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COVID-19 Imaging: What We Know Now and What Remains Unknown

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Infection with SARS-CoV-2 ranges from an asymptomatic condition to a severe and sometimes fatal disease, with mortality most frequently being the result of acute lung injury. The role of imaging has evolved during the pandemic, with CT initially being an alternative and possibly superior testing method compared with reverse transcriptase–polymerase chain reaction (RT-PCR) testing and evolving to having a more limited role based on specific indications. Several classification and reporting schemes were developed for chest imaging early during the pandemic for patients suspected of having COVID-19 to aid in triage when the availability of RT-PCR testing was limited and its level of performance was unclear. Interobserver agreement for categories with findings typical of COVID-19 and those suggesting an alternative diagnosis is high across multiple studies. Furthermore, some studies looking at the extent of lung involvement on chest radiographs and CT images showed correlations with critical illness and a need for mechanical ventilation. In addition to pulmonary manifestations, cardiovascular complications such as thromboembolism and myocarditis have been ascribed to COVID-19, sometimes contributing to neurologic and abdominal manifestations. Finally, artificial intelligence has shown promise for use in determining both the diagnosis and prognosis of COVID-19 pneumonia with respect to both radiography and CT.

Since the first imaging summaries of COVID-19, the disease caused by SARS-CoV-2 infection, were published (1,2), much has been learned about the clinical and radiologic manifestations of COVID-19. As it has evolved from a disease isolated in the Hubei Province of China to a global pandemic resulting in more than 2 million deaths worldwide, larger and more comprehensive studies have been published, the physiologic and biologic heterogeneity of the disease has been explored, and extrathoracic manifestations of COVID-19 have been reported. In this review, we aim to summarize what is known about COVID-19 with respect to imaging and state what is not yet known.

Indications for Imaging in COVID-19

The clinical indications for imaging, specifically chest radiography and chest CT, have evolved since the initial discovery of disease in Wuhan, China, and since the World Health Organization officially characterized COVID-19 as a pandemic on March 11, 2020. Although some early proponents, particularly in China, advocated for routine diagnostic imaging in patients suspected of having COVID-19 pneumonia, others, particularly in the United States and Europe, proposed a more conservative approach (3). Societies such as the American College of Radiology (4), the Society of Thoracic Radiology, and the American Society of Emergency Radiology (5) recommended against the use of routine imaging, particularly CT, as a first-line diagnostic test.

Experts felt that the value of CT was limited because the diagnosis of COVID-19 is primarily based on nucleic acid testing, because of concern that frequent CT examinations increase the potential for infection transmission to other patients and health care staff, because the CT findings of COVID-19 overlap with those of other causes of acute lung injury or can even be normal, and because results from CT infrequently alter disease management (3). Ultimately, the precise role of imaging remains somewhat controversial and varies on the basis of country and institution.

In April of 2020, the Fleischner Society published a multinational consensus statement to offer guidance to clinicians on the use of thoracic imaging across a spectrum of health care environments and scenarios (6). The statement structure is centered around three clinical scenarios of patients who have or are suspected of having COVID-19 infection with varying severities of illness (mild, moderate to severe, and moderate to severe in a resource-constrained environment). On the basis of expert opinions of panel members, recommendations were issued that included no indication for routine imaging as a screening test for COVID-19 in asymptomatic individuals, no indication for daily chest radiography in stable intubated patients with COVID-19, and an indication

Abbreviations

AI = artificial intelligence, GGO = ground-glass opacity, ICU = intensive care unit, PE = pulmonary embolism, RT-PCR = reverse transcriptase–polymerase chain reaction

Summary

Since the publication of initial reports on imaging manifestations of COVID-19, imaging classification systems and artificial intelligence applications have been developed, indications for chest imaging have been refined, and diverse complications have been recognized.

Essentials

- Imaging findings of COVID-19 pneumonia and the evolution of findings over time are well described: an organizing pneumonia pattern of lung injury is most common, with some patients developing diffuse alveolar damage, and patients with few or no symptoms may have normal imaging findings.
- COVID-19 imaging classification systems have high interobserver agreement, and artificial intelligence has shown diagnostic and prognostic promise.
- Cardiovascular complications include thromboembolic disease, myocarditis, and multisystem inflammatory syndrome in children; abdominal complications may be due to cardiovascular effects or critical illness; and neurologic complications are not well defined.

for CT in patients with functional impairment, hypoxemia, or both after recovery from infection.

Imaging Features of COVID-19 on Chest Radiographs and CT Images

Chest imaging findings of SARS-CoV-2 infection overlap with or mimic those of other infections, including those caused by other human coronaviruses (severe acute respiratory syndrome coronavirus, or SARS-CoV; Middle East respiratory syndrome coronavirus, or MERS-CoV); influenza A virus, or H1N1, and other influenza virotypes; and acute lung injuries from drug reactions and connective tissue diseases (7). Given that the outbreak heightened during the influenza season in many regions, this further limited the specificity of using chest radiography and CT for diagnosis.

Findings of COVID-19 on chest radiographs vary, ranging from normal in the early stages of disease to unilateral or bilateral lung opacities, sometimes with a basilar and strikingly peripheral distribution (Fig 1) (7,8). Early research reported a relatively low sensitivity (69%) for the diagnosis of COVID-19 using baseline chest radiography. Although underlying comorbidities such as chronic lung disease or congestive heart failure may confound chest radiograph interpretation, studies have shown that many of the hallmark chest CT findings are apparent on chest radiographs (8–10).

The typical appearance of COVID-19 pneumonia on chest CT images is bilateral peripheral opacities with a lower lung distribution (Fig 2). The opacities are usually ground-glass opacities (GGOs), sometimes with areas of consolidation, and are often nodular or masslike, thereby resembling an organizing pneumonia pattern (11,12). Additional imaging patterns resembling organizing pneumonia include a perilobular pattern of opacification and a so-called reverse halo sign, defined as a focal and rounded area of GGO surrounded by a ring or arc of denser consolidation (Figs 3, 4). Diffuse GGOs, which can mimic other infections, drug toxicities, and inhalational lung disease, have also been reported (12). Although prototypical features of COVID-19 pneumonia on CT images are well described, in clinical practice many patients will have some but not all the imaging manifestations. For example, the opacities may be unilateral but have a rounded morphologic presentation. Alternatively, the opacities may have an upper lobe predominance but still retain a peripheral or subpleural distribution.

CT image features that are indeterminate for COVID-19 have also been described and classified in guidelines such as the Radiological Society of North America, or RSNA, consensus statement on CT reporting (12). These include imaging findings that have been reported in COVID-19 but are not specific enough to arrive at a relatively confident radiologic diagnosis (Fig 5). For example, diffuse or perihilar GGOs, with or without consolidation, or scattered nonrounded opacities can occur in a variety of other infectious and in some noninfectious processes such as edema or alveolar hemorrhage. Certain CT features are uncommonly seen in COVID-19 pneumonia, including lobar or segmental consolidation without GGOs, discrete small pulmonary nodules, pulmonary cavitation, septal thickening, pleural effusion, and pneumothorax. Interestingly, the rate of barotrauma in mechanically ventilated patients with COVID-19 has been reported to be much higher than that in patients with other causes of acute respiratory distress syndrome (24% vs 11%) (13). A comprehensive review of the various scoring and assessment systems developed for CT lung findings is discussed in detail in a later section.

Change in COVID-19 Findings over Time on Chest Radiographs and CT Images

Although the presence of characteristic COVID-19 imaging findings is helpful in diagnosis and risk stratification, it is noteworthy that both chest radiographs and chest CT images may lack lung abnormalities in the earliest stages of infection, with rates of normal CT findings as high as 56% in patients imaged within 2 days of symptom onset (Fig 6) (14). Therefore, normal chest radiographic and CT findings do not reliably exclude disease.

Pan et al (15) described four temporal stages of acute and subacute COVID-19 on CT images, including an initial phase in which abnormalities manifest as GGOs, may be unilateral, and tend to lack the characteristic peripheral lung distribution. Patients often experience progression from day 5 to day 8, when pulmonary opacities become more extensive and confluent with more common bilateral lung involvement (Fig 4). The peak stage occurs around 9–13 days and features more extensive consolidation, which parallels the evolution of acute lung injury (2,14,15). This dovetails with investigators finding that abnormalities on chest radiographs are most extensive 10–12 days after symptom onset (8). There is variation among patients, but beginning at about 2 weeks, many enter the absorption stage (16). During this period, consolidation may wane, and other manifestations absent in

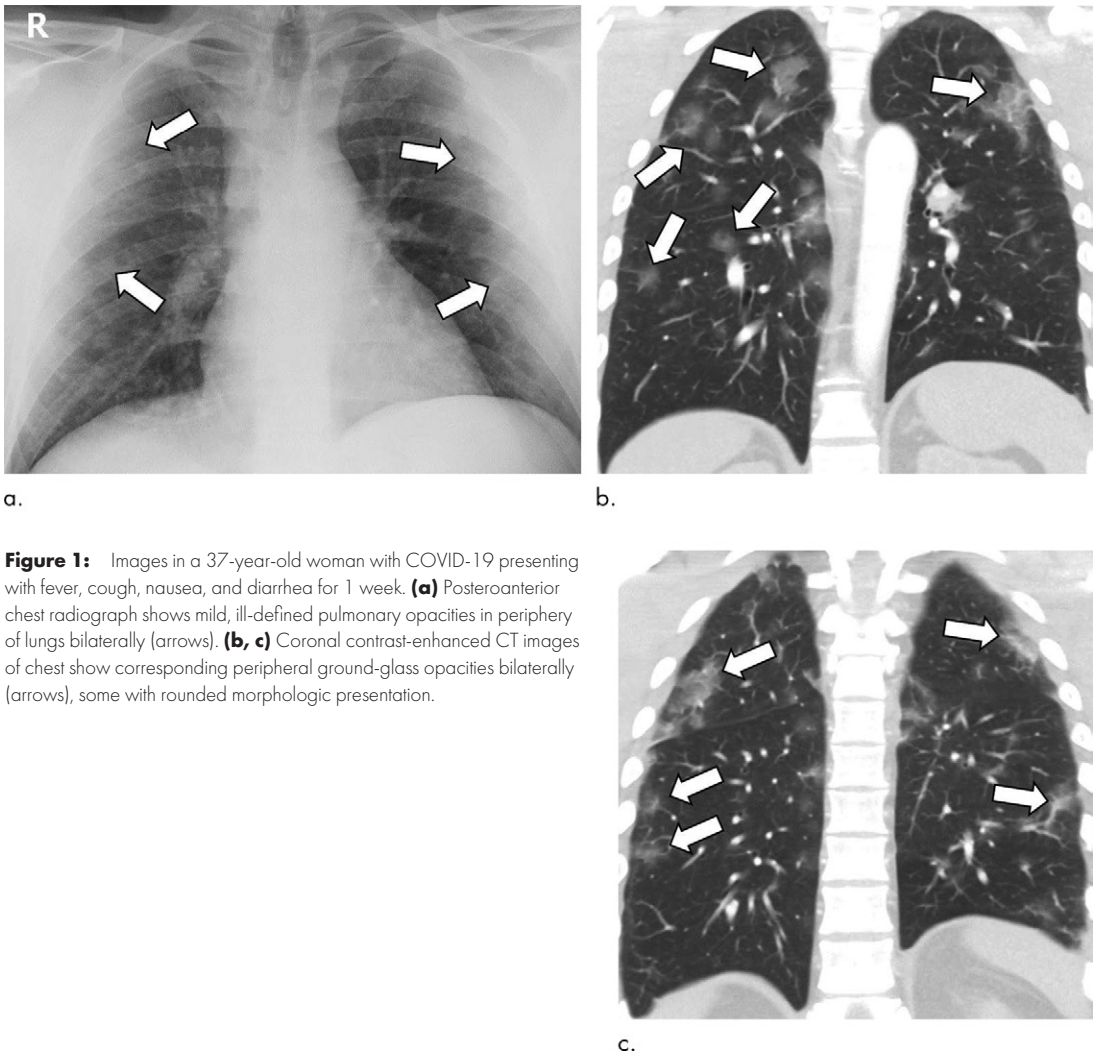


Figure 1: Images in a 37-year-old woman with COVID-19 presenting with fever, cough, nausea, and diarrhea for 1 week. **(a)** Posteroanterior chest radiograph shows mild, ill-defined pulmonary opacities in periphery of lungs bilaterally (arrows). **(b, c)** Coronal contrast-enhanced CT images of chest show corresponding peripheral ground-glass opacities bilaterally (arrows), some with rounded morphologic presentation.

the earlier phases of acute infection, such as linear opacities, a reverse halo sign, and a so-called crazy-paving pattern, may emerge. During the first several weeks of infection, pleural effusions are uncommon, cavitation is rare, and pulmonary fibrosis is not expected.

Over weeks, COVID-19 pulmonary findings on both chest radiographs and CT images resolve or can evolve into a more structured and organized phase, in which case GGOs and consolidation transform into more reticular opacities and may be associated with fibrosis, volume loss, architectural distortion, and traction bronchiectasis.

What Role Does Severity of Disease on CT Images Play in Disease Evaluation?

Assessment of disease severity with imaging in COVID-19 may inform clinical decisions related to the need for hospital admission, timing of intubation, patient course and prognosis, and therapeutic efficacy. CT may enable reproducible quantitative severity scoring and can be particularly helpful in detecting mild disease, characterizing longitudinal change, and assessing the extent of disease in the setting of baseline pulmonary abnormalities.

A variety of methods have been used to assess lung involvement at CT in COVID-19. Qualitative methods classify parenchymal disease as mild, moderate, or severe. Semiquantitative methods estimate lobar or zonal involvement by quartiles (0%–25%, 26%–49%, 50%–75%, and 76%–100%) (17), with less than 5% lobar involvement also sometimes used (18). Software-based quantitative methods, including those using machine learning, can be used to calculate the total lung involvement as well as the percentage of GGO and consolidation, and may have higher accuracy than human semiquantitative estimates (19–21).

Several studies have shown correlations between the extent of parenchymal involvement at CT and the clinical assessment of COVID-19 disease severity as defined by parameters such as the severity of symptoms, oxygenation status, and certain laboratory measures of infection and inflammation. Semiquantitative and quantitative studies have shown CT severity scores for patients with severe and critical disease that are significantly higher than those for patients with less severe disease (17,22–25). For example, in one study of 189 inpatients, the average volume of lung involvement measured by using semiautomated segmentation of parenchymal opacities on CT images was higher in critically ill

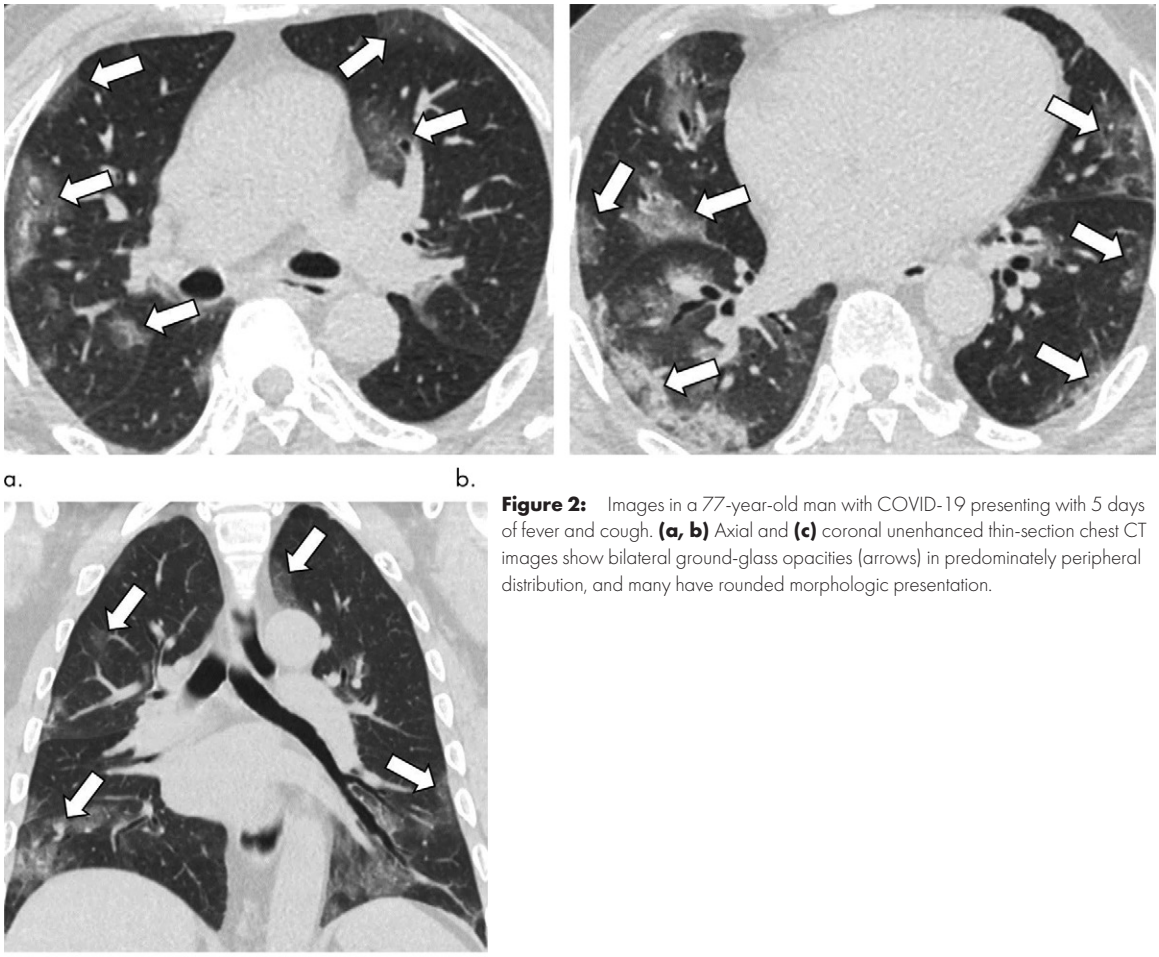


Figure 2: Images in a 77-year-old man with COVID-19 presenting with 5 days of fever and cough. **(a, b)** Axial and **(c)** coronal unenhanced thin-section chest CT images show bilateral ground-glass opacities (arrows) in predominately peripheral distribution, and many have rounded morphologic presentation.

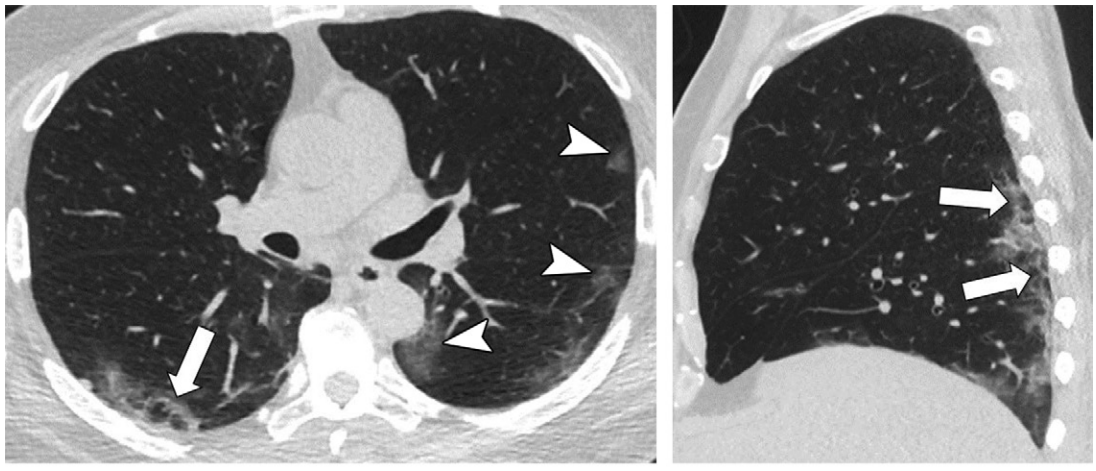
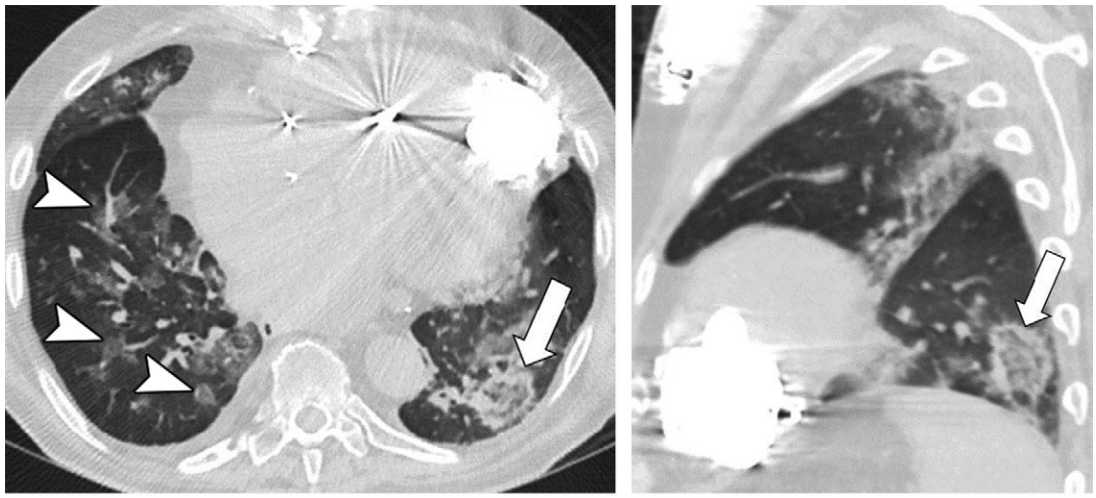


Figure 3: Images in a 57-year-old man with COVID-19 presenting with 4 days of cough. **(a)** Axial and **(b)** sagittal unenhanced thin-section chest CT images show bilateral ground-glass opacities in peripheral distribution in left lung, some with rounded morphologic presentation (arrowheads). There are also arcadelike opacities in subpleural right lower lobe (arrows), indicative of perilobular pattern of disease.

patients (38.5%) than in non–critically ill patients (5.8%), with a threshold of 23% distinguishing these two groups with 96% sensitivity and specificity (22). In another study of 78 patients, a semiquantitative total CT severity score ranging from 0 to 20 distinguished mild, moderate, and severe clinical disease with high accuracy (82.6% sensitivity and 100% specificity for a cut-off score of 7.5) and a high interclass correlation between readers of 0.976 (17).



a. b.

Figure 4: Images in a 72-year-old man with COVID-19 and a history of heart failure presenting with 10 days of cough. **(a)** Axial and **(b)** sagittal unenhanced thin-section chest CT images show peribronchial ground-glass opacities (arrowheads), as well as ground-glass opacity in left lower lobe with ring of denser consolidation (reverse halo sign) (arrow).

CT severity scores also show correlations with serum markers of disease severity. A study of 84 hospitalized patients with COVID-19 showed significant correlations with the lymphocyte count and percentage, neutrophil percentage, and C-reactive protein and procalcitonin levels ($P < .05$ for all) (26). Another semiquantitative study of 106 inpatients with COVID-19 pneumonia showed significant positive correlations between the CT severity and the levels of inflammatory cytokines such as interleukin 6 and interleukin 2R (27). Additional studies have observed similar correlations (22,28,29).

CT severity scoring may show promise for use in clinical triage and assessment of prognosis, and the higher CT severity scores can be used to predict clinical outcomes in COVID-19 (29,30). In a study of 572 hospitalized patients, 70% of patients with total lung involvement greater than 50% were admitted to the intensive care unit (ICU) or died within 7 days of a CT scan being performed at admission, whereas these rates were lower for lung involvement of 26%–50% (41%) and less than 25% (23%) (18). Semiquantitative CT severity scores of 18 or greater on a scale from 0 to 25 correlated with increased mortality risk in another study of 130 patients in the emergency department setting (hazard ratio, 3.7; $P = .03$).

Semiquantitative CT severity scores of 18 or greater on a scale from 0 to 25 correlated with increased mortality risk in another study of 130 patients in the emergency department setting (hazard ratio, 3.7; $P = .03$) (28). Higher semiquantitative total severity scores and multilobar involvement were associated with increased fatality risk in a study of 128 patients with COVID-19 hospitalized for observation; death was more common in patients with a CT severity score of 15 or greater (odds ratio, 53; $P = .003$), and the CT severity score was the only independent risk factor for mortality in a multivariate analysis that incorporated age and several inflammatory serum markers (30).

However, CT severity scores are just one of many clinical and laboratory parameters that correlate with patient prognosis (31). In addition, a significant percentage of patients with asymptomatic infection may have parenchymal involvement at CT that overlaps in severity with that of symptomatic patients (32), and CT severity scores of clinically severe cases of COVID-19 pneumonia may overlap with those of moderate clinical severity (30), underscoring limitations in drawing clinical conclusions from CT severity alone. Although initial evidence is promising, clinical studies of the usefulness of CT severity scoring in management of patients with COVID-19 are still awaited.

What Role Does Severity of Disease on Chest Radiographs Play in Disease Evaluation?

Chest radiography is commonly used as the initial diagnostic imaging test to evaluate patients who have or who are suspected of having COVID-19. Several studies investigating the relationship of the severity of lung abnormalities on chest radiographs with disease severity have shown scores reflecting an increased extent and intensity of lung opacities to be associated with more severe clinical manifestations, higher rates of ICU admission, and death (10,33,34). In one retrospective study of 338 young adults (median age, 39 years), a chest radiographic severity score greater than or equal to 2 out of a maximum score of 6 (odds ratio, 6.2) and the presence of obesity (odds ratio, 2.4) were independent predictors of hospital admission. Among those admitted to the hospital, a chest radiographic severity score greater than or equal to 3 was an independent predictor of endotracheal intubation (10). Another study of 1157 patients that looked at a variety of clinical factors, including the radiologic assessment of lung edema score, found that with each unit increase of the radiologic assessment of lung edema score, the hazard increased by 1.49 for ICU admission and by 1.23 for death (33). A group from the Netherlands created a risk model from a retrospective study of 356 hospitalized patients with COVID-19 that included a chest radiographic score of 0–8 based on four zones and a severity level of 0–2. Patients who required ICU admission or died had significantly higher radiographic scores (mean, 4.4) than those who did not (mean, 3.3) ($P < .01$). Furthermore, bilateral lung involvement at presentation

was present in 86% of patients with critical illness compared with 73% without critical illness ($P = .06$) (34).

Patients with COVID-19 and normal or near-normal chest radiographs typically have a benign clinical course. A retrospective study of 109 patients with COVID-19 using a 72-point chest radiographic severity score showed that a severity score less than 5 between 6–10 days after the onset of symptoms had a negative predictive value of 95.5% for supplemental oxygen being required and a negative predictive value of 100.00% for ICU admission being required (35). A retrospective study of 5621 asymptomatic or minimally symptomatic male patients with COVID-19, 1964 of whom underwent chest radiography, showed normal results in 98%. Supplemental oxygen and inpatient treatment were only necessary for four patients (0.2%) (36). These studies support recommendations that imaging is not usually indicated for patients with COVID-19 who have few or no symptoms. Routine radiographic monitoring of stable patients with COVID-19, including those requiring mechanical ventilation, is not recommended (6).

Studies comparing the various scoring systems have not been performed, and each system has its own merits. In routine clinical practice, patients with COVID-19 and normal or minimal findings on chest radiographs will likely have a benign clinical course, whereas patients with more extensive lung opacities are much more likely to require supplemental oxygen, ICU admission, and mechanical ventilation.

What Reporting Systems Have Been Found Useful for Conveying Suspicion of COVID-19 at CT and Radiography?

Early during the COVID-19 pandemic when access to accurate reverse transcriptase–polymerase chain reaction (RT-PCR) testing was limited, several reporting systems were proposed for reporting the chest radiographic and CT results of patients who are suspected of having COVID-19 in a high-disease-prevalence setting. These systems provide standardized language and diagnostic categories aiming to convey the likelihood that lung abnormalities on CT images represent COVID-19. Reporting systems include the RSNA Expert Consensus Statement system (Table 1) (12), the COVID-19 Reporting and Data System developed by the Dutch Radiologic Society (Table 2) (37), the British Society of Thoracic Imaging system (Table 3) (38), the COVID-19 Imaging Reporting and Data System (Table 4) (39), and a COVID-19 structured reporting system (Table 5) (40). One study of the RSNA Expert Consensus Statement found excellent interobserver agreement among thoracic radiologists in a retrospective review of approximately 300 patients suspected of having COVID-19 (41). In this study, the Fleiss κ value for all observers was almost perfect for typical (Fleiss κ, 0.815), atypical (Fleiss κ, 0.806), and negative (Fleiss κ, 0.962) COVID-19 categories ($P < .001$) and was substantial (Fleiss κ, 0.636) for indeterminate COVID-19 categories. A retrospective study of chest CT images in 572 symptomatic patients (142 with RT-PCR–confirmed COVID-19 and 430 without confirmed COVID-19) showed moderate agreement for COVID-19 Reporting and Data System rating among all readers (Fleiss κ, 0.43), with a substantial agreement being shown for COVID-19 Reporting and Data System category 1 (Fleiss κ, 0.61) and moderate agreement being shown for COVID-19 Reporting and Data System category 5 (Fleiss κ, 0.60). A COVID-19 Reporting and Data System score greater than or equal to 4 was identified by receiver operating characteristic analysis as the optimal threshold, demonstrating a cumulative area under the curve of 0.72, a sensitivity of 61%, and a specificity of 81% (42).

Table 1: Summary of Radiological Society of North America Expert Consensus Reporting System for COVID-19

Category and Description
Typical appearance
Peripheral, bilateral GGO with or without consolidation or visible intralobular lines (crazy paving)
Multifocal GGO of rounded morphologic presentation with or without consolidation or visible intralobular lines (crazy paving)
Reverse halo sign or other findings of organizing pneumonia (seen later in the disease)
Indeterminate appearance
Absence of typical features AND presence of:
Multifocal, diffuse, perihilar, or unilateral GGOs with or without consolidation that lack a specific distribution; that are nonrounded or nonperipheral and lack a specific distribution; or that are nonrounded or nonperipheral
Few very small GGOs with a nonrounded and nonperipheral distribution
Atypical appearance
Absence of typical or indeterminate features AND presence of:
Isolated lobar or segmental consolidation without GGO
Discrete small nodules (centrilobular, "tree-in-bud")
Lung cavitation
Smooth interlobular septal thickening with pleural effusion
Negative for pneumonia
No CT features to suggest pneumonia

Note.—Summary is compiled from reference 12. GGO = ground-glass opacity.

Proposed chest radiographic reporting language and categories include those of the British Society of Thoracic Imaging (38,43) and a multicenter U.S. group (44) (Table 6). A retrospective study of the British Society of Thoracic Imaging guidelines found substantial interobserver agreement (Fleiss κ, 0.61) for "classic" and "probable categories." Agreement was fair for the "indeterminate for COVID-19" (κ, 0.23) and "non–COVID-19" (κ, 0.37) categories (45). The authors of this study suggest combining the latter two categories into a single "not classic of COVID-19" category to improve interobserver agreement and to avoid labeling patients with COVID-19 as being in the "non–COVID-19" category.

Despite routine use of CT as a triage tool early in the outbreak in China, the role of CT has been more limited elsewhere in the world, where use has been mostly limited to specific indications such as pulmonary embolism (PE) (6). With increased access to RT-PCR testing and faster result reporting, the prospective value of these classification systems in patients with COVID-19 is unclear. The positive predictive value of all of these systems varies greatly with the prevalence of COVID-19 in the community.

Table 2: Summary of CO-RADS

Category and Description
6: Proven
RT-PCR test is positive for SARS-CoV-2
5: Very high suspicion: typical for COVID-19
GGO, with or without consolidations, in lung regions close to visceral pleural surfaces, including the fissures (subpleural sparing is allowed) and multifocal bilateral distribution AND at least one of the following:
Ground-glass regions
Nonsharp demarcation, (half) rounded shape
Sharp demarcation, outlining the shape of multiple adjacent secondary pulmonary lobules
Crazy paving
Patterns compatible with organizing pneumonia
Thickened vessels within parenchymal abnormalities found in all confirmatory patterns
4: High suspicion: suspicious for COVID-19
Findings are similar to those for CO-RADS 5 category but
Not in contact with the visceral pleura
Not located strictly unilaterally in a predominant peribronchovascular distribution
Superimposed on severe diffuse preexisting pulmonary abnormalities
3: Equivocal/unsure: features compatible with COVID-19 but also other diseases
Perihilar GGO
Homogeneous extensive GGO with or without sparing of some secondary pulmonary lobules
GGO together with smooth interlobular septal thickening with or without pleural effusion in the absence of other typical CT findings
Small GGOs that are not centrilobular or not located close to the visceral pleura
Patterns of consolidation compatible with organizing pneumonia without other typical findings of COVID-19
2: Low suspicion: typical for other infection but not for COVID-19
CT findings in the lungs typical of infectious origin that are considered incompatible with COVID-19. Examples include the following:
Bronchitis
Infectious bronchiolitis
Bronchopneumonia
Lobar pneumonia
Pulmonary abscess
Features including the following:
Tree-in-bud sign
Centrilobular nodular pattern
Lobar or segmental consolidation
Lung cavitation
1: Very low suspicion
Normal or noninfectious
0: Not interpretable
Image technically insufficient for assigning a score

Note.—Summary is compiled from reference 37. CO-RADS = COVID-19 Reporting and Data System, GGO = ground-glass opacity, RT-PCR = reverse transcriptase–polymerase chain reaction.

Table 3: Summary of British Society of Thoracic Imaging System

Category and Description
Classic COVID-19: 100% confidence
Lower lobe predominant, peripheral predominant, multiple, bilateral foci of GGO, with or without:
Crazy paving
Peripheral consolidation
Air bronchograms
Reverse halo or perilobular pattern
Probable COVID-19: 71%–99% confidence
Lower lobe predominant mix of bronchocentric and peripheral consolidation
Reverse halo or perilobular pattern
GGOs scarce
Indeterminate: <70% confidence for COVID-19
Does not fit into definite, probable, or non–COVID-19
Manifests above patterns, but the clinical context is wrong or suggests an alternative diagnosis
Non–COVID-19: 70% confidence for alternative
Lobar pneumonia
Cavitating infections
Tree-in-bud or centrilobular nodularity
Lymphadenopathy, effusions
Established pulmonary fibrosis

Note.—Summary is compiled from reference 38. GGO = ground-glass opacity.

However, further investigation is warranted to evaluate the diagnostic performance of CT for patients who are not clinically suspected of having COVID-19 but who have highly suggestive CT findings (6,46).

Although each classification system is likely to be helpful in suggesting the presence or absence of COVID-19 when typical findings are present or absent, respectively, the value of any one system will vary depending on disease prevalence and the level of access to and rapidity of RT-PCR testing. Radiologist experience may also play a role.

Why Has CT Detection versus RT-PCR Detection of COVID-19 Been Controversial?

The diagnosis of viral infection, including infection with SARS-CoV-2, relies on the use of RT-PCR testing for identifying genetic material in biologic samples (47,48). However, the availability of RT-PCR testing was limited in the first half of 2020, and for this reason, CT was used for early triage and management of COVID-19 pneumonia. Because of this, the specific definition of SARS-CoV-2 infection in the early literature is unclear, with the CT definition and RT-PCR definitions being complementary. Although RT-PCR testing is considered the reference standard in diagnosing SARS-CoV-2 infection, it is far from perfect.

RT-PCR testing is subject to false-negative results because its diagnostic performance can be influenced by multiple factors, such as inadequate sampling and improper extraction of nucleic acids from biologic materials, variations

Table 4: Summary of COVID-RADS

Category and Description
3: High suspicion
Typical findings
Multifocal GGO
GGO with superimposed consolidation
Consolidation predominant pattern (late or complicated)
Linear opacities (late or complicated)
Crazy-paving pattern (late or complicated)
Melted sugar sign (late or remission)
2A: Moderate suspicion
Fairly typical findings
Single GGO (early)
Consolidation without GGO (late or complicated)
Focal pleural thickening associated with GGO or consolidation
Vascular dilation or mural thickening
Air bronchogram
Bronchial wall thickening
White lung stage (late or complicated)
Parenchymal fibrotic bands (late or remission)
2B: Moderate suspicion
Combination of atypical findings with typical or fairly typical findings
1: Low suspicion
Atypical findings:
Pleural effusion
Cavity
Pulmonary nodule(s)
Nodular pattern
Lymphadenopathy
Peribronchovascular distribution
Halo sign
Tree-in-bud sign
Bronchiectasis
Airway secretions
Pulmonary emphysema
Pulmonary fibrosis
Isolated pleural thickening
Pneumothorax
Pericardial effusion
0: Low suspicion
Normal

Note.—Summary is compiled from reference 39. COVID-RADS = COVID-19 Imaging Reporting and Data System, GGO = ground-glass opacity.

Table 5: Summary of COVID-19 Structured Reporting System

Category and Description
Compatible with COVID-19
Bilateral elementary COVID-19 lesions only or predominantly in lower zones (lower zones with or without upper and middle zones)
Bilateral elementary COVID-19 lesions in all zones without predominance
Elementary lesions defined as pure GGO or GGO with consolidation (consolidation may be smaller in the central region of the lesion or may occupy most of the lesion [halo sign]) that has the following characteristics:
Rounded or lobulated or geographic contours (not diffuse)
Discrete or coalescent
Peripheral with or without bronchocentric (not central)
Predominantly posterior localization
Accompanying intralesional intralobular reticulations (crazy paving), bronchial dilation, air bronchogram, vascular enlargement, air bubble, curvilinear irregular thick lines, perilobular sparing, or reverse halo sign
Indeterminate
Bilateral elementary COVID-19 lesions located predominantly in upper or middle zones
Single or multiple elementary COVID-19 lesions in single lower zone unless consolidation is dominant
Unilateral elementary COVID-19 lesions predominantly in lower zone
GGO that does not have the characteristic of an elementary COVID-19 lesion, but does not exactly fit any other diagnosis
Alternative diagnosis
Unilateral elementary COVID-19 lesions located predominantly in upper or middle zones
Absence of typical features of an elementary COVID-19 lesion and presence of:
Opacity that affects a large and continuous area of a lobe (lobar pneumonia) or of one or more secondary lobules of a lung presenting segmental consolidation (bronchopneumonia)
Bronchiolitis (tree-in-bud sign or centrilobular nodularity)
Cavitating infection
Bronchial wall thickening
Lymphadenopathy, pleural effusions
Smooth interlobular septal thickening
Normal
No CT features to suggest pneumonia

Note.—Summary is compiled from reference 40. GGO = ground-glass opacity.

in the accuracies of different tests, or low initial or late viral load (49,50). False-negative CT results have also been reported in 3%–56% of patients with positive RT-PCR test results (14,51,52). Signs of pneumonia on CT images represent a potential manifestation of COVID-19 severity and tend to develop later in the disease course, typically 6–11 days after infection (53).

Studies in symptomatic patients have reported higher sensitivity with the use of CT than with the use of RT-PCR testing (51,53). It has been advocated that such findings could be due to several factors, particularly the inclusion of only patients with moderate to severe symptoms (54).

The interpretation of the RT-PCR and CT mismatch is difficult and is confounded by a variety of factors (55). In a large meta-analysis (56), the pooled sensitivity with use of CT was 94% (95% CI: 91, 96), and the pooled sensitivity with use of RT-PCR testing was 89% (95% CI: 81, 94). In this study, the lower sensitivity associated with the use of CT

Table 6: Reporting Systems for Chest Radiography

British Society of Thoracic Imaging	U.S. Multicenter
Classic or probable COVID-19	Typical appearance
Lower lobe and peripheral predominant multiple opacities that are bilateral	Multifocal bilateral, peripheral opacities
Indeterminate for COVID-19	Opacities with rounded morphologic presentation
Does not fit classic or non–COVID-19 descriptors	Lower lung–predominant distribution
Non–COVID-19	Indeterminate appearance
Pneumothorax	Absence of typical findings AND
Lobar pneumonia	Unilateral, central, or upper lung–predominant distribution
Pleural effusion	Atypical appearance
Pulmonary edema	Pneumothorax
Other	Pleural effusion
Normal	Pulmonary edema
	Lobar consolidation
	Solitary lung nodule or mass
	Diffuse tiny nodules
	Cavity
	Negative for pneumonia
	No lung opacities

Note.—Summaries are compiled from references 38 and 43 (British Society of Thoracic Imaging) and reference 44 (U.S. multicenter).

was reported as a function of symptoms and disease severity, whereas these factors did not influence RT-PCR performance, underscoring that imaging is not meant for screening asymptomatic patients (6,36).

The specificity of RT-PCR testing is optimal, whereas the CT findings of COVID-19 pneumonia are far from pathognomonic. A systematic review from Cochrane Database (57) reported a substantial reduction of sensitivity and specificity in studies that included suspected cases. The chances of a positive CT result were 86% in patients with a SARS-CoV-2 infection and 82% in patients without an infection. Therefore, the specificity when using CT is too weak to justify its use for the diagnosis of COVID-19 pneumonia.

The accuracy of imaging tests in diagnosing COVID-19 and in any clinical setting is influenced by the prevalence of both COVID-19 and comparable viral pneumonias as well as other clinical-radiologic mimickers. This issue was witnessed in regions with a low rate of COVID-19 (<10%), where the positive predictive value of using chest CT was trivial (56).

What Is the Role of Artificial Intelligence in COVID-19 Evaluation?

Artificial intelligence (AI) based on imaging has a potentially important role in the diagnosis, disease quantification, severity assessment, and prognosis determination in COVID-19 pneumonia. AI has been proposed as a tool to reduce radiologists' workload, streamline the workflow, improve diagnostic accuracy, and facilitate resource allocation.

Published studies have focused on using CT and chest radiography to distinguish COVID-19 from other types of pneumonia and predict disease severity (Table 7). Li et al (58) developed a fully automatic framework on 4352 chest CT images from 3322 patients to distinguish COVID-19 pneumonia from community-acquired pneumonia and other lung conditions. The COVID-19 Detection Neural Network achieved a per-image sensitivity of 90% (95% CI: 83, 94) and specificity of 96% (95% CI: 93, 98) for detecting COVID-19 on the test set with an receiver operating characteristic area under the curve of 0.96. Another study by Bai et al (59) used CT images from 1186 patients (521 COVID-19 cases and 665 non–COVID-19 pneumonia cases) to distinguish COVID-19 from pneumonia due to another lung disease. On independent testing, the model achieved an accuracy of 87% (95% CI: 82, 90), sensitivity of 89% (95% CI: 81, 94), and specificity of 86% (95% CI: 80, 90). Furthermore, the authors demonstrated the ability of AI to improve radiologists' performance. In another study of 905 patients from Chinese hospitals, Mei et al (60) developed AI algorithms to integrate chest CT findings with clinical symptoms, exposure history, and laboratory testing results for rapid diagnosis of COVID-19. In a test set of 279 patients, the AI system achieved an area under the curve of 0.92 and had sensitivity equal to that of a senior thoracic radiologist. In addition, the AI system improved the detection of patients who were positive for COVID-19 according to RT-PCR testing results who presented with normal findings at CT, correctly identifying 17 of 25 (68%) patients.

To our knowledge, Zhang et al (61) have performed the largest and most comprehensive study to use AI to diagnose COVID-19 pneumonia and predict patient prognosis, using 6752 chest CT images from 4154 patients. To validate the ability of the AI system to distinguish patients with COVID-19 pneumonia from patients with community-acquired pneumonia and normal control participants, the authors conducted three prospective pilot studies in China and externally tested the model on a cohort of patients from Ecuador. The AI system achieved stable and good results, with an overall performance superior to

Table 7: Summary of Artificial Intelligence Studies for COVID-19

Study	Journal	Country	Modality	No. of Patients	Purpose	EV	Acc	AUC	PR AUC	Sen	Spec	C Index	F_1 Score
Li et al (58)	*Radiology*	China	CT	3322	Diagnosis	No	NA	0.96	NA	0.90	0.96	NA	NA
Bai et al (59)	*Radiology*	U.S.	CT	1186	Diagnosis	Yes	0.87	0.90	0.87	0.89	0.86	NA	NA
Mei et al (60)	*Nature Medicine*	U.S.	CT	905	Diagnosis	No	NA	0.92	NA	0.84	0.83	NA	NA
Zhang et al (61)	*Cell*	China	CT	3777	Diagnosis, severity assessment	Yes	0.91	0.97	NA	0.93	0.86	NA	NA
Murphy et al (62)	*Radiology*	Nl	Radiography	1549	Diagnosis	Yes	NA	0.81	NA	0.85	0.61	NA	NA
Lessmann et al (63)	*Radiology*	Nl	CT	843	Severity assessment	Yes	NA	0.88	NA	0.82	0.81	NA	NA
Liu et al (64)	*Theranostics*	China	CT	134	Prognosis	No	NA	0.93	NA	NA	NA	0.88	NA
Wang et al (65)	*European Respiratory Journal*	China	CT	5372	Diagnosis, prognosis	Yes	0.78	0.87	NA	0.80	0.77	NA	0.77
Harmon et al (66)	*Nature Communications*	U.S.	CT	2617	Diagnosis	Yes	0.90	0.94	NA	0.85	0.92	NA	NA
Ning et al (67)	*Nature Biomedical Engineering*	China	CT	1521	Prognosis	Yes	0.76	0.81	NA	0.76	0.76	NA	NA
Jin et al (68)	*Nature Communications*	China	CT	9025	Diagnosis	Yes	NA	0.93	NA	0.94	0.66	NA	NA
Zhang et al (69)	*Radiology*	U.S.	Radiography	5208	Diagnosis	No	NA	0.92	NA	0.88	0.79	NA	NA

Note.—Deep learning technique was used for all studies. Acc = accuracy, AUC = area under the curve, EV = external validation, NA = not applicable, Nl = the Netherlands, PR = precision-recall, Sen = sensitivity, Spec = specificity, U.S. = United States.

that of junior radiologists and comparable to that of more experienced radiologists.

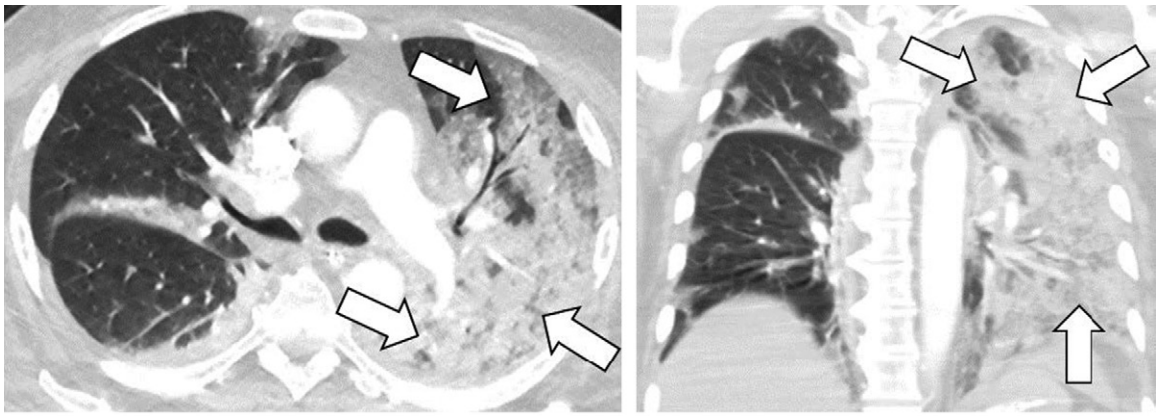
Several studies provided proof-of-concept for deep learning–based triage of COVID-19 cases using chest radiography. For example, Murphy et al (62) evaluated the performance of an AI system (CAD4COVID-Xray; Thirona) trained on 24 678 chest radiographs and compared performance to that of six radiologists on a test set of 454 chest radiographs of patients suspected of having COVID-19 pneumonia. The AI system correctly classified chest radiographs as demonstrating COVID-19 pneumonia with an area under the curve of 0.81 and significantly outperformed each reader at their highest possible sensitivities. A summary of the important studies published using AI based on imaging is shown in Table 7. Li et al (70) developed a Siamese neural network–based severity score that correlated with radiologist-annotated pulmonary disease severity scores assigned to chest radiographs in the internal and external test sets (r = 0.86 [95% CI: 0.80, 0.90]) and (r = 0.86 [95% CI: 0.79, 9.90]), respectively. In patients not intubated at admission chest radiography, the severity score enabled prediction of subsequent intubation or death within 3 days of hospital admission, with an area under the curve of 0.80 (95% CI: 0.75, 0.85). Bai et al (H.B., unpublished data, July 2020) investigated the performance of an AI system that combined chest radiographic features and clinical data to predict future critical events of ICU admission, mechanical ventilation, or death for patients with COVID-19.

In summary, AI based on chest CT and chest radiography has demonstrated potential in both diagnosing and determining the prognosis of COVID-19 pneumonia. However, to integrate these AI algorithms into routine clinical care in the fight against this pandemic, we advocate the following. First, open-source data sets and code are strongly advocated so that the broader community can train, test, and evaluate the performance of the machine learning classifiers. This is exemplified by the recent publication of the RSNA International COVID-19 Open Annotated Radiology Database (71). Second, true generalizability will need to be assessed in real time in a prospective study design. If one or a few of these models can be validated prospectively, then they could inform treatment algorithms and guidelines customized for patients with COVID-19 manifestations across the spectrum, ranging from mild symptoms to death, and pave the way for a bigger role for AI-based imaging in COVID-19 resurgence and future pandemics.

What Are the Pulmonary Vascular Effects of COVID-19?

Pulmonary macrovascular and microvascular manifestations of COVID-19, initially underrecognized, have received increasing attention in the radiologic, clinical, and pathologic literature. Our current understanding reflects intensive study that has predominantly focused on patients with severe disease and has been limited by a marked paucity of data regarding asymptomatic patients and those with mild infection. The highest level of evidence, from prospective randomized trials with outcome data, is also presently lacking.

Diagnostic imaging pathways have evolved, often radically, during the COVID-19 pandemic. These changes vary



a. b.

Figure 5: Images in a 74-year-old man with COVID-19 presenting with 7 days of cough. **(a)** Axial and **(b)** coronal contrast-enhanced thin-section chest CT images show diffuse ground-glass opacity and consolidation in left lung (arrows). These findings would be classified as indeterminate as per the Radiological Society of North America, British Society of Thoracic Imaging, and COVID-19 structured reporting assessment systems; these findings would be classified as equivocal/unsure as per the COVID-19 Reporting and Data System.

widely among different countries, regions, and institutions, reflecting differences in guidelines, the availability of resources, the prevalence of COVID-19, and institutional expertise. Variability in data resulting from differences in diagnostic imaging use in different populations during the pandemic and compared with practice prior to the pandemic remains an analytic dilemma. This is particularly true for acute PE imaging, which has performance characteristics that have been shown to be greatly impacted by disease prevalence (pretest probability) and the diagnostic modality used (72).

Although CT pulmonary angiography remains a dominant diagnostic imaging test for acute PE, point-of-care US is commonly performed in critically ill patients in the ICU (73). Patients with COVID-19 and elevated D-dimer levels along with signs of right heart strain may receive a clinical diagnosis of PE. Changes to the use of the ventilation–perfusion lung scans during COVID-19 have received attention because of infection control concerns related to the risks of the leakage of aerosolized ventilation agents. Some centers have been performing perfusion-only scans for stable patients with COVID-19 and normal chest radiographic findings (74).

The preponderance of evidence suggests that there is a real increased incidence of acute PE and other thrombotic events among patients with COVID-19. Helms et al (75) described a prospective cohort of 150 patients with COVID-19 (81% men; mean age, 63 years) with acute respiratory distress syndrome from four ICUs in France. The primary outcome was any thrombotic event. There were 64 thrombotic complications diagnosed by using CT, with most of them being PE. When compared with a prospective cohort with non–COVID-19 acute respiratory distress syndrome that was matched by clinical history, patients with COVID-19 had a higher rate of PE (11.7% vs 2.1%; P = .008), despite prophylactic or therapeutic anticoagulation being used in all patients.

Kaminetzky et al (76) described a retrospective cohort of 62 patients (65% men; mean age, 58 years) with COVID-19 who underwent CT pulmonary angiography and 62 matched patients from the pre–COVID-19 era from a single New York institution. They found a CT pulmonary angiography–defined positivity rate for patients with COVID-19 that was higher than that of patients in the non–COVID-19 cohort (37.1% vs 14.5%). One observational cohort study of 3334 (60% men; median age, 64 years) hospitalized patients with COVID-19 from the same New York institution found a 16% rate of thrombotic complications, which included acute PE in 3.2% (n = 106) (77). Other series have described the prevalence of acute PE at CT pulmonary angiography in hospitalized patients with COVID-19 as ranging from 6.4% to 30% (6.4% [78], 18% [79], 23% [80], 30% [81]).

The dilated vessel sign (pulmonary artery) was reported in the lungs early during the pandemic on unenhanced chest CT images, with some debate regarding its etiology. Possible explanations include small PEs, in situ pulmonary vascular thrombosis, and increased pulmonary blood flow (Fig 7). There are imaging and pathologic data to support both processes, and additional study will be useful for further elucidation (82,83).

In situ thrombosis of the pulmonary arteries in the lungs of patients with COVID-19 is supported by cohort studies that demonstrated clots being disproportionately located in the distal pulmonary vasculature along with lower-than-expected rates of concurrent deep vein thrombosis. In a retrospective cohort study, Van Dam et al (84) compared CT pulmonary angiography findings indicative of in situ thrombosis in 23 patients with COVID-19 and 100 control participants. Thrombotic lesions affected COVID-19–involved lung in all cases, with a lower thrombus burden and lower rate of proximal pulmonary artery involvement being shown in patients with COVID-19 compared with control participants. Cavagna et al (85) reported similar results in

a study of an Italian population of 101 patients with COVID-19 who underwent CT pulmonary angiography, with positive results found in 41%. Pulmonary emboli or thrombi were present in the segmental and more distal vessels in more than 90% of patients, representing the most proximal clot in 52% (22 of 41); deep vein thrombosis prevalence was only 12% (five of 41).

Autopsy studies have shown various pulmonary vascular abnormalities in patients who have died of COVID-19. Although representing only the most severe (fatal) disease spectrum, they shed light on the pathophysiologic characteristics and imaging findings. In a prospective series, Lax et al (86) found thrombosis of small to midsized pulmonary arteries in all patients, none of whom were clinically suspected of having thrombosis, despite prophylactic anticoagulation in 91% of patients (10 of 11). Fox et al (87) found a dominant pattern of diffuse small-vessel thrombosis associated with inflammation and hemorrhage in addition to diffuse alveolar damage. Ackermann et al (88) found distinctive vascular features, which included severe endothelial injury with intracellular virus and thrombosis with microangiopathy throughout the pulmonary vascular bed, including alveolar capillary microthrombi. They also found extensive new vessel growth predominantly through intussusceptive angiogenesis, which occurs in response to increased blood flow, vascular dilation, and the resultant mural wall stress (89).

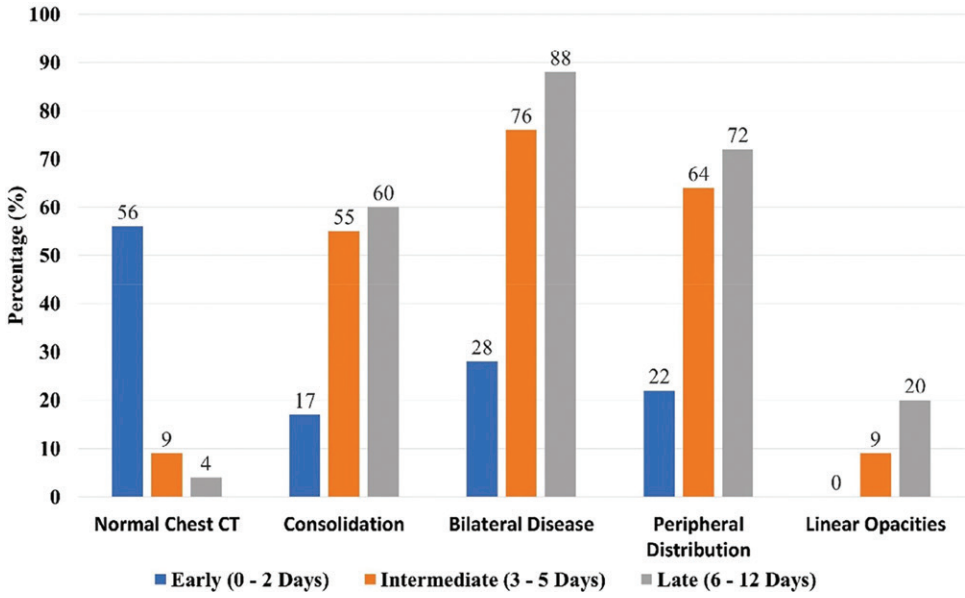


Figure 6: Graph shows frequency of selected chest CT findings as function of time course from symptom onset. Adapted, with permission, from reference 14.

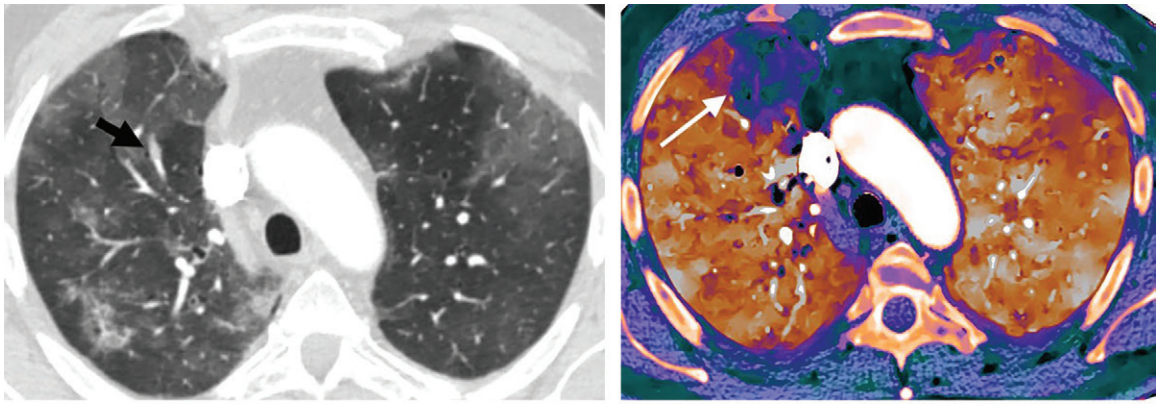
Lang et al (90) described pulmonary vessel dilation and increased perfusion proximal and distal to lung opacities in patients with COVID-19 and without PE. They proposed this was caused by regional vasodilation rather than by the normal vasoconstriction due to a dysfunctional diffuse inflammatory process. This paradoxical shunting to the hypoventilated regions may, in part, explain the poorly understood clinical phenomenon of "happy hypoxia"—profound hypoxia occurring in a patient with COVID-19 who appears well.

In severe COVID-19, it has been difficult to assess the contribution of PE to mortality in those patients who may have multiorgan failure, acute respiratory distress syndrome, and/or thromboses in different vessels, among other complexities. However, with increased recognition of thrombotic complications and the issuing of anticoagulation recommendations (91), there is an evidence base suggesting that anticoagulation is associated with improved survival (92). The National Institute of Public Health of the Netherlands recommends prophylactic low-molecular-weight heparin for all hospitalized patients with COVID-19 and monitoring of D-dimer levels to guide the use of prophylactic anticoagulation and the decision to image for deep vein thrombosis or PE, in concert with the clinical picture and YEARS criteria (91).

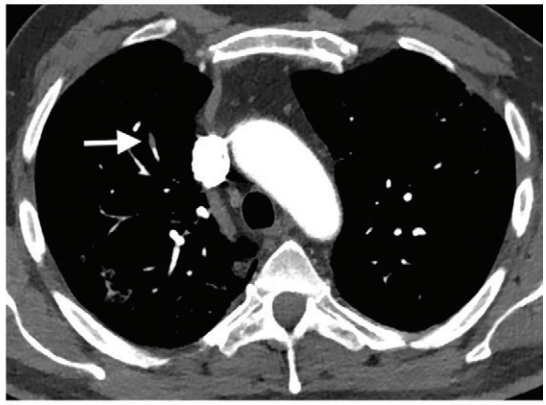
Cardiac Manifestations

Cardiac manifestations associated with COVID-19 include myocarditis, acute myocardial infarction, and coronary artery aneurysms, which have received particular attention as a component of the recently described multisystem inflammatory syndrome in children and can be associated with myocarditis.

Viral infection is the most common cause of myocarditis, whereas cardiac injury as a component of the inflammatory response commonly occurs in severely ill patients. Active investigation is in progress to determine whether myocarditis incidence is elevated with SARS-CoV-2 compared with other viral infections. MRI is the reference standard for myocarditis, and although available data are limited, its exquisite tissue characterization has shown abnormalities (Fig 8) in most imaged patients with COVID-19, in both symptomatic and asymptomatic cases. In a prospective observational cohort study, Puntmann et al (93) performed cardiac MRI in 100 patients recovering from COVID-19 (33% hospitalized), 50 healthy control participants, and 57 risk factor–matched patients. A median 71 days after COVID-19 diagnosis, 78% of cardiac MRI studies were abnormal, demonstrating elevated native T1 and T2 values, a lower left ventricular ejection fraction, higher left ventricular volumes, late gadolinium enhancement in 32%, and pericardial enhancement in 22%. Huang et al described a series of 26 symptomatic patients with COVID-19 who

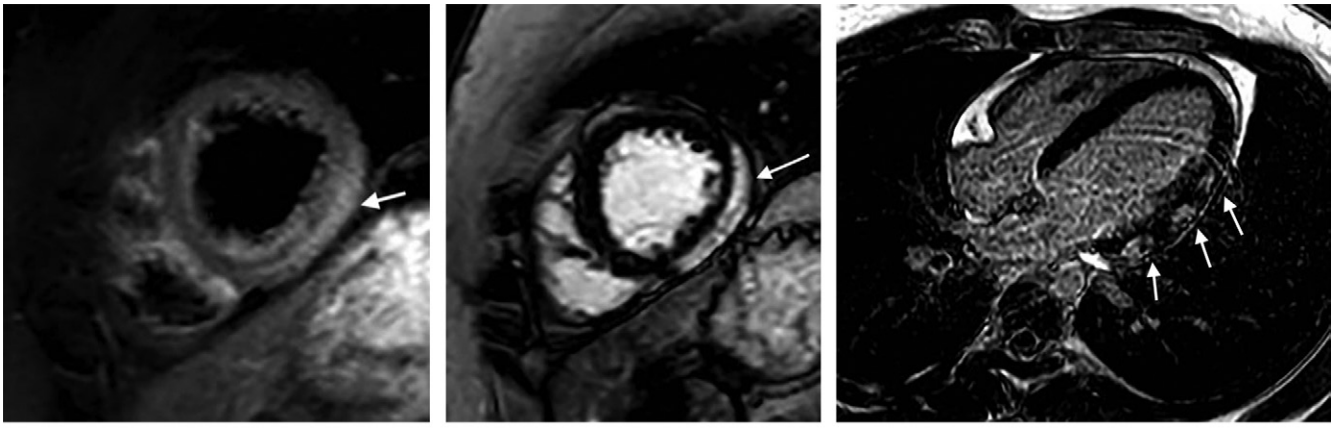


a. b.



c.

Figure 7: Images in a 59-year-old man with COVID-19, diabetes, hypertension, and coronary arterial disease presenting with shortness of breath and fever. **(a)** Contrast-enhanced CT angiographic image (lung window settings) shows bilateral peripheral ground-glass opacity. Dilated vessel (arrow) is present in anterior right upper lobe within region of lung opacity. **(b)** Spectral contrast-enhanced CT pulmonary blood volume map shows subsegmental perfusion defect (arrow) in anterior right upper lobe, in territory of dilated vessel. **(c)** Contrast-enhanced CT angiographic image (vascular window settings) shows isolated subsegmental filling defect (arrow) corresponding to dilated vessel in subsegmental anterior right upper lobe pulmonary artery, which is consistent with acute pulmonary embolism or in situ thrombus.



a. b. c.

Figure 8: Images in a 22-year-old man with COVID-19, shortness of breath, and chest pain. Cardiac MRI demonstrates mildly reduced left ventricular systolic function with ejection fraction of 47%. **(a)** T2 short-axis image through apical segments demonstrates subepicardial edema (high signal, arrow) along lateral wall. **(b, c)** There is corresponding subepicardial lateral wall late gadolinium enhancement on short-axis (arrow in **b**) and four-chamber (arrows in **c**) images.

underwent cardiac MRI compared with 20 control participants; 58% of patients with COVID-19 (15 of 26) had abnormalities at MRI, including edema in 54% (14) and late gadolinium enhancement in 31% (8); additional parameters were abnormal only among this positive subset (94). Rajpal et al (95) described cardiac MRI findings for 26 competitive college athletes (54% [14 of 26] were asymptomatic) with COVID-19 imaged 11–53 days after diagnosis. All had normal ventricular volumes and function, 45% (12 of 26) had late gadolinium enhancement, and four met modified Lake Louise Criteria for myocarditis with myocardial edema (two with pericardial effusion).

The overall incidence of myocardial infarction in COVID-19 is uncertain, but Bilaloglu et al (77) reported myocardial infarction in 9% of 3334 hospitalized patients with COVID-19. Proposed mechanisms include direct viral infection of coronary endothelium through angiotensin-converting enzyme 2 receptors, microangiopathy and

thrombosis, plaque instability related to a severe inflammatory response, and demand ischemia. Catheterization with percutaneous coronary intervention remains the standard treatment for ST-elevation myocardial infarction, but use has been reduced during the COVID-19 pandemic (96,97). CT coronary angiography has a role in low- to intermediate-risk patients with chest pain in assessing the patency of the epicardial coronary arteries (96,97).

In multisystem inflammatory syndrome in children, coronary arterial aneurysms have been described in close to 10% of hospitalized children (98). CT coronary angiography has the capacity to exquisitely demonstrate coronary arterial aneurysms, which is particularly useful for children with limited echocardiographic windows.

Are There Abdominal Findings in COVID-19?

Although diagnostic imaging in COVID-19 has centered on the lungs and pulmonary manifestations of the disease, abdominal organs are also affected, most notably the liver, biliary tree, gastrointestinal tract, and abdominal vasculature (99). The affinity of SARS-CoV-2 for cells with surface expression of receptors for angiotensin-converting enzyme 2 forms a basis for preferential COVID-19 involvement of abdominal organs as well as the lungs (100). Within the abdomen, angiotensin-converting enzyme 2 expression predominates in small-bowel enterocytes, the vascular endothelium, and the biliary epithelium (99,101).

Thromboembolic complications of COVID-19 have been reported across a variety of vascular beds and have been attributed to both microvascular inflammation and coagulopathy, leading to thrombosis and embolization (101–103). Most abdominopelvic manifestations are associated with microvascular involvement and thus manifest as end-organ ischemia or infarction involving the bowel, spleen, kidneys, and liver (99,103), with rare reports of COVID-19 being associated with superior mesenteric artery or portal vein thrombosis (101,104).

Because the use of abdominal imaging in association with COVID-19 is substantially less frequent than its use for thoracic manifestations, the evidence base is limited to small case series and case reports with limited data to support SARS-CoV-2 causation versus association.

Abdominal pain and sepsis are the most common indication for abdominal imaging in COVID-19. Among patients hospitalized with COVID-19, cross-sectional abdominal imaging has been reported in 17%, with equal use of US and CT, and is significantly more likely among patients admitted to the ICU (99).

Common findings observed on abdominal CT images include colorectal and small-bowel wall thickening, fluid-filled colon, and infarction of the kidney, spleen, or liver. Pneumatosis and portal venous gas without vascular involvement may be associated with ischemic enteritis and necrosis or pneumatosis cystoides intestinalis (105). Direct viral infection, small-vessel thrombosis, and nonocclusive mesenteric ischemia have been proposed as causes for the spectrum of bowel findings in COVID-19 (99).

Right upper abdominal US most commonly reveals signs of cholestasis, particularly gallbladder distension and sludge and fatty liver (106). Acute cholecystitis, which can be acalculous, including a case of ischemic gangrenous cholecystitis, has been reported in COVID-19 (106–108). In the latter instance, the gallbladder specimen lacked direct evidence of viral shedding, but medium-vessel thrombosis, endothelial overexpression, and invasion by macrophages and T cells supported a diagnosis of gallbladder vasculitis.

Serologic evidence of pancreatic injury was reported in nine of 52 of patients hospitalized for COVID-19 pneumonia (109). Whether the mechanism of injury results from local cytopathic effects of the virus or an indirect injury to systemic inflammatory response is not known. Although CT findings of pancreatic edema and mild peripancreatic fluid collections in association with COVID-19 appear in case reports (110,111), reports of pancreatic imaging findings are rare.

Are There Any Neuroimaging Findings in COVID-19 That Are Concerning and Consistent in the Literature?

Neurologic symptoms in COVID-19 are relatively uncommon, being seen in about 5% of patients overall. The most common clinical symptoms include anosmia, headache, confusion, and encephalopathy. Large-vessel ischemic stroke as well as Guillain-Barré syndrome are less common clinical presentations that have received substantial interest in the literature. At this time, it is difficult or impossible to determine the exact proportion of patients infected with SARS-CoV-2 who experience each of these specific neurologic symptoms. In the ICU setting, approximately 20% of patients will have some type of neurologic impairment (112).

Approximately one-half of patients who have undergone neuroimaging in the setting of COVID-19 have abnormal findings (113). The primary patterns of abnormalities include ischemic and hemorrhagic stroke, leptomeningeal enhancement, encephalomyelitis, and widespread white matter hyperintensities, which may be associated with multiple microhemorrhages (114–117). Unfortunately, for many or most of these imaging findings, it remains unclear whether they are related to the underlying infection or to the multiple confounding comorbidities, including prolonged hypoxia and deranged coagulation parameters (118). For example, the widespread microhemorrhages are striking but have been previously reported in seriously ill ICU patients without COVID-19 (119). A recent postmortem report noted that hemorrhagic transformation was rare, with "pronounced neuroinflammatory changes" representing the dominant pathologic findings (120). A rarity of hemorrhagic findings was also observed in a recent systematic review (121). Large-vessel occlusions have been seen in patients with COVID-19, which is unsurprising given the prothrombotic effects of the underlying infection. Anosmia, a common presenting symptom, was shown to be associated with T2 hyperintensity and volume loss in the olfactory bulb at MRI, but it remains unclear whether these imaging findings relate to direct viral involvement or postinflammatory changes (122,123). A recent report of olfactory epithelial biopsy highlighted its disruption, suggesting that direct neural invasion was not the primary culprit in anosmia (124).

The virus itself has been isolated from the cerebral spinal fluid in very few reports (125), again lending credence to the hypothesis that neuroimaging findings are at least in part

related to the associated systemic manifestations of the disease (116). Given the myriad presenting neurologic symptoms, the frequency of normal imaging findings in symptomatic patients, the wide range of neuroimaging findings, and the lack of clear evidence of direct central nervous system involvement with SARS-CoV-2, it remains difficult or impossible to draw meaningful conclusions about the role of neuroimaging in this pandemic (126).

Remaining Questions

Although our knowledge of COVID-19 and the role imaging plays in diagnosis and management has greatly increased since the infection became a global pandemic, many questions remain unanswered:

- What are the long-term sequelae of COVID-19 in the lungs and cardiovascular system?
- Are there long-term sequelae of COVID-19 outside of the cardiovascular system that have yet to be determined?
- Do classification systems of CT and chest radiographic findings sufficiently predict prognosis and is the extent of disease enough?
- Can imaging be used to reduce hospital admissions?
- How will the role of imaging change with the winter season of respiratory illnesses in the northern hemisphere?

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