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Review of Thoracic Imaging Manifestations of COVID-19 and Other Pathologic Coronaviruses



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KEYWORDS

- Coronavirus disease 2019 (COVID-19)
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- Computed tomography
- Severe acute respiratory syndrome coronavirus (SARS-CoV)
- Middle East respiratory syndrome coronavirus (MERS-CoV)

KEY POINTS

- Chest radiography (CXR) is often used as an initial diagnostic imaging tool in patients presenting with respiratory complaints.
- Computed tomography (CT) is more sensitive and specific than radiography for identifying lung abnormalities in patients with COVID-19.
- Common early imaging manifestations of COVID-19 on CT include ground-glass opacities, sometimes with a rounded morphology, and often with a peripheral and lower lobe predominant distribution.
- Several scoring methods have been proposed to evaluate the severity of lung disease on CXR and CT, and reporting guidelines have been produced by societies to assist in standardizing radiology reporting and guiding imaging in the postacute stage.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an easily transmissible coronavirus that emerged in late 2019 and has caused a global pandemic characterized by acute respiratory disease named coronavirus disease 2019 (COVID-19).¹ Although COVID-19 was first reported in the city of Wuhan, the capital city of central China's Hubei Province, it rapidly spread throughout the world and became one of the greatest global health crises of this century.² To date, there are more than 235 million people worldwide with documented SARS-CoV-2 infection and more than 4.8 million deaths.^{3,4}

SARS-CoV-2 belongs to a family of viruses known as coronaviridae. To date, 7 coronaviruses that infect humans have been identified,⁵ which include severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV).⁶ SARS-CoV emerged in 2002 and led to an epidemic in southeast China, which ultimately resulted in 774 deaths out of 8098 total cases.⁷ MERS originated in Saudi Arabia in 2012 and ultimately resulted in 858 deaths out of 2494 infected individuals.⁸ The SARS outbreak of 2002 was eradicated and has never resurfaced, with the last case being reported in 2003. MERS, however, continues to have

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episodic small outbreaks, often clustered in families or hospitals but usually limited to a single geographic location. The number of people infected with COVID-19 has far surpassed both SARS and MERS, but COVID-19 has a much lower mortality rate than both diseases.⁹ The remaining coronaviruses known to infect humans are (HCoV)-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1.⁵ These are relatively benign respiratory pathogens in humans (often children), typically causing upper respiratory tract disease and common cold symptoms.⁵

Most of the COVID-19 diagnostic assays available to date require the collection of nasopharyngeal swab to assess for SARS-CoV-2 viral RNA.² Although diagnosis of COVID-19 is definitively made through laboratory testing, diagnostic imaging can be helpful as a complementary tool in supporting the diagnosis or identifying alternative pathology. In this article, the authors aim to review the thoracic imaging manifestations of COVID-19.

CLINICAL MANIFESTATIONS

SARS-CoV-2 infection has been estimated to have a mean incubation period of 5.1 to 6.4 days, with most of the patients (97.5%) developing symptoms within 11.5 days.² SARS-CoV-2 typically affects the lower respiratory tract. It can present clinically with a multitude of symptoms, with the most common including fever, cough, and dyspnea. Patients with COVID-19 may be asymptomatic or show symptoms ranging from mild to severe. In severe cases, symptoms can escalate into acute respiratory distress syndrome (ARDS), and this can develop in 17% to 29% of patients.^{10,11} Complicated COVID-19 infection can result in multiorgan dysfunction characterized by respiratory failure, encephalopathy, coagulopathy and vasculopathy, acute cardiac injury and cardiac failure, renal failure, and other end-organ damage.^{2,11} Studies suggest that most of the COVID-19 mortalities occur among patients with ARDS in the intensive care unit (ICU).¹²

DIAGNOSTIC CONFIRMATION OF COVID-19

Current detection methods rely on real-time reverse transcription polymerase chain reaction (RT-PCR) to test mucosal swabs of suspected patients. However, some false-negative RT-PCR results were reported in the early stages of the disease, possibly because of inadequate viral material in the sample or technical issues during nucleic acid extraction.¹³ In the early stages of the pandemic, there was limited availability of RT-PCR in some locations because of a lack of

testing kits and reagents. Turnaround times for test results were (and continue to be) variable, ranging from hours to days.¹⁴

The role of radiology in COVID-19 is evolving and may vary depending on local disease prevalence and availability of laboratory testing.

THE ROLE OF IMAGING

Chest computed tomography (CT) findings have proved to be diagnostic in several cases with an initial false-negative RT-PCR screening test.¹³ The positive and negative predictive value of chest CT for COVID-19 are estimated at 92% and 42%, respectively, in a population with high pretest probability for the disease (eg, 85% prevalence by RT-PCR).¹⁵ The potential value of CT is that it is widely available and can be performed rapidly. However, findings on chest imaging in COVID-19 are somewhat nonspecific in many cases and may overlap with other pulmonary infections.¹⁶ In addition, there are concerns regarding time management in the CT scanner, given that scan rooms must be thoroughly cleaned after imaging a suspected COVID-19 patient, and the air needs to be recirculated.² Currently, the Centers for Disease Control and Prevention (CDC), the American College of Radiology (ACR), the Society of Thoracic Radiology (STR), and the American Society of Emergency Radiology (ASER) have all recommended against the use of CT for routine screening and diagnosis of COVID-19 pneumonia, reserving CT for cases in which there is clinical suspicion of a complication of the disease or another diagnosis.^{17,18}

Several scoring methods have been proposed to evaluate the severity of lung inflammation on chest radiography (CXR) and CT. One chest CT severity score proposed by Yang and colleagues calculated individual scores from 20 lung regions; scores of 0, 1, and 2 were assigned for each region if parenchymal opacification involved 0%, less than 50%, or equal to or more than 50% of each region, respectively. The CT severity score was higher in patients with severe COVID-19 in comparison to patients with mild disease.¹⁹

ACUTE IMAGING MANIFESTATIONS

Chest Radiography

CXR is often used as an initial diagnostic imaging tool in patients presenting with respiratory complaints. Radiography in patients with COVID-19 can vary from normal to hazy pulmonary opacities with a peripheral and lower lung distribution to frank diffuse pulmonary opacification depending on the severity of illness (**Fig. 1**). These findings

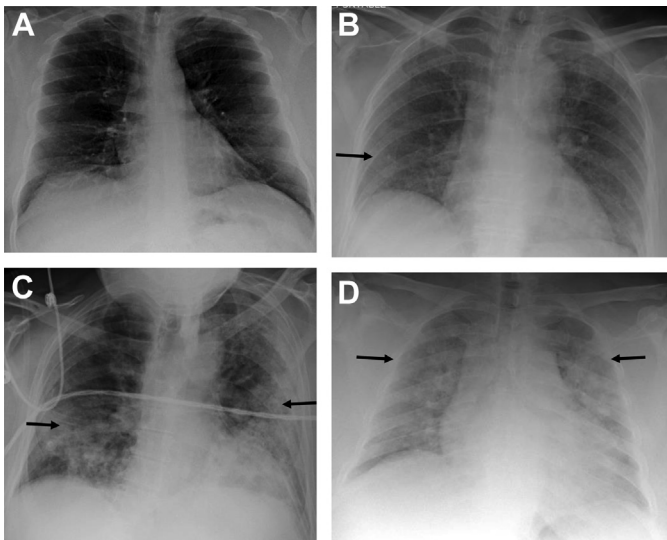


Fig. 1. Spectrum severity of COVID-19 on chest radiography. (A) No acute consolidation or other radiographic findings. (B) Mild bilateral ill-defined hazy opacities (arrow) in a peripheral and lower lobe distribution. (C) Moderate multifocal patchy opacities (arrows) in a predominately peripheral distribution. (D) Severe bilateral diffuse patchy opacities (arrows).

may be nonspecific and can overlap with imaging findings in other diseases such as influenza, organizing pneumonia, and other acute lung injuries.²⁰ Radiography is less sensitive than CT, with a reported baseline CXR sensitivity of 69%.²¹ CXR is an effective way to assess progress/resolution of disease over time while minimizing radiation dose (Fig. 2).

Prognostic Value of Chest Radiography

It has been suggested that imaging in the acute phase can help predict disease severity in COVID-19. One study performed in patients aged 21 to 50 years with COVID-19 presenting to the emergency department demonstrated that a CXR

severity score was predictive of risk for hospital admission and intubation.²² Another study performed by Schalekamp and colleagues evaluated patients requiring hospitalization due to COVID-19 in the Netherlands. They found that patients who developed critical illness more often had higher initial chest radiography scores and bilateral involvement at admission.²³

Computed Tomography

CT is more sensitive and specific than radiography for identifying lung abnormalities in patients with COVID-19 (Fig. 3).²⁰ Investigators have demonstrated that COVID-19 on CT most commonly produces a pattern of bilateral ground-glass opacities

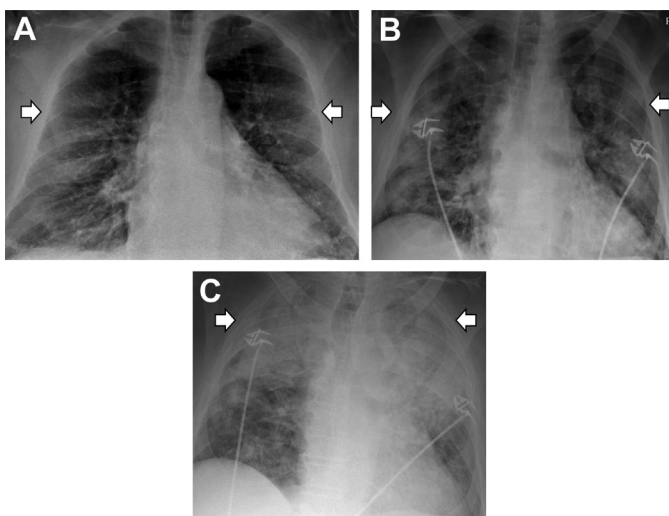


Fig. 2. A 75-year-old man with fever and cough. (A) CXR on admission shows mild multifocal hazy and patchy opacities in a peripheral distribution (arrows). (B) Follow-up CXR performed 5 days later shows worsening now moderate multifocal peripheral opacities (arrow). (C) Repeat CXR 14 days later shows interval worsening large consolidations in the upper to mid-lungs (arrows).

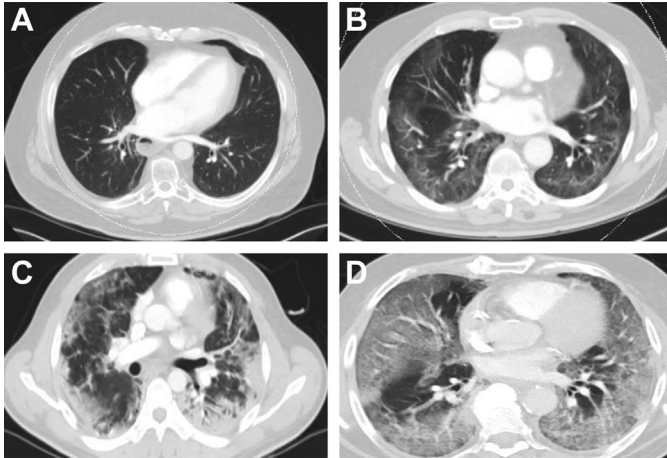


Fig. 3. Severity of COVID-19 on CT. (A) No acute pulmonary findings. (B) Mild bilateral ground-glass and reticular densities in a peripheral distribution. (C) Moderate bilateral peripheral consolidative and ground-glass opacities. (D) Severe diffuse peripheral ground-glass opacities.

(GGO), sometimes with a rounded morphology or with a “crazy paving” pattern (which is defined as GGO with superimposed interlobular septal thickening and visible intralobular lines) (Fig. 4).²⁴ The opacities often have a peripheral distribution, mainly in the lower lobes, with the right middle lobe typically being the least involved (Fig. 5). Additional less common imaging findings include interlobular septal thickening, bronchial dilatation, pleural thickening, and pleural effusions (Figs. 6 and 7).¹² Consolidation is considered an indication of disease progression.²⁵ A study by Pan and colleagues in China showed that the most severe lung abnormalities on CT in patients with COVID-19 were obtained approximately 10 days after symptom onset²⁵ (Fig. 8).

Chest CT findings in COVID-19 evolve as the illness progresses, similar to other causes of acute lung injury. In one study from the beginning of the pandemic, imaging findings related to disease

progression were separated into phases based on the number of days from symptom onset to initial CT—early (0–2 days); intermediate (3–5 days); late (6–12 days); absorption stage/fourth stage (>14 days). Patients imaged in the early stage often had a negative chest CT (56%), with the remaining patients having GGO or consolidation that were often unilateral. Most patients in the intermediate, late, and absorption stage had bilateral GGO and consolidation (55%) with a peripheral lung distribution.²⁶ Bao and colleagues found that the right lower lobe and left lower lobe were the most commonly involved lobes in COVID-19 (Fig. 9).²⁷

Additional Imaging Modalities

To date, there are limited data on the pulmonary MR imaging manifestations of COVID-19. Limitations to thoracic MR imaging implementation include longer scan time and increased cost



Fig. 4. A 60-year-old positive man with COVID-19 with focal ground-glass exhibiting a “crazy paving” pattern (arrow).

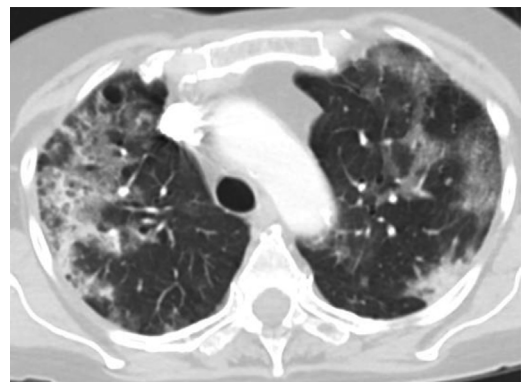


Fig. 5. A 70-year-old positive patient with COVID-19 with bilateral ground-glass opacities in a peripheral distribution.

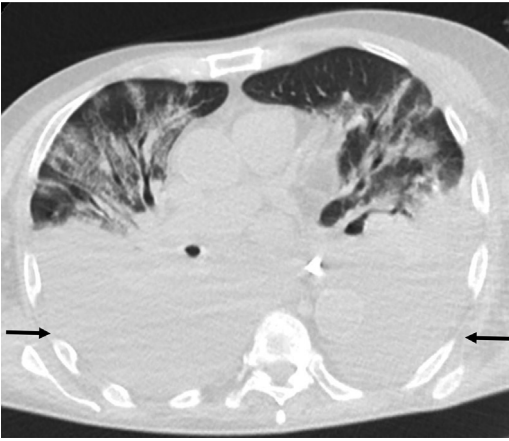


Fig. 6. A 74-year-old positive man with COVID-19 with large bilateral pleural effusions (arrows).

compared with CXR and CT. Nonetheless, MR imaging performed for unrelated indications such as cardiac, vascular, and musculoskeletal indications can demonstrate incidental findings related to COVID-19 in the lungs. The pulmonary distribution of COVID-19 on MR imaging mirrors CT and CXR, featuring basilar and peripheral predominant disease (**Fig. 10**). On MR imaging, the parenchymal changes of COVID-19 pneumonia seem as regions of abnormal increased signal intensity on both T1- and T2-weighted sequences, corresponding to the ground-glass or consolidative opacities seen on CXR and CT.^{28,29}

The literature on imaging manifestations of COVID-19 on PET with fludeoxyglucose F 18 integrated with computed tomography (18F-FDG PET/CT) is currently limited to mostly case reports in which patients were incidentally found to have COVID-19 during a PET/CT scan for oncologic staging.³⁰ These reports demonstrate elevated FDG avidity in areas of pulmonary opacity^{30,31} (**Fig. 11**). Reported maximum standardized uptake

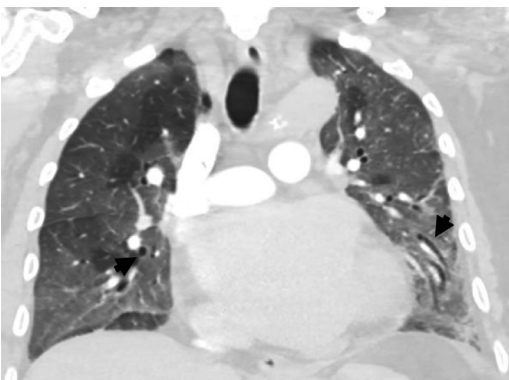


Fig. 7. A 79-year-old man with diffuse ground-glass opacification and mild bibasilar predominant bronchial dilatation (arrows).

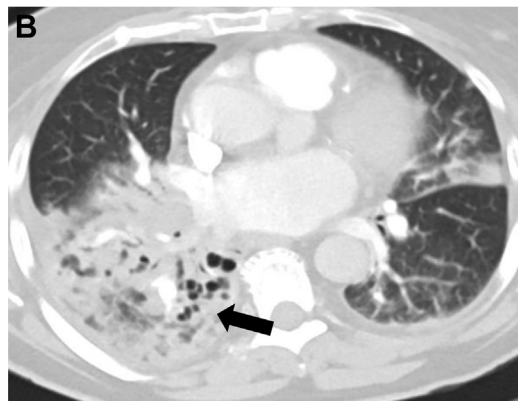
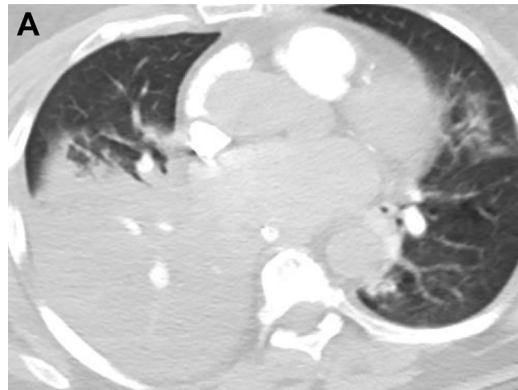


Fig. 8. Necrotizing pneumonia in a 69-year-old woman with RT-PCR-test-proven COVID-19. (A) Admission CT shows a large dense right lower lobe consolidation. (B) Follow-up CT performed 10 days later due to worsening respiratory symptoms shows new numerous air-filled cystic lucencies (arrow) within the consolidation, which suggests necrotizing pneumonia.

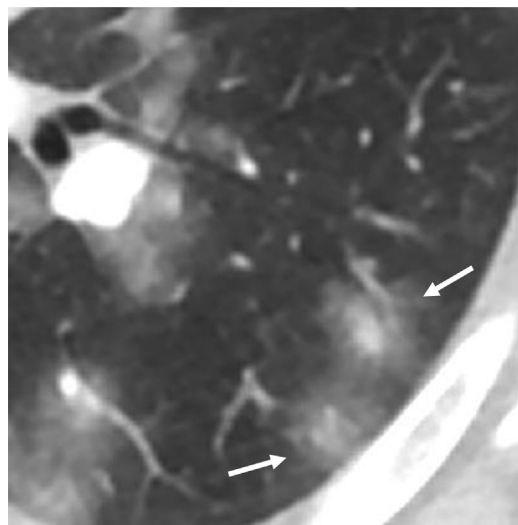


Fig. 9. Halo sign in a 31-year-old man with RT-PCR-test-proven COVID-19. Axial chest CT images show rounded dense consolidations surrounded by ground-glass opacities (arrows) in the left lower lobe, findings consistent with the halo sign.

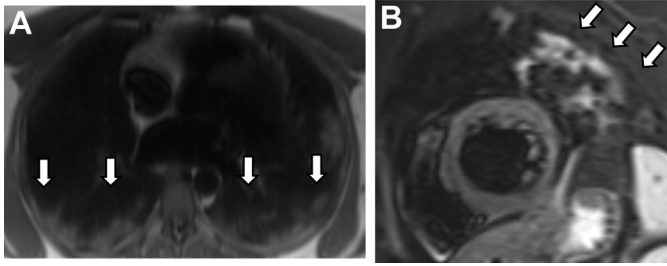


Fig. 10. Cardiac MR imaging performed in a 38-year-old woman with new-onset cardiomyopathy in the setting of COVID-19. (A) Axial T2-weighted sequence demonstrates multifocal areas of increased signal intensity (*arrows*) in a peripheral distribution. (B) Short-axis STIR sequence shows increased STIR signal in the corresponding areas of abnormality (*arrows*). STIR, short tau inversion recovery.

values have ranged from 4.6 to 12.2.^{30,32} There may be some utility in monitoring disease severity on PET/CT. A study by Qin and colleagues found that patients with higher FDG uptake in lung lesions take longer to heal and are positively correlated with erythrocyte sedimentation rate.³³

IMAGING REPORTING

In early 2020, globally increasing rates of COVID-19 necessitated the development of an organized, systematic, and reproducible approach for radiologists to report COVID-related findings and improve communication with referring clinicians.³³ An expert consensus panel assembled by the Radiological Society of North America (RSNA) developed guidelines for reporting chest CT findings potentially attributable to COVID-19 pneumonia. Four categories for standardized COVID-19 reporting were proposed, which include “typical appearance,” “indeterminate appearance,” “atypical appearance,” and “negative for pneumonia” (**Fig. 12**).¹⁸ The RSNA guidelines have not been universally accepted by radiologists, given differences in practice patterns across institutions. In addition, categorizing patients into a specific category can be difficult or somewhat subjective in patients who have mixed imaging

findings that include both typical and atypical features for COVID-19.

The COVID-19 Reporting and Data System (CO-RADS) is another categorical assessment system proposed in 2020. CO-RADS assesses the suspicion for pulmonary involvement of COVID-19 on a scale from 1 (very low) to 5 (very high).^{34,35} The CO-RADS scaling is similar to other frequently used standardized reporting systems in radiology such as Lung Imaging Reporting and Data System, Prostate Imaging Reporting and Data System, and Breast Imaging Reporting and Data System. CO-RADS has been helpful in some settings, but in practice its widespread adoption in the United States has been limited. Some radiologists believe they can adequately identify and communicate findings without the formal structure of a recently introduced reporting system that many clinicians are unfamiliar with. In addition, the accuracy of the CO-RADS system depends on the prevalence of the disease in the population at any given point in time in addition to the prevalence of other diseases with overlapping CT morphology.

PULMONARY EMBOLISM IN COVID-19

Although the causes of mortality due to COVID-19 are multifactorial, respiratory failure from pneumonia

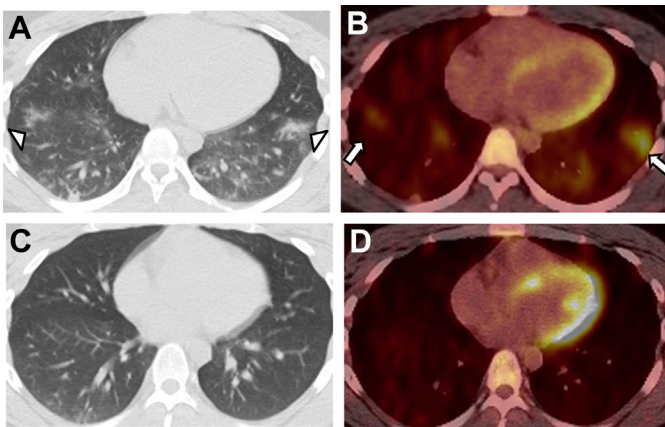


Fig. 11. A 19-year-old man with metastatic alveolar rhabdomyosarcoma presenting for follow-up PET/CT after radiation therapy. Incidentally found to be COVID positive. (A, B) CT demonstrates mild multifocal bibasilar ground-glass opacities (*arrowheads*) with corresponding FDG uptake (*arrows*) on the fused PET image. (C, D) Follow-up PET/CT performed 4 months later shows resolution of ground-glass opacity and FDG uptake.

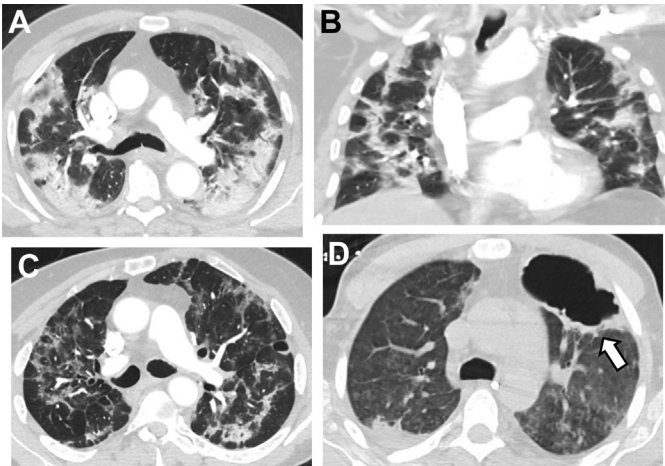


Fig. 12. Examples of COVID-19 categorization endorsed by the RSNA. (A, B) Axial and coronal views of a patient exhibiting commonly reported imaging features of COVID-19 pneumonia including peripheral, bilateral, ground-glass opacities. (C) Indeterminate appearance showing bilateral reticular and ground-glass opacities lacking typical COVID features. (D) Atypical appearance showing uncommonly or not reported features of COVID-19 pneumonia such as cavitation (arrow).

and subsequent ARDS is a primary contributor.³⁶ In addition, there is growing evidence of coagulopathy related to COVID-19, which may predispose patients to thromboembolic complications including deep venous thrombosis, pulmonary embolism (PE), limb ischemia, stroke, and myocardial infarction (Fig. 13).³⁷ A study performed by Suh and colleagues found the PE incidence was higher in patients with COVID-19 than in patients with non-COVID-19 viral pneumonia who were admitted to the ICU, patients with acute respiratory distress syndrome, or patients with H1N1 influenza (swine flu).³⁸ The presence of thromboembolic disease seems to be an added factor in worsened patient outcomes.³⁹

APPROACH TO EVALUATION OF PULMONARY EMBOLISM IN PATIENTS WITH COVID

Deciding whether or not to image a patient for a PE can be challenging, given that the symptoms of PE

and COVID overlap significantly.³⁹ Moreover, many patients infected with COVID-19 have an elevated D-dimer.³⁷ Overall, the clinical index of suspicion should dictate decision-making on whether to pursue chest CT angiography (CTA) based on evaluation of symptoms and risk factors. Clinicians can consider ordering lower extremity duplex ultrasonography first to rule out deep venous thrombosis if the clinical suspicion is relatively low. If the decision is made to perform a chest CTA, some advocate performing the study as a dual-energy CT if available because it can help characterize pulmonary blood volume and patterns of pulmonary perfusion (Fig. 14).⁴⁰

POSTACUTE SEQUELAE OF COVID-19

Radiologic changes in patients who have recovered from COVID-19 comprise an active area of continued research efforts. Some patients have complete resolution of pulmonary findings

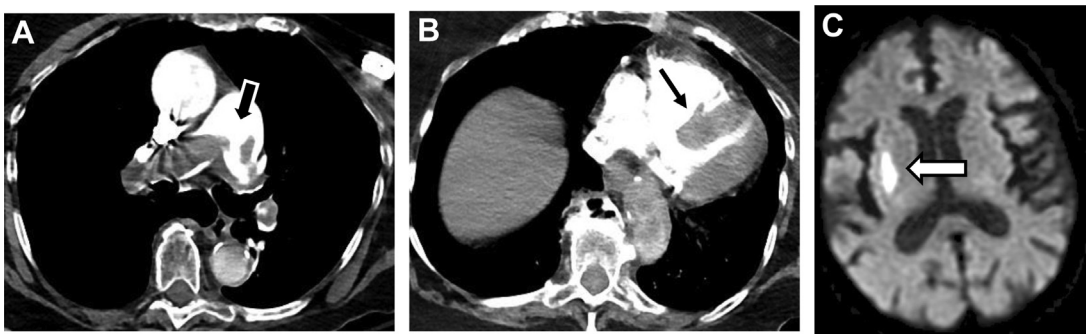


Fig. 13. CTA chest radiography in a 98-year-old man with dyspnea in the setting of COVID-19. (A) Large saddle pulmonary embolism (arrow) extending to the lobar branches. (B) There is mild right ventricular enlargement with flattening of the interventricular septum (arrow), which suggests right heart strain. (C) Brain MR imaging performed concurrently shows a small area of infarct (arrow) in the right middle cerebral artery (MCA) territory.

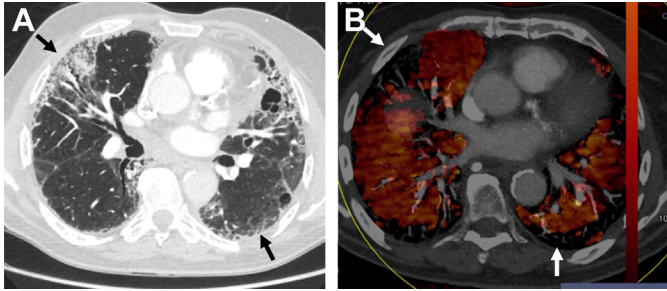


Fig. 14. A 50-year-old man presenting 1 month after recovering from COVID-19. (A) Chest CT shows moderate multifocal peripheral reticular opacities (arrows) with scattered areas of traction bronchiectasis. (B) DECT images obtained concurrently show perfusion defects (arrows) in the corresponding areas of lung involvement. DECT, dual-energy CT.

(**Fig. 15**). A subset of patients has CT abnormalities that persist 3 months after acute infection. The most commonly reported CT abnormalities at 3 months include GGO and subpleural bands (**Fig. 16**).⁴¹ A study of 3-month scans in 48 survivors of severe COVID-19 who required mechanical ventilation found that 89% of patients had GGO and 67% had signs of fibrosis. At 6 months after acute infection, some patients have resolution of GGOs and development of fibrotic-like changes.⁴² Fibrotic-like changes are described as coarse fibrous bands either with or without obvious parenchymal distortion, bronchiectasis, and bronchiolectasis⁴¹ (**Fig. 17**). A study by Han and colleagues evaluated 6-month follow-up CT scans in 114 patients who recovered from severe COVID-19 pneumonia. Thirty-five percent of the patients had follow-up CTs showing fibrotic-like changes in the lungs.⁴³ A recent study performed by Caruso and colleagues found similar results. In their cohort of 118 patients with a history of moderate-to-severe COVID-19 pneumonia, 72% of patients showed fibrotic-like changes months after recovery.⁴⁴ Several studies suggest that older age is a potential predictor of 6-month fibrotic-like changes.^{44,45} It is unclear if postacute changes are the sequelae of acute lung injury/ARDS, the effects of mechanical ventilation, or direct injury from the virus. Whether or not these fibrotic-like changes reflect permanent, irreversible change in the lungs remains to be known with certainty.

APPROACH TO LONG-TERM FOLLOW-UP IMAGING IN PATIENTS WITH COVID-19

There is no clear consensus at this time regarding the recommended frequency of follow-up imaging in patients who have recovered from COVID-19. Currently, follow-up imaging is dictated by the clinical symptoms of each individual patient. Recent studies have shown that in patients who had severe disease and recovered or had milder disease with lingering respiratory symptoms, CT surveillance can provide helpful information.⁴³ Radiologists can assess for evolution and organization of abnormality with time and quantify the amount of fibrosis. Evaluating the degree of fibrosis is of particular interest, given that there is ongoing research about the potential utility of anti-fibrotic therapies in attenuating profibrotic pathways in SARS-CoV-2 infection.⁴⁶

IMAGING FOLLOWING COVID-19 VACCINATION

Vaccines have emerged as a vital tool in the battle against COVID-19. Thoracic lymphadenopathy ipsilateral to the injected deltoid muscle has become an important radiologic finding postvaccine that may present as a diagnostic dilemma on imaging studies performed in the oncology population⁴⁷ (**Fig. 18**). Some radiology consensus groups recommend scheduling routine imaging examinations such as those for oncologic screening at least 6 weeks after the final

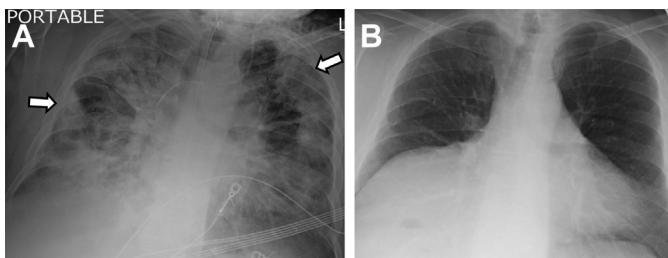


Fig. 15. A 64-year-old COVID-19 positive male. (A) Portable CXR on admission shows severe bilateral patchy opacities (arrows). (B) Follow-up CXR 1 year later shows complete resolution of pulmonary findings.

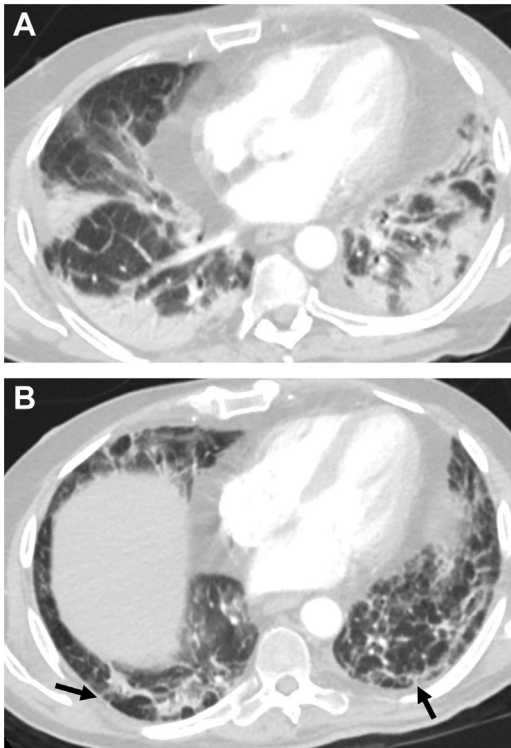


Fig. 16. A 71-year-old COVID-19 positive patient showing evolution of pathology over the span of 3 months. (A) CT in the acute phase shows severe bilateral dense peripheral consolidations. (B) Follow-up scan 3 months later shows resolution of ground-glass and consolidative densities with evolution into moderate mostly peripheral subpleural reticulation (arrows) and scarring with regions of bronchiectasis, findings consistent with fibrosis.

vaccination dose to allow for any reactive adenopathy to resolve.⁴⁸

IMAGING OF OTHER CORONAVIRUSES

COVID-19 is related to the same family of coronaviruses that caused the SARS and MERS outbreaks during 2003 and 2012, respectively.⁴⁹

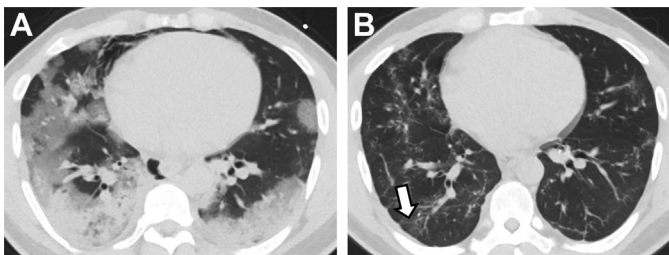


Fig. 17. A 38-year-old man with shortness of breath found to be COVID-19 positive on PCR. (A) Scan performed on admission demonstrates severe bilateral multifocal dense and ground-glass opacities in a peripheral distribution. (B) Follow-up CT scan performed 1 year later demonstrates mild fibrotic-like changes including mild reticular opacities (arrow) with traction bronchiectasis.

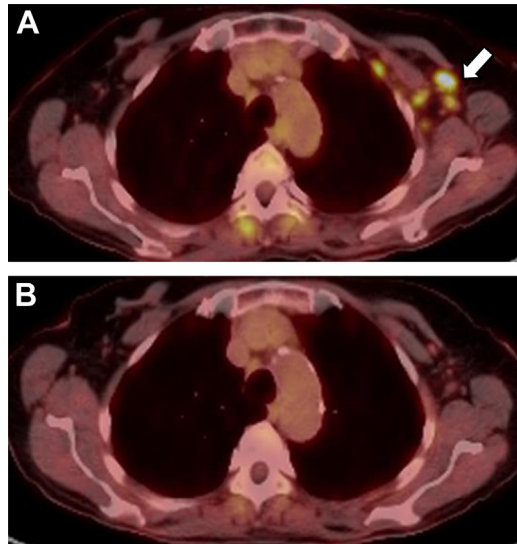


Fig. 18. PET/CT in a patient with a history of squamous cell carcinoma of the pharynx. (A) PET/CT performed 1 week following administration of the COVID vaccine in the left arm shows multiple enlarged and hypermetabolic left axillary lymph nodes (arrow). (B) Follow-up PET performed 2 months later shows decrease in size and FDG avidity within these lymph nodes.

Some CT features of patients with confirmed COVID-19 are similar to those described in SARS and MERS, including peripheral and lower lobe predominant GGO, interlobular septal thickening, and air trapping. In addition, all 3 of these related viruses rarely cause pneumothorax, lung cavitation, or lymphadenopathy.¹⁴ In contrast to COVID-19, SARS tends to be unilateral and focal in distribution (50%). In addition, patients with MERS have been reported to develop pleural effusions more commonly (33%).^{6,50} Both SARS and MERS are associated with constriction of the pulmonary vasculature, whereas enlargement of the vasculature has been reported in COVID-19.⁵¹

SUMMARY

With widespread global health implications related to COVID-19, a comprehensive understanding of the diagnostic thoracic imaging hallmarks is essential for effective diagnosis and management.

CLINICS CARE POINTS

- Chest radiography is an effective way to assess progression/resolution of COVID pneumonia over time while minimizing radiation dose.
- CT is more sensitive and specific than radiography for identifying lung abnormalities.
- Imaging findings in COVID-19 evolve as the illness progresses.
- A subset of patients will have CT abnormalities that persist after acute infection.

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