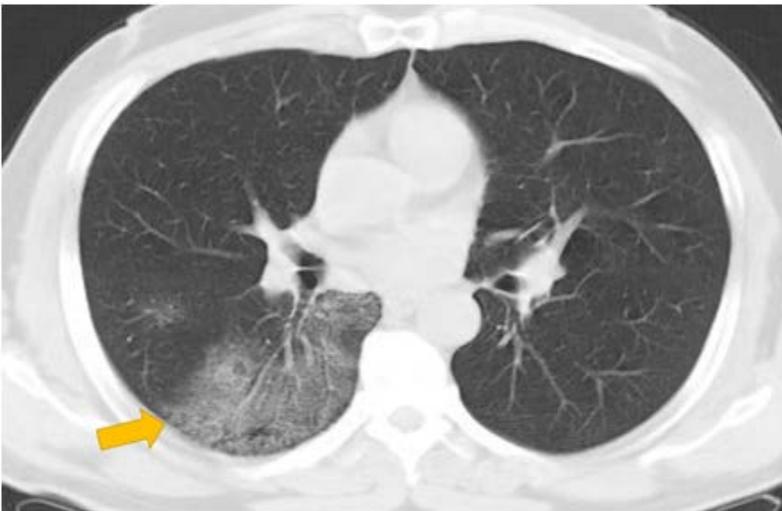
Figure 3. Crazy paving pattern in a 66-year-old man with COVID-19. Axial chest CT scan shows ground-glass density superimposed with interlobular septal thickening (yellow arrow), consistent with crazy-paving pattern.

terns. This pattern may be associated with interlobular and intralobular interstitial hyperplasia and may show interstitial inflammation and alveolar damage in lungs of COVID-19 patients. Various chest CT results were present in 10-70% of COVID-19 cases proven by the RT-PCR test and the crazy paving pattern was reported as 34.9% . The prevalence of the crazy paving pattern has been reported between 5% and 89%.

Most of the patients show more ground-glass density and fewer retained lobes than subsequent follow-up screenings in the early stages. However, the condensation of the crazy paving pattern over time, a rising in the number of related lobes, and consolidation densities occur in many patients. Tabatabaei et al. found in a selected cohort of 120 consecutive patients that intensive care unit patients had significantly greater consolidation, air-bronchograms, "crazy paving", and central involvement of the lungs compared to other hospitalized patients. On average, CT findings become evident on the 10th day of the disease. A reduction in the number of related lobes and an improvement in imaging results, including resolution of the crazy paving pattern and consolidated densities, were reported in 75% of patients after day 14. The most common results in follow-up CT have been reported to be an increase in consolidation densities and a loss in the crazy paving pattern in other published studies in the literature. The increase in the intensity of ground glass density occurs at the intermediate stages of the disease and indicates that these areas gradually transform into multifocal consolidation, septal thickening, and the emergence of crazy paving pattern. The combination of the crazy paving pattern with consolidation is considered the peak point of disease or progression.

Pulmonary vascular enlargement

Common pulmonary vascular abnormalities in COVID-19 pneumonia; can be described as vascular enlargement and regional mosaic perfusion patterns. The high prevalence of vascular enlargement and thickening in areas of pulmonary parenchymal opacity in COVID-19 patients is noteworthy and is evidence of the important role of vascular pathology in the pathophysiology of COVID-19 pneumonia. When there is a larger than expected vessel diameter within the point in the vascular tree, pulmonary vascular enlargement can be mentioned (**Figure 4**).

On CT, it is described as the enlargement of the subsegmental pulmonary vessel (pulmonary arteries and veins) with a diameter of more than 3 mm around and / or within the opacity. The vascular diameter greater than that of
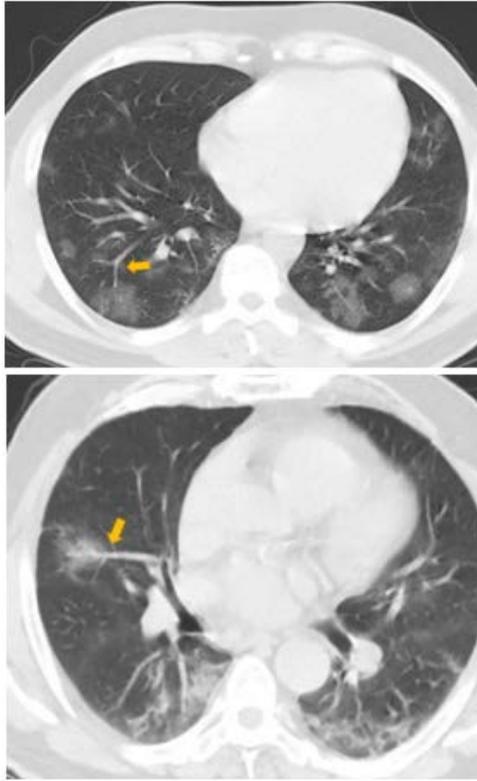
Figure 4. a) Vascular enlargement sign in a 38-year-old man with COVID-19 who presented with persistent fever and cough. Axial chest CT image shows multifocal bilateral areas of GGD with vascular enlargement (yellow arrow). **b)** 41-year-old man with COVID-19 patient presenting with fever. Axial CT scan shows bilateral ground-glass densities and vascular enlargement sign in the right middle and lower lobes (yellow arrow).

adjacent parts of the disease-free lung is characterized by a vascular diameter larger than that of the disease-free comparable regions of the contralateral lung or by the focal, continuous expansion of vessels towards the peripheral region of lungs. Quantitative methods will be more accurate since the evaluation of vascular enlargement and mosaic perfusion may be subjective.

It is reported to be positive in 70% of the cases. It is thought to be secondary to inflammation-related vascular involvement in this region even though the exact cause is not known. Ye et al. suggested that vascular enlargement may be due to proinflammatory factors. PVE is a potential diagnostic sign for COVID-19 even though the pathophysiology is not fully understood.

PVE has been reported in 45.2% to 89.2% of COVID-19 patients. In addition, Bai et al. reported that PVE was significantly associated with COVID-19 in a comparison of CT results in patients with COVID-19 pneumonia and non-COVID-19 pneumonia.

Halo and reverse halo (or atoll) sign

More atypical signs such as halo and reverse halo (or atoll) have been described less frequently in COVID-19 patients. These signs are not present at the onset of the disease and usually occur later. The reverse halo sign is surrounded by denser ring-like or crescent-shaped consolidation indicating a central ground-glass density and is also known as the atoll sign while the halo sign identifies a nodule or mass surrounded by ground-glass density (**Figure 5**).

Although this finding is known to be non-specific, reverse halo signs have been reported in several COVID-19 cases. Opportunistic invasive fungal infections in immunocompromised patients (e.g., aspergillosis, mucor mycosis), as well as in immunocompromised patients previously diagnosed withnon-fungal endemic infection, cryptogenic organized pneumonia, vasculitis, neoplasm, hypervascular pulmonary metastases, and inflammatory diseases. It should be kept in mind that it can also be seen in opportunistic

Figure 5. Halo sign in a 51-year-old man with COVID-19. Axial contrast-enhanced CT scan revealed ground-glass densities in both lungs and a nodule surrounded by ground-glass density consistent with a halo sign.

invasive fungal infections in immunocompromised patients (e.g., aspergillosis, mucor mycosis), non-fungal endemic infection, cryptogenic organizing pneumonia, vasculitis, neoplasia, hypervascular pulmonary metastasis and inflammatory diseases.

Reticular pattern

The reticular pattern is the pathological process of pulmonary interstitium or consists of fine subpleural reticulation without gross linear or curvilinear opacity or a significant amount of ground-glass density. It is characterized by interlobular septal thickening and prominent intralobular lines. (**Figure 6**).

The reticular pattern is seen in COVID-19 patients with a longer disease process and usually with pneumonia. The prevalence of reticular pattern and linear opacification is quite variable, between 1% and 81%. Also, in COVID-19 patients, subpleural curvilinear lines and fibrous bands are observed as a result of the replacement of cellular components and fibrosis.

Reticular opacities can accompany ground-glass density areas and can be well defined on standard chest radiographs. Fibrotic changes in the form of traction bronchiectasis, volume loss, structural distortion and, subpleural reticular opacity develop in the later stages of the disease. Generally, the peripheral and basal lungs are the areas where these reticular opacities are observed. On CT scans, it has been reported that COVID-19 patients with pneumonia may have persistent reticular opacities after treatment.

Figure 6. A 74yearold male COVID-19 patient presenting with persistent cough. Axial CT scan shows bilateral reticular pattern (yellow arrow) superimposed on the background of the groundglass density.

Pleural and pericardial effusion

Pleural effusion (5.2%) and pericardial effusion (2.7%) were rarely reported on chest CT in many COVID-19 cases. A recent study reported that 1 in 90 patients with COVID-19 pneumonia had pericardial effusion. The cardiac injury occurs in 12.5% to 19.7% of patients hospitalized with COVID-19 and is a risk factor that increases mortality. It has been reported that the frequency of pericardial effusion is higher in COVID-19 patients with serious disease than those without critical disease. Pericardial effusion may develop as a result of inflammation in the myocardium or pericardium in COVID-19 and may be a sign of cardiac damage. However, it should be kept in mind that elderly patients and those with heart failure may have pericardial effusion independent of COVID-19. Radiologists should consider the possibility of cardiac injury associated with COVID-19 in the presence of pericardial effusion on chest CT images even though pericardial effusion is a non-specific result.

Pleural effusion and focal pleural thickening, which may be associated with intense pleural inflammation, have been rarely reported among pleural pathologies, which are usually seen in the advanced stages of the disease. Furthermore, the addition of pleural effusion to COVID-19 pneumonia is thought to be associated with a poor prognosis. The prevalence of pleural effusion has been reported between 0% and 20% in COVID-19 patients.

Pulmonary thromboembolism

SARS-CoV-2 can induce coagulation cascade activation or local or systemic inflammation. Therefore, COVID-19 patients are at risk of developing increasingly defined thromboembolic complications. In pulmonary CT angiography, it has been reported that the incidence of pulmonary embolism (PE) in COVID-19 patients ranges from 17% to 35%. Patients with mild disease may also develop acute PE, but its prevalence is higher in critically ill patients. Regarding the location and distribution of the thrombus, PE is more common in the segmental and lobar branches and less frequent in the central pulmonary arteries. The need for mechanical ventilation is higher in COVID-19 patients with PE and D-dimer levels of patients with severe COVID-19 pneumonia are significantly increased. Although there is no age-adjusted D-dimer cut-off level in COVID-19 patients, it has been reported that D-dimer levels are associated with both the presence of PE and the degree of pulmonary artery occlusion.

Non-contrast chest CT is recommended by current guidelines in patients with risk factors and/or in patients with suspected COVID-19 whose clinical

findings are severe and critical. The definitive contribution of PE to mortality in COVID-19 patients remains unknown due to the lack of routine CT pulmonary angiography in all patients and the limited number of autopsy studies available. In addition, the risk of deep vein thrombosis and PE is increased, especially in those who receive treatment in the ICU and those who receive mechanical ventilation therapy (e.g., hemoptysis, unexplained tachycardia, or signs and symptoms of deep vein thrombosis and acute worsening of patient mobilization. Pulmonary CT angiography (CTA) should be considered to evaluate pulmonary parenchyma and vascular complications in patients with high clinical suspicion for PE with symptoms suggestive of hemoptysis, unexplained tachycardia, acute worsening of patient mobilization, or deep vein thrombosis. The British Society of Thoracic Imaging recommends that patients with COVID-19 undergo a non-contrast chest CT prior to CTA, as mosaic attenuation in CTA can cause difficulty in differentiating with ground glass density.

Ultrasonography

Lung ultrasonography (USG) has been defined for the evaluation of lung involvement in patients with suspected COVID-19 in cases where other imaging sources are not available or appropriate. Exposure decreases with a single operator, bedside examination, and easy disinfection, and the spread rate of infection decreases. Intensive care units reduce mortality and morbidity rates by providing rapid and critical clinical decision-making in emergency triage, obstetrics, and pediatric clinics and in rural areas where transportation and accessibility are limited. Repeatable and portable, easy to disinfect, radiation-free, and low-cost are other advantages of US. Lung ultrasonographic characteristics of patients with COVID-19 have been identified as follows:

1. Thickening with irregularity in the pleural line;
2. B lines in patterns that vary focally, multifocally, and confluently under the pleura;
3. Consolidations in varying patterns in translobar form with multifocal small, non-translobar, and mobile air bronchograms;
4. The emergence of A-lines during the recovery phase;
5. Pleural effusions are not common.

The results of lung USG characteristics vary in relation to the stage of the disease and the severity of the lung injury. The interstitial pattern may be

slightly alveolar or bilateral. In addition, consolidated areas can be observed. These two main findings, which differ in relation to the stage of lung injury, are the dominant pattern. Thickening of the pleural line in the inferior and posterolateral regions is the most common symptom in pneumonia or ARDS. In cases of bacterial pneumonia or superinfection or congestive heart failure, it should be considered in the differential diagnosis due to the presence of pleural effusion. The accuracy of USG in detecting pleural effusions was 93%.

In the early stages of COVID-19, the changes seen in the subpleural regions of the lung are more localized. Subsequently, air loss involving multiple lobes and consolidation of some lesions surrounded by the B line is observed. A white area is observed in which neither A-lines nor separated B-lines are visible on the USG in ARDS, including ARDS caused by COVID-19. This image is called the "white lung".

Whether pulmonary edema is of cardiogenic origin can be distinguished by careful examination of the pleura with USG. The presence of pulmonary USG changes in COVID-19 in both lungs is helpful in distinguishing from influenza and bacterial pneumonia but is not specific to any infection. In addition, the difficulty in detecting lesions deep in the lungs due to reduced transmission in the ventilated tissues is a known limitation of lung USG. Chest CT will be a good solution to detect pneumonia that does not extend to the pleural surface.

DIFFERENTIAL DIAGNOSIS

Other viral pneumonia factors (influenza, parainfluenza, adenovirus, respiratory syncytial virus, rhinovirus, etc.) are primarily present in the differential diagnosis of COVID-19. CT results are similar to other viral pneumonia. H1N1 virus pneumonia has ground-glass densities, interlobular septal thickening, and accompanying centrilobular nodules. Adenovirus pneumonia often has lobar or segmental consolidations that accompany ground-glass densities. Peribronchial thickening and centrilobular nodules are distinguishing results from other viral pneumonia in parainfluenza pneumonia. Small centrilobular nodules with asymmetric distribution on CT and asymmetric consolidation areas can be observed in respiratory syncytial virus pneumonia. Influenza pneumonia CT result is usually in the form of irregular ground-glass densities that may be associated with focal consolidation areas in the lower lobes. Similar results can be found in SARS and MERS pneumonia since they are from the same virus family. A definitive diagnosis can be made as a result of

laboratory examinations in which the virus is isolated in viral pneumonia. Chlamydia pneumonia is among the differential diagnoses of infectious origin of COVID-19 in mycoplasma pneumonia and bacterial pneumonia. Other diseases in the differential diagnosis include acute interstitial pneumonia, connective tissue-related lung disease, and cryptogenic organized pneumonia.

## TEMPORAL CHANGES IN COVID-19 PNEUMONIA

Changes in lung results develop over time in COVID-19 pneumonia. The final stage of COVID-19 lung involvement is acute respiratory distress syndrome as with severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS). Four different stages have been identified for COVID-19. 1. The most common result in the stage (0-4 days) is Ground-Glass Densities. The square and size of ground-glass densities increase, and it is observed that the result of crazy paving is accompanied in the second stage (5-8 days). 3. Consolidations are seen to be more dominant in the stage (days 9-13) and the result of crazy paving with ground-glass areas begins to regress. It has been reported that consolidation areas begin to regress in the final 4th stage and are accompanied by fibrotic batches. It was reported in another study that pure ground-glass densities were the most common result with the onset of symptoms. Ground-glass densities and accompanying linear densities have been reported to peak between the 6th and 11th days. Consolidations may extend and expand to the upper lobes, pleural or pericardial effusion, pneumothorax, and cavitation may develop in the late period. Secondary infections, sepsis, cardiac and multi-organ failure, and ARDS are the causes of mortality (**Figure 7**).

CT SCORING SYSTEM

CO-RADS

Four categories for COVID-19 pneumonia were identified by the Radiological Society of North America (RSNA) for standardization of CT reports of suspected COVID-19 subjects (negative for typical appearance, vague appearance, atypical appearance, and pneumonia). In addition, the Radiological Society of the Netherlands (Nederlandse Vereniging voor Radiologie) developed a classification indicating suspicion in patients suspected of COVID-19
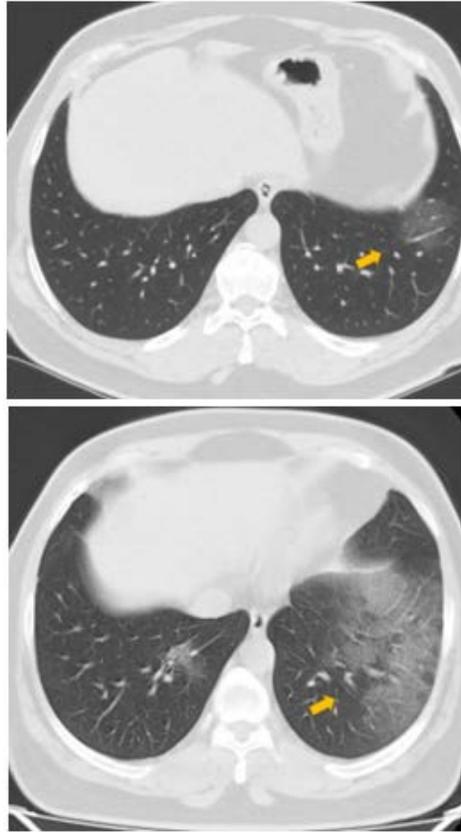
Figure 7. Axial CT scans in 49-year-old man with COVID-19. (a) Scan obtained on day 5 of illness shows diffuse ground-glass densities that affected left lower lobe. (b) Scan obtained on day 11 of illness shows that an increase in the areas of ground glass densities is observed (yellow arrow)

on April 7, 2020. CO-RADS is used to evaluate suspicion in the evaluation of pulmonary involvement (**Table**).

Table . CO-RADS Categories		
	CO-RADS Category	Level of suspicion for pulmonary involvement
0	Not interpretable	Scan technically insufficent for assigning a score
1	Very low	Normal
2	Low	Typical for other infection but not COVID-19
3	Equivocal/unsure	Features compatible with COVID-19 but also other diseases
4	High	Suspicious for COVID-19

| 5 | Very High | Typical for COVID-19 |
| 6 | Proven | RT-PCR positive for SARS-CoV-2 |

CO-RADS Category 0: This category should be reported when there is a common artifact in CT images and insufficient quality CT images.

CO-RADS Category 1: This category is defined for normal CT results or noninfectious CT results. Noninfectious results include emphysema, perifissural nodules, lung tumors, and fibrosis.

CO-RADS Category 2: This category is used due to results that are considered infectious and are not compatible with COVID-19. This category should be selected in results suggesting non-COVID-19 infection such as lobar pneumonia, tree-in-bud sign, and an abscess.

CO-RADS Category 3: Category 3 indicates suspicious results of COVID-19 in terms of lung involvement, such as non-infectious causes (such as perihilar ground-glass densities, presence of pleural effusion, and interlobular septa, organized pneumonia), and other viral pneumonia results.

CO-RADS Category 4: This category is reported as a high suspect in the presence of pulmonary results that may overlap with other viral pneumonia causes along with typical results for COVID-19.

CO-RADS Category 5: Category 5 should be selected in the presence of COVID-19 typical results indicating high suspicion for lung involvement. The presence of patchy ground-glass densities, crazy paving, multifocal involvement, and other accompanying typical results is significant for Category 5.

CO-RADS Category 6: It is used for patients with proven COVID-19 with coronavirus positive PCR results.

Severity Score

COVID-19 has been clinically classified as mild, common, severe, and critical. Patchy ground-glass densities with multilobar involvement are the most common results in chest CT, and ARDS and death may develop in severe and critical cases. Some scoring was performed semiquantitative in order to contribute to the prognosis. Pan et al. scored the involvement of each of the five lung lobes as less than 5% 1 point, 5-25% 2 points, 26-50% 3 points, 51-75% 4 points, and 76-100% 5 points. They reported that the total score increased until day 10. Yang et al. scored 20 pulmonary segments as 0, 1-50%, and more than 51% with 0.1 and 2 points. They proposed the threshold value as 19.5 points in order to distinguish between severe and mild cases in this study. Yang et al. evaluated the performance of a semi-quantitative score that calcu-

lated the degree of pulmonary opacification in 20 pulmonary segments as a surrogate for 33 disease burdens. Each lung opacity was given a score of 0, 1, or 2 based on whether parenchymal opacity was less than 0.50%, equal to, or greater than 50% of each region (total score: 0-40 points). A threshold of 19.5 was identified to distinguish between 83% sensitivity and 94% specificity between severe and mild cases. The severity of lung parenchymal involvement, which is visually scored, is calculated as a percentage in similar studies.

CONCLUSION

COVID-19 early diagnosis is very important for filiation efforts and prevention of transmission. With imaging methods, especially patients with pulmonary involvement are diagnosed with high sensitivity and specificity. Imaging will also have an important place in the diagnosis of viral infections targeting multiple organ systems and the late-stage complications of this disease.

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