



# COVID-19 pneumonia: lessons learned, challenges, and preparing for the future

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## ABSTRACT

Coronavirus disease 2019 (COVID-19) is a viral disease that causes life-threatening health problems during acute illness, causing a pandemic and millions of deaths. Although computed tomography (CT) was used as a diagnostic tool for COVID-19 in the early period of the pandemic due to the inaccessibility or long duration of the polymerase chain reaction tests, current studies have revealed that CT scan should not be used to diagnose COVID-19. However, radiologic findings are vital in assessing pneumonia severity and investigating complications in patients with COVID-19. Long-term symptoms, also known as long COVID, in people recovering from COVID-19 affect patients' quality of life and cause global health problems. Herein, we aimed to summarize the lessons learned in COVID-19 pneumonia, the challenges in diagnosing the disease and complications, and the prospects for future studies.

At the end of 2019, pneumonia cases of unknown cause emerged in Wuhan, China. Later, scientists determined that this pneumonia agent was a previously unknown betacoronavirus [severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)].<sup>1</sup> Then, the World Health Organization declared the disease [coronavirus disease 2019 (COVID-19)] caused by SARS-CoV-2 a pandemic.<sup>2</sup> The most prevalent problems in COVID-19 patients during acute illness are pneumonia, respiratory failure, sepsis, and death. In addition to patient-related factors, coinfections and superinfections are essential causes of poor prognosis in COVID-19 patients during acute illness.<sup>3</sup> Radiologic findings are vital in assessing pneumonia severity, prognosis, the presence of coinfections, and investigating complications in COVID-19.<sup>4-6</sup> In addition to acute illness, long-term symptoms experienced by people recovering from COVID-19 are also significant health problems reported more frequently.<sup>7</sup> Herein, we provide an overview of the lessons learned in patients with COVID-19 pneumonia, the early and long-term complications of COVID-19 pneumonia, and the prospects for future studies.

## Clinical features of COVID-19

The clinical manifestations of SARS-CoV-2 infection are very variable and range from asymptomatic to severe illness requiring mechanical ventilation. A large meta-analysis involving approximately 30 million tested individuals showed that 40.5% of cases infected with SARS-CoV-2 were asymptomatic.<sup>8</sup> Older age, male gender, underlying comorbidities, and being unvaccinated are risk factors for severe disease.<sup>9</sup> Some SARS-CoV-2 variants have been associated with less frequent risks of severe disease.<sup>10</sup> Moreover, vaccination against COVID-19 reduces the risk of severe disease, leads to less pneumonia at chest computed tomography (CT), and is associated with good prognosis.<sup>11,12</sup>

The median incubation period of SARS-CoV-2 is approximately 4-5 days after exposure. Cough, fever, myalgia, diarrhea, smell or taste abnormalities, and headache are the frequently reported symptoms of COVID-19.<sup>1,3-6,12,13</sup> Mild upper respiratory symptoms (e.g., sore throat, sneezing, and nasal congestion) have been more commonly reported with the Delta (B.1.617.2) and Omicron (B.1.1.529) variants.<sup>10,14</sup> Pneumonia is the most common serious presentation of SARS-Cov-2 infection, and no specific symptoms can reliably

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distinguish COVID-19 from other infectious agents. However, some clinical features (notably, smell or taste abnormalities) are more frequent in COVID-19 than in other respiratory infections.<sup>15</sup>

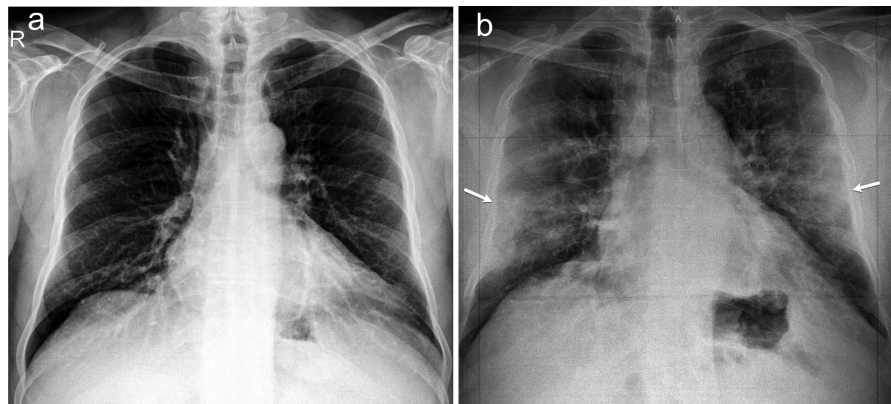
## Imaging findings of COVID-19 pneumonia

### Chest radiograph

Although the chest radiograph (CR) may be completely normal in the early stages of COVID-19 or mild disease, it has been shown that approximately 74% of patients have an abnormal CR at the time of diagnosis or follow-up.<sup>16</sup> While there is no specific imaging feature in CR to diagnose COVID-19 pneumonia, the most common abnormalities are bilateral, basal predominant consolidation, and ground-glass opacities (GGOs)<sup>4-6,16</sup> (Figure 1). The British Chest Imaging Society has developed a simple CR reporting template to help facilitate the consistency of CR reporting in patients with suspected COVID-19.<sup>17</sup> For classic/probable disease described in this guideline,<sup>17</sup> moderate sensitivity (44%), excellent specificity (100%), and significant agreement between observers ( $\kappa=0.61$ ) have been demonstrated. The advantages of CR are that it is easily accessible and contains a low radiation dose compared to chest CT. Therefore, it is the preferred imaging tool in pregnant and pediatric patients. Moreover, CR plays a crucial role in the clinical triage of COVID-19 patients, and the percentage opacification score in CR is an essential predictor of the prognosis.<sup>16-18</sup>

### Lung ultrasound

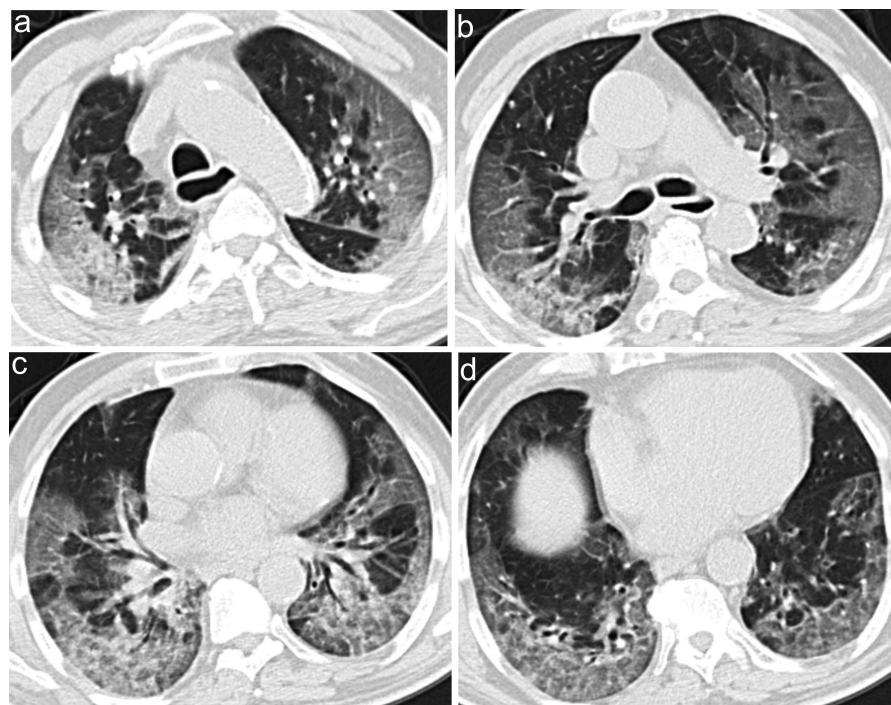
Lung ultrasound (US) is a radiation-free, non-invasive, well-tolerated, feasible, and low-cost imaging tool.<sup>19</sup> Since lung lesions



**Figure 1. a, b.** A 48-year-old man with acute severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Posteroanterior chest radiograph (CR) at the time of diagnosis reveals no signs of pneumonia (a). Posteroanterior CR 6 days later shows peripheral and basal predominant opacities (arrows), consistent with COVID-19 pneumonia (b).

due to COVID-19 pneumonia mainly affect peripheral lung regions, it is possible to evaluate COVID-19 pneumonia by lung US.<sup>19,20</sup> Lung US can make an essential contribution to assessing the presence and extent of COVID-19 pneumonia, as it allows quick and bedside examination, especially in mechanically ventilated patients.<sup>20,21</sup> The most crucial disadvantage of lung US is its user dependency.<sup>19,21</sup> Diagnosis of lung abnormalities in the US is based on artifacts created by peripheral pulmonary lesions. The US can demonstrate the typical features of interstitial pneumonia, including

B lines (focal, multifocal, or confluent), pleural irregularities, air bronchograms, thickening of the pleural line, and discontinuous (interrupted) pleural line.<sup>19</sup> Different severity scores have been proposed for assessing the extent of COVID-19 pneumonia by lung US based on segmentation of the lungs and semiquantitative analysis of the findings in each lung segment.<sup>20</sup> It has also been shown that lung US can reveal critical respiratory conditions requiring mechanical ventilation and can be used to monitor the development of acute respiratory distress syndrome (ARDS).<sup>22</sup> In addition, lung



**Figure 2. a-d.** A 57-year-old man with acute SARS-CoV-2 infection. Unenhanced axial computed tomography (CT) images at presentation demonstrate peripheral and basilar predominant ground-glass opacities (GGOs), (a-d).

### Main points

- Radiologic findings are vital in assessing pneumonia severity, prognosis, the presence of coinfections, and investigating complications in COVID-19.
- Pulmonary thromboembolism is a poor prognostic factor for COVID-19 patients.
- Long-term symptoms experienced by people recovering from COVID-19 (Long COVID) are also significant health problems.
- There is an increased risk of secondary infections, some of which can be fatal, in COVID-19 patients.

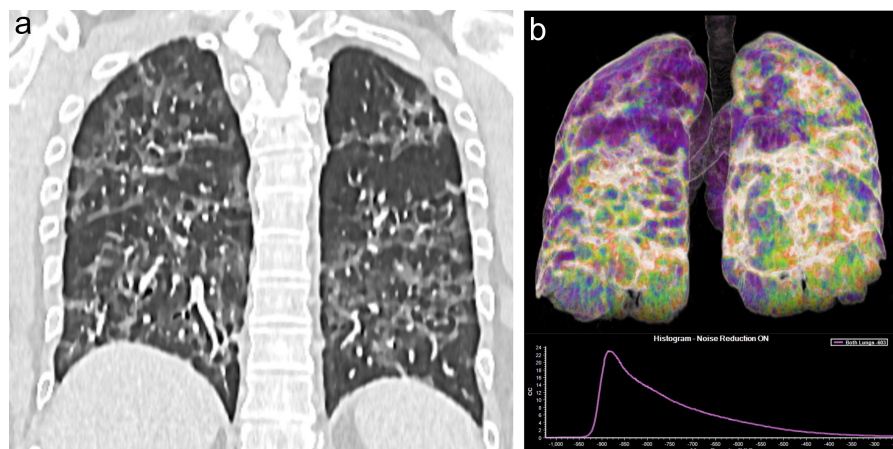
US can be used in intensive care unit (ICU) patients to recognize complications such as pneumothorax, guide invasive procedures, and evaluate the correct endotracheal tube position.<sup>23,24</sup>

### Magnetic resonance imaging

Apart from case reports, there are few studies investigating the characteristics of COVID-19 pneumonia in pulmonary magnetic resonance imaging (MRI). Torkian et al.<sup>25</sup> showed that parenchymal lesions (GGOs, areas of consolidation, and reticulation) could be visualized on pulmonary MRI similarly to chest CT. Ates and colleagues<sup>26</sup> reported no significant difference between MRI and CT in detecting COVID-19-related parenchymal lesions, and they also reported that MRI had high accuracy for COVID-19 pneumonia assessment. Similarly, Yang et al.<sup>27</sup> also revealed the high agreement between chest CT and ultra-short echo-time MRI in COVID-19-related parenchymal lesion detection. While MRI successfully diagnoses pulmonary lesions, it is recommended to limit the use of MRI in patients with confirmed or suspected COVID-19.<sup>28</sup> In addition to concerns about infectious transmission, the limitations of pulmonary MRI are its sensitivity to motion artifacts, low signal intensity of the parenchyma, and susceptibility artifacts.<sup>25,27</sup> Although pulmonary MRI is not routinely accepted to evaluate for COVID-19 pneumonia, pulmonary MRI may provide a viable alternative in high-risk patient groups without ionizing radiation.<sup>25-27</sup>

### Chest CT

Early studies have reported high sensitivity of chest CT for diagnosing COVID-19, especially in regions with limited access to polymerase chain reaction (PCR) tests.<sup>29-31</sup> However, these early publications did not include any control group; therefore, the specificity of chest CT was unknown. Furthermore, most of these studies suffered from patient selection bias, and the patient population of these studies was ambiguous (probably most had COVID-19 patients with severe clinical symptoms).<sup>29-31</sup> Later studies have shown that CT sensitivity and specificity are low (<50%) in the early phase of illness and asymptomatic or mildly symptomatic cases.<sup>32</sup> In a real-world study, the positive predictive value of chest CT for COVID-19 diagnosis was only 52%, and a significant overlap in CT findings was

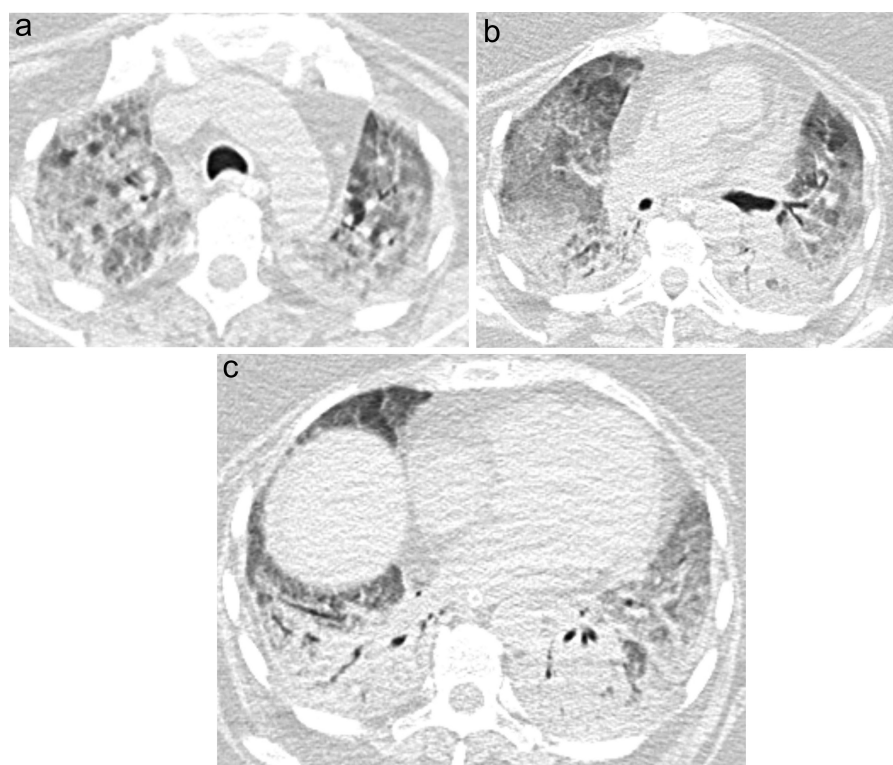


**Figure 3.** a, b. A 42-year-old man with acute SARS-CoV-2 infection. Unenhanced coronal CT image during the seventh day of illness shows patchy GGOs in both lungs (a). The corresponding quantitative CT image shows the CT attenuation histogram and reveals the ground-glass areas colored according to the CT density values (b).

observed between COVID-19 pneumonia, influenza pneumonia, and non-infectious organizing pneumonia.<sup>33</sup> For all these reasons, in the diagnosis of COVID-19, chest CT should not be used alone.

Imaging may vary depending on the patient's immunity, vaccination history, and the type of SARS-CoV-2 variant. The most frequently reported chest CT findings of COVID-19 pneumonia are peripheral and basilar predominant GGOs and areas

of consolidation<sup>4,6,34,35</sup> (Figure 2). Moreover, vascular enlargement, pleural thickening, halo sign, crazy-paving pattern, reversed halo sign, pulmonary nodules, and bronchial wall thickening are also frequently reported chest CT findings. Pleural effusion, pericardial effusion, central distribution of opacities, mediastinal or hilar lymphadenopathy, tree-in-bud sign, and cavitation are atypical features of COVID-19 pneumonia.<sup>4,6,29-31,35</sup> Recently, Yoon et al.<sup>34</sup>



**Figure 4.** a-c. A 61-year-old woman with early SARS-CoV-2 infection and acute respiratory distress syndrome (ARDS). Non-contrast enhanced axial CT images at presentation demonstrate extensive GGOs, dependent consolidation areas, and areas of crazy paving (a-c).



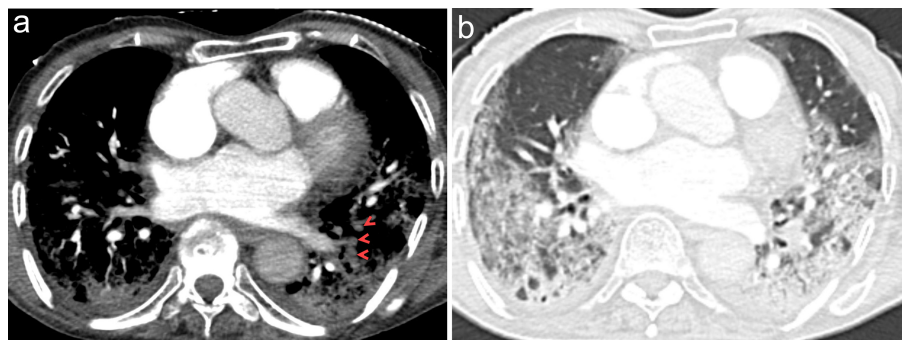
demonstrated that the Omicron variant showed more frequent atypical chest CT findings than the Delta variant. They also showed no difference between these 2 variants for pneumonia extent.<sup>34</sup>

#### Chest CT protocol and radiation dose exposure

Ionizing radiation is a carcinogenic factor, and radiation dose and age of radiation exposure are 2 critical modifiers of cancer risk from ionizing radiation. It is essential to be aware of the ionizing radiation risk in CT as most cases with SARS-CoV-2 infection survive.<sup>4,6,35,36</sup> Scanning protocols and radiation doses in the use of chest CT scan in COVID-19 cases have been shown to vary considerably around the world.<sup>36</sup> Coşkun et al.<sup>37</sup> revealed that the total radiation exposure for infectious indications increased almost 6 times during the pandemic compared to the previous year. This widespread radiation dose exposure paves the way for a significant global health problem.<sup>36,37</sup> Tabatabaei et al.<sup>38</sup> revealed that low-dose chest CT is reliable in detecting COVID-19 pneumonia with a significant dose reduction. Similarly, Hosseini Nasab et al.<sup>39</sup> showed that for assessing COVID-19 pneumonia, a range of tube currents of 20-50 mAs could produce acceptable chest CT images regarding radiation dose and diagnostic quality. Considering all these results, choosing the most appropriate CT protocol to reduce the radiation dose is crucial. Moreover, in COVID-19 cases, if vascular pathology is not suspected, non-contrast chest CT should be preferred when necessary.<sup>6,35,36,40</sup>

#### Reporting and communicating chest CT findings

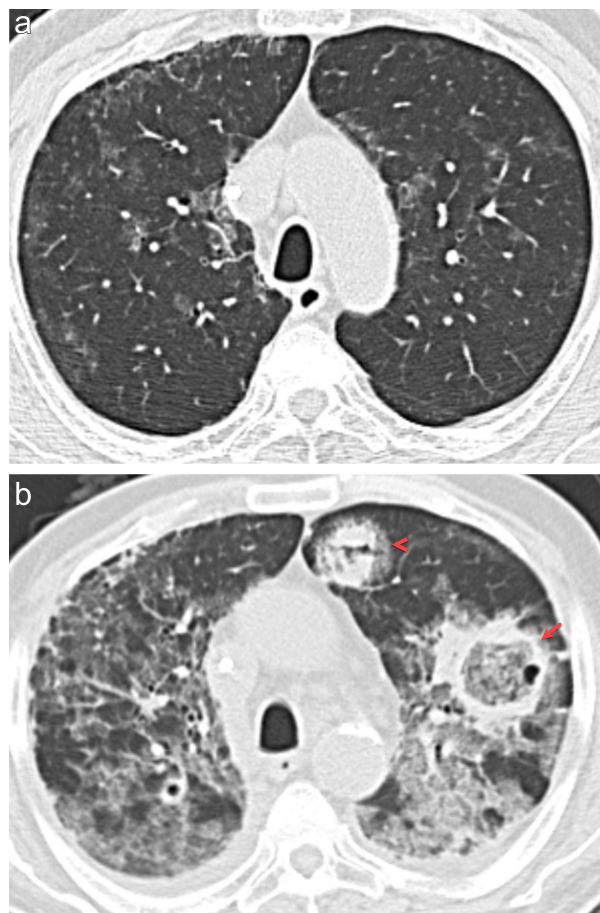
PCR tests are the gold standard for diagnosing COVID-19, and chest CT scanning is only recommended for patients in a limited population.<sup>40</sup> Chest CT findings of many diseases can mimic COVID-19, and various assessment systems have been published to standardize CT reporting. The Radiological Society of North America (RSNA) recommended a chest CT classification for COVID-19 pneumonia that includes 4 categories (i.e., typical appearance, uncertain appearance, atypical appearance, and negative for pneumonia). Dutch researchers defined the CO-RADS (COVID-19 reporting and data system) for the probability of COVID-19 pneumonia.<sup>41</sup> They created a categorical assessment scheme representing the level of suspicion



**Figure 5.** a, b. A 55-year-old man with early SARS-CoV-2 infection and pulmonary thromboembolism. Contrast-enhanced axial pulmonary CT angiography images with (a) mediastinum and (b) lung window settings show acute pulmonary embolism in the left lower segmental pulmonary arteries (arrowheads) and bilateral GGOs.

of pulmonary involvement in patients with suspected COVID-19. Salehi et al.<sup>42</sup> described the COVID-RADS (COVID-19 imaging reporting and data system), and Gezer et al.<sup>43</sup> defined the COVID-19 S for the probability of COVID-19 pneumonia. Inui et al.'s study<sup>44</sup> comparing COVID-19

CT reporting systems (RSNA statement, CO-RADS, and COVID-RADS) showed good interobserver agreement ( $\kappa=0.61-0.63$ ) and good diagnostic performance compared with the PCR test results. Moreover, Abdel-Tawab et al.<sup>45</sup> demonstrated that CO-RADS and RSNA chest CT classification



**Figure 6.** a, b. A 73-year-old male with a history of autologous bone marrow transplantation due to mantle cell lymphoma. He presented with recent-onset fever and cough due to acute SARS-CoV-2 infection. Unenhanced axial CT images at presentation demonstrate patchy peripheral and peribronchial patchy GGOs (a). Axial chest CT image 13 days later shows extensive GGOs and newly emerged lesions with halo sign (arrowhead) and reverse halo sign (arrow) in the left upper lobe (b). A transbronchial biopsy was performed, and a histopathological diagnosis of pulmonary mucormycosis was made.

systems could be used to diagnose COVID-19 pneumonia with high sensitivity and reliability.

#### Role of chest CT for prognostication

Many studies have shown that an increase in the extent of pneumonia in chest CT indicates a poor prognosis.<sup>5,9,40,46</sup> Pneumonia severity can be evaluated with visual (semi-quantitative evaluation) and computer-aided software (quantitative evaluation). In semiquantitative evaluation, each lung lobe's involvement percentage is calculated visually, and the pneumonia severity score of the whole lung is determined by summing up the involvement rates.<sup>5,46</sup> Quantitative CT evaluation is a method that provides an objective and rapid assessment of COVID-19 pneumonia extent and predicts patient prognosis<sup>47-49</sup> (Figure 3). Ufuk et al.<sup>46</sup> demonstrated that pneumonia severity was an independent predictor of prolonged hospitalization (adjusted odds ratio [OR]: 1.20,  $P < .001$ ), intubation (OR: 1.73,  $P < .001$ ), and death (OR: 2.13,  $P = .026$ ). Kaya et al.<sup>47</sup> reported that quantitative CT assessment had high sensitivity and specificity in distinguishing disease severity and predicting prolonged hospitalization. Salvatore et al.<sup>50</sup> reported that an overall pneumonia severity score of  $\geq 50\%$  indicates a poor prognosis. Moreover, Colombi et al.<sup>51</sup> showed that a visually well-aerated lung volume  $< 73\%$  (OR: 5.4,  $P < .001$ ) was a predictor of ICU admission or death.

#### Temporal changes of COVID-19 pneumonia at chest CT

Chest CT findings show temporal changes in COVID-19 pneumonia, and predominant CT findings may vary according to the disease period in which CT was obtained. Wang et al.<sup>52</sup> and Pan et al.<sup>53</sup> reported that after symptom onset, the predominant parenchymal abnormality was GGO. Wang et al.<sup>52</sup> showed that the extent of pneumonia progressed rapidly after symptom onset and peaked during illness days 6-11, and the percentage of mixed opacities (GGO and consolidation) peaked at disease days 12-17. Pan et al.<sup>53</sup> reported that parenchymal lesions were slowly resorbed 2 weeks after COVID-19 pneumonia.

#### Disease course and acute complications

The clinical features of symptomatic SARS-CoV-2 infection can range from mild to critical.<sup>4,8,40</sup> Symptoms may progress

rapidly in some patients, and several acute complications of COVID-19 have been described and discussed under the following subheadings.

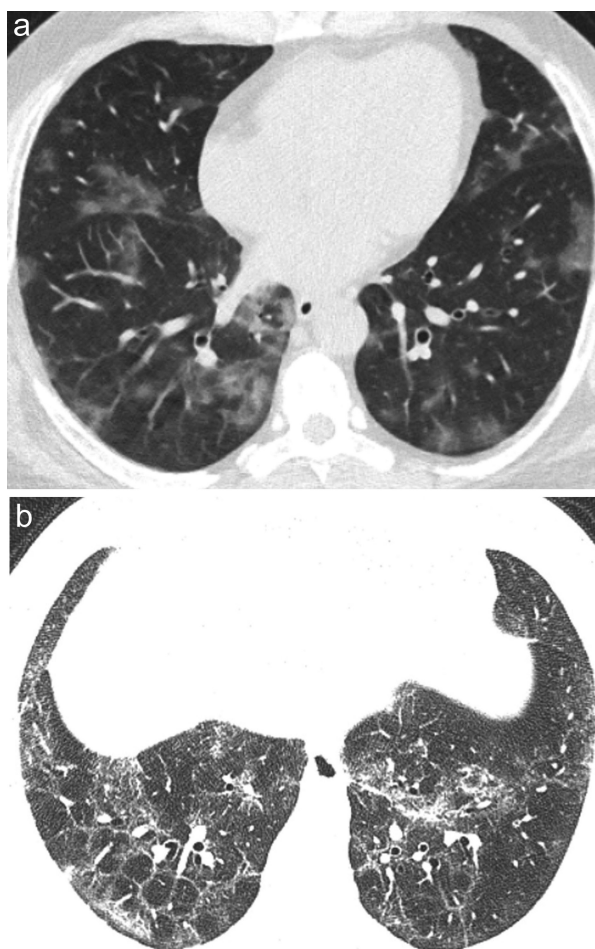
#### ARDS and Respiratory Failure

Respiratory failure and ARDS are the major complications of COVID-19 pneumonia and can manifest shortly after dyspnea. These conditions are associated with diffuse alveolar damage (DAD) and capillary endothelial injury.<sup>54</sup> Respiratory failure requiring mechanical ventilation can be seen in approximately one-fifth of hospitalized patients with COVID-19.<sup>9,41,42,46</sup> A significant positive correlation was demonstrated between respiratory failure and CT severity score in COVID-19 patients.<sup>5,46-51</sup> In the early phase of ARDS, diffuse GGOs and consolidations with an anterior-posterior gradient can be seen on chest CT. In the later period, diffuse GGOs and bronchial dilatation

within areas of GGO are frequently reported CT findings<sup>22,52</sup> (Figure 4).

#### Pulmonary thromboembolism

Pulmonary thromboembolism (PTE) is a poor prognostic factor for COVID-19 patients, and PTE is associated with a higher pneumonia severity score and lower saturation level.<sup>55</sup> In the meta-analysis of Suh and colleagues,<sup>56</sup> the pooled incidence of PTE was reported as 16.5% in 3342 COVID-19 patients. They also showed that embolism was in peripheral pulmonary arteries in the vast majority of patients (60.4%) and a higher incidence of PTE in patients admitted to the ICU<sup>56</sup> (Figure 5). The D-dimer test results have been reported to have high sensitivity and low specificity.<sup>55-57</sup> Higher D-dimer levels are associated with a poor prognosis, and it has been suggested that D-dimer levels should be the driving force in decision-making.<sup>56</sup>



**Figure 7. a, b.** A 59-year-old man with fibrosis resulting from SARS-CoV-2 infection. Unenhanced axial chest CT image at presentation demonstrates peripheral and peribronchial patchy GGOs (a). Axial high-resolution CT image 12 months after SARS-CoV-2 infection shows GGOs and newly emerged peribronchial, perilobular, and peripheral reticulations (b).



## Secondary infections

There is an increased risk of bacterial/fungal secondary infections, some of which can be fatal, in COVID-19 patients. Rawson et al.<sup>58</sup> revealed that 62 of 806 (8%) COVID-19 patients experienced coinfection during hospitalization. Musuuzza et al.<sup>3</sup> showed that 19% of COVID-19 patients have secondary infections, and the secondary infections were associated with a poor prognosis. *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Hemophilus influenzae*, *Escherichia coli*, and *Pseudomonas aeruginosa* were the most common coinfecting pathogens, *Acinetobacter* spp., Epstein-Barr virus, and invasive pulmonary aspergillosis were the most commonly reported secondary infections.<sup>3,58</sup> Fungal superinfections are rarely seen in COVID-19 patients but have high mortality. Immunosuppression, diabetes mellitus, corticosteroids, and immunosuppressive agents are risk factors for fungal superinfections<sup>3</sup> (Figure 6). The presence of atypical findings, such as isolated lobar or segmental consolidation, centrilobular lung nodules, lung nodules with a tree-in-bud sign, and cavity, in chest CT should suggest secondary infection.<sup>35,40,41</sup>

## Inflammatory complications

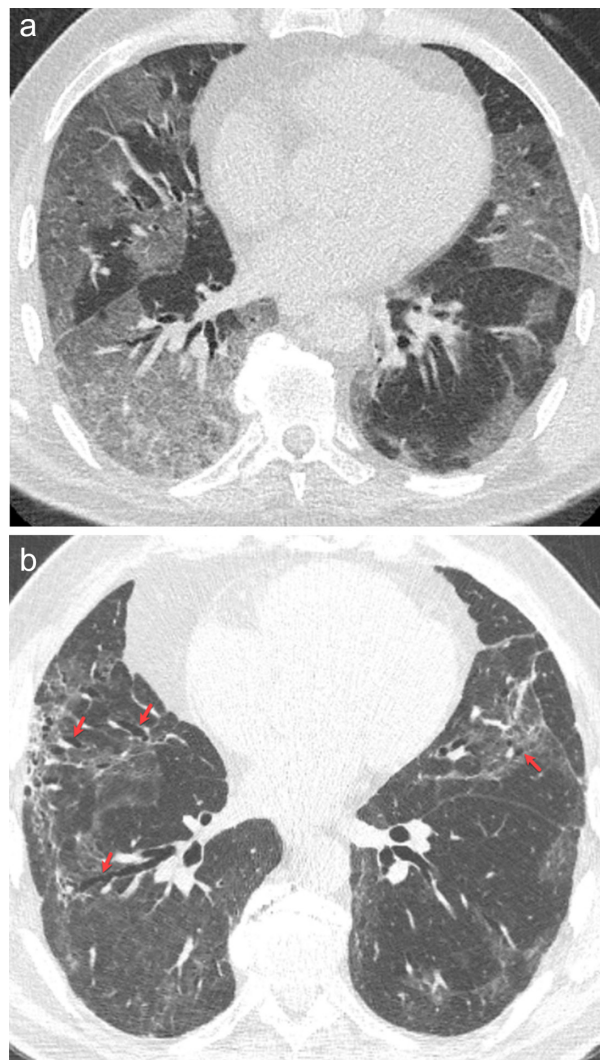
In some cases with severe COVID-19, a multisystemic hyperinflammation (mHI; persistent fever, skin rashes, elevated proinflammatory cytokines, multiorgan dysfunction, and hepatosplenomegaly) can occur.<sup>59,60</sup> An mHI characterized by clinical features similar to Kawasaki disease or toxic shock syndrome has also been described in children with COVID-19 [multi-system inflammatory syndrome in children (MIS-C)].<sup>60</sup> Although MIS-C is predominantly characterized by cardiopulmonary abnormalities (heart failure, cardiomegaly, myocarditis, coronary artery aneurysms, pulmonary edema, pleural effusion, pericardial effusion, consolidation, and ARDS), hepatomegaly, ascites, and intestinal abnormalities were reported.<sup>60,61</sup> Rarely, an MIS in adults, characterized by markedly elevated proinflammatory cytokines and multiorgan dysfunction similar to MIS-C, can be seen.<sup>59</sup>

## Long-term pulmonary sequelae

Post-COVID-19 condition, which is also known as long-term sequelae of COVID-19 or long COVID, has been frequently described in the literature recently.<sup>7,62-65</sup>

However, the causes of post-COVID-19 condition and persistent respiratory symptoms are currently poorly understood. Pulmonary function tests (PFTs), CR, chest CT, pulmonary MRI, and 6-minute walk test have been used to evaluate patients with post-COVID-19 respiratory complaints.<sup>62-65</sup> Long COVID is characterized by multiorgan involvement, prolonged symptoms, and significant disability in individuals recovering from COVID-19.<sup>65</sup> The leading causes of pulmonary sequelae of viral pneumonia are direct injury by viral organisms (bronchiolitis, bronchitis, and DAD) and the host's immune response. In the middle-long term (approximately 1 year later) after COVID-19 pneumonia, fibrosis-like changes can be seen on chest CT in about one-third of the cases. The most common CT findings were architectural distortion,

GGOs, traction bronchiectasis, honeycombing, septal thickening, and reticulation<sup>62,65</sup> (Figure 7). Moreover, post-viral obliterative (or constrictive) bronchiolitis can be seen and cause dyspnea with an obstructive defect in PFTs, mosaic attenuation, air trapping, and tubular bronchiectasis on chest CT.<sup>62-64</sup> Pulmonary fibrosis due to DAD is associated with the development of traction bronchiectasis and reticulation and is associated with restrictive physiology in PFTs (Figure 8). Han et al.<sup>62</sup> demonstrated that approximately half of the patients showed evidence of fibrosis-like changes on chest CT obtained six months after COVID-19, and these fibrosis-like changes are similar to that described in the 2002-2003 SARS epidemic. In a study of patients with post-COVID-19 respiratory symptoms, Cho et al.<sup>63</sup> showed that air trapping was present on CT



**Figure 8.** a, b. A 48-year-old man with fibrosis resulting from SARS-CoV-2 infection. Unenhanced axial CT image at presentation shows extensive peripheral predominant GGO areas (a). Unenhanced axial CT image 7 months later shows marked clearing of GGO but development of reticulation and mild bronchial dilations (arrows) (b).

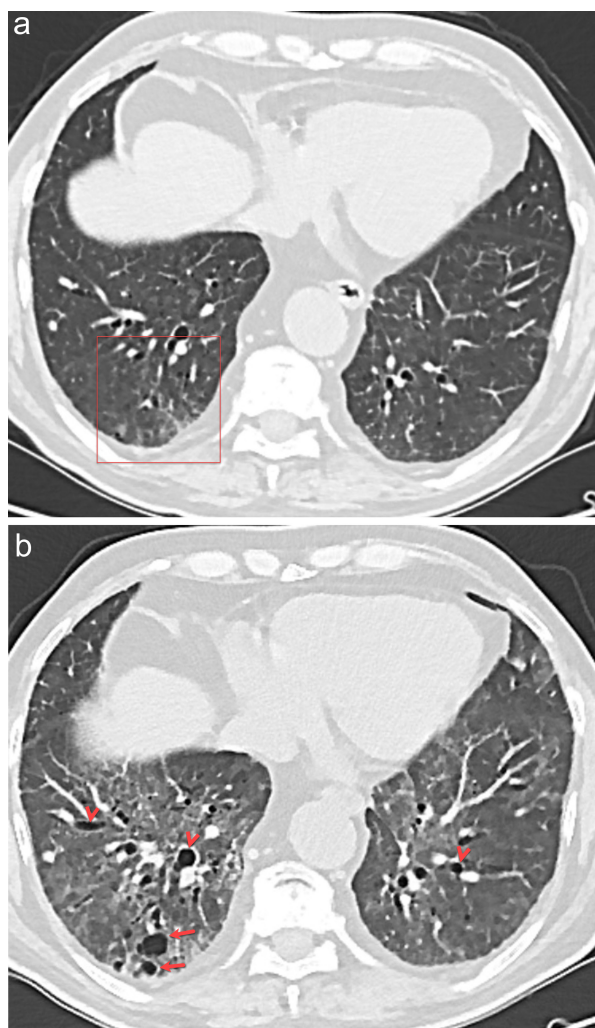
in more than half of the participants following COVID-19, indicating post-viral constrictive bronchiolitis. Moreover, Cho et al.<sup>63</sup> demonstrated that ICU-admitted patients had restrictions on PFTs and frequently had fibrosis-like changes on chest CT, which may be contributed by post-ventilatory fibrosis<sup>63</sup> (Figures 9 and 10). Matheson and colleagues<sup>64</sup> showed that inhaled hyperpolarized xenon-129 (129Xe) gas exchange MR spectroscopy and CT vascular density measurements were abnormal and correlated with PFTs in patients with post-COVID-19 condition. Based on the evidence in this study, Matheson et al.<sup>64</sup> suggested that pulmonary symptoms may result from microvascular abnormalities. Similarly, Grist et al.<sup>65</sup> demonstrated that participants with post-COVID-19 respiratory symptoms and

normal chest CT scans had significantly impaired gas transfer with hyperpolarized 129Xe MRI. Currently, there are no optimal evidence-based treatment guidelines targeting patients with post-COVID-19 condition and respiratory symptoms. Therefore, more extensive studies are needed to identify factors associated with respiratory symptoms after COVID-19 and to provide treatment options for patients with post-COVID-19 condition.

#### COVID-19 vaccination-related complications

The infection rate and lethality of SARS-CoV-2 have been reduced with vaccinations. However, some side effects of the COVID-19 vaccinations, most of which are clinically insignificant, have been reported.

The most commonly reported side effects of COVID-19 vaccinations are headache, pain at the injection site, weakness, and fatigue, which are usually mild to moderate and disappear within a few days. Severe reactions after vaccination are rare, and cases of anaphylaxis, thrombosis with thrombocytopenia syndrome, Guillain-Barré syndrome, and myopericarditis have been reported.<sup>66</sup> COVID-19 vaccine-associated axillary adenopathy (AA) is of great importance in cancer patients, as it can be confused with malignant infiltration or metastasis of axillary lymph nodes on imaging examinations. In studies, the frequency of AA in COVID-19 vaccine recipients has been very variable, ranging from 0.3% to 29%.<sup>66,67</sup> Horvat et al.<sup>67</sup> found the frequency of AA in COVID-19 vaccine recipients was 29%, and they suggested that ipsilateral AA in a COVID-19 vaccine recipient should be considered probably benign in patients without malignant lesions on breast imaging and with low suspicion for cancer relapse. Younger patients are more likely to develop AA than older patients,<sup>66,67</sup> and ipsilateral AA occurred more frequently in patients receiving the Moderna (Spikevax) vaccine than in patients receiving the Pfizer-BioNTech (COMIRNATY) vaccine.<sup>67</sup> When incidental AA is detected in thoracic imaging, the patient's vaccination history, vaccination dates, and laterality should be questioned, and an US examination should be performed for adenopathy. Moreover, breast imaging should be performed, and if there is low suspicion of malignancy, adenopathy should be followed. Tissue sampling may be preferred in the presence of high suspicion of malignancy and the management of complex cases.<sup>66,67</sup>

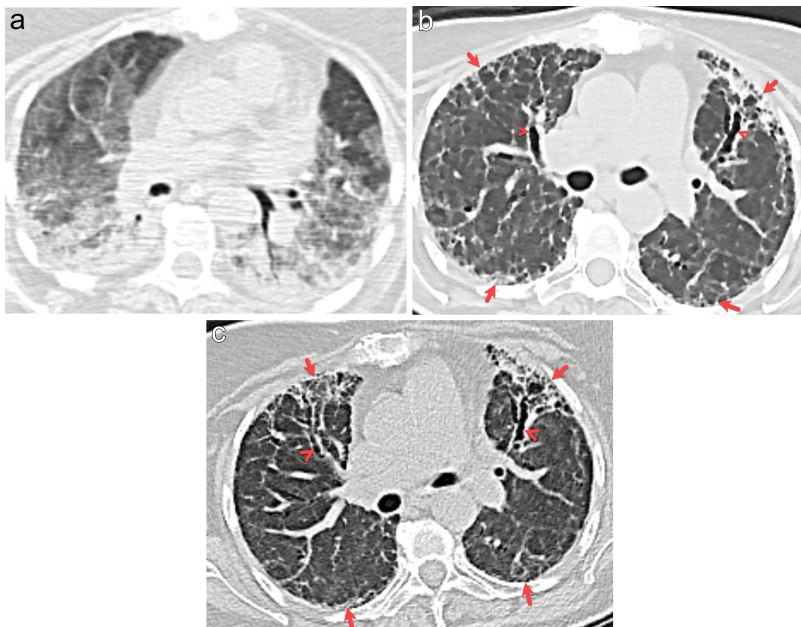


**Figure 9.** a, b. A 51-year-old woman with bronchiectasis/bronchiolectasis resulting from SARS-CoV-2 infection. Unenhanced axial CT image at presentation shows focal peripheral GGO in the right lower lobe. Respiratory failure developed a few days after CT; she was then intubated (a). Unenhanced axial CT image 6 months later shows marked decrease of diffuse GGOs in both lower lobes and development of bronchial dilations (arrowheads) and bronchiectasis/bronchiolectasis (arrows) (b).

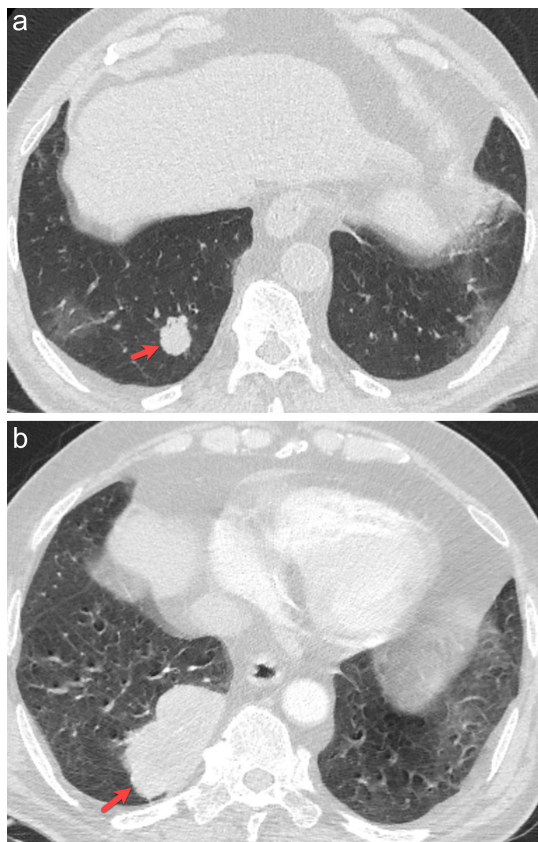
#### Artificial intelligence in COVID-19 pneumonia

Artificial intelligence (AI)-based models can accurately detect COVID-19 from CT and CR images, determine disease severity, distinguish it from other lung diseases, triage COVID-19 patients, and predict disease prognosis.<sup>68-71</sup> In addition, AI-based models can be applied to COVID-19 patients to reduce the significant impact on workload. For example, Li et al.<sup>68</sup> showed that an AI-based model achieved high accuracy in detecting COVID-19 pneumonia on CT images in an average time of 4.51 seconds. Zou and colleagues<sup>71</sup> reported that AI-based chest CT analysis correlated well with quantitative pulmonary fibrosis scores





**Figure 10.** a-c. A 63-year-old woman with fibrosis resulting from SARS-CoV-2 infection and ventilation. Unenhanced axial CT image during acute infection shows extensive areas of GGO and dependent consolidation, indicative for ARDS (a). Unenhanced axial CT image 8 months later shows decrease of GGOs and development of bronchial dilations (arrowheads) and reticulations (arrows) (b). Unenhanced axial CT image 14 months later infection shows the persistence of bronchial dilations (arrowheads) and reticulations (arrows) (c).



**Figure 11.** a, b. A 55-year-old man with a delayed diagnosis of lung cancer. Unenhanced axial CT image during acute infection shows peripheral areas of GGO and a solid ill-defined nodule in the right lower lobe (arrow). A biopsy was recommended, but the patient was lost to follow-up (a). Unenhanced axial CT image 16 months later shows a significant increase in the size of the nodule (arrow) (b). Histopathological analysis of the biopsy obtained from the mass showed the diagnosis of lung adenocarcinoma.

in patients with post-COVID-19 fibrosis. We suggest that studies with AI-based models that combine clinical and imaging-based data are needed to predict patients with long COVID and develop effective treatments.

### Radiology department and personnel preparedness

SARS-CoV-2 has infected many people worldwide, and the disease remains a pandemic. Imaging methods in the early stages of the COVID-19 pandemic significantly impacted the management.<sup>4,6,29-31</sup> During the early pandemic, patient circulation in radiology departments increased significantly, and the importance of keeping radiology departments and personnel as safe as possible increased even more. To keep the radiology departments and personnel to be safer, it is recommended to meet the following conditions<sup>72,73</sup>: (1) screening patients at the front desk for COVID-19, (2) training radiology staff on infection control, (3) ensuring the use and access of personal protective equipment, (4) implementing standard operating procedures for COVID-19 patients and suspected cases of COVID-19, (5) dedicating imaging systems such as CT, US, and CR only to COVID-19 patients, (6) using appropriate disinfection protocols after each patient for decontamination of rooms and devices, (7) providing remote access of radiological images for interpretations, (8) creating a dedicated radiography team to screen COVID-19 patients, (9) provisioning of negative pressure rooms for CT and CR examinations in hospitals, (10) encouraging universal masking and vaccination. With a comprehensive approach to radiology department preparedness, medical imaging can effectively participate in the battle against current and future virus outbreaks.

### Impact of COVID-19 on lung cancer

A remarkable decrease in new cancer diagnoses during the pandemic has been reported. Cantini et al.<sup>74</sup> revealed that the pandemic caused a delay in the diagnosis of lung cancer and that the probability of being diagnosed with stage IV disease in diagnosed lung cancer cases was higher than before the pandemic (Figure 11). The repercussions of COVID-19 on cancer diagnosis and treatment are likely to be felt for years to come.<sup>37,40,74</sup> As the negative consequences of delaying routine cancer screening and treatment strategies are emerging



due to the pandemic, it is essential to maintain care and screening for this patient population.

## Conclusion

Chest imaging can be used to evaluate COVID-19 pneumonia severity and investigate complications in the acute disease period. Imaging findings and PFTs provide essential information in evaluating post-COVID-19 respiratory complaints. Moreover, AI-based models can successfully distinguish COVID-19 from other lung diseases using CT images and provide information that can predict disease prognosis. Recent studies show that many patients recovering from COVID-19 experience long COVID, and there is no specific treatment yet. We believe that further radiological studies will enable us to understand better the pathophysiology of symptoms in patients with long COVID and help develop specific treatment.

## Conflict of interest disclosure

The authors declared no conflicts of interest.

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