

COVID-19: A Review of Imaging Manifestations and the Current Role of Radiology

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Abstract

Imaging must be utilized judiciously for the management of coronavirus disease 2019, to minimize the inadvertent risk of transmission of the virus. Currently, known imaging manifestations encompass a broad spectrum of non-specific findings which radiologists must recognize. Chest radiography has a lower sensitivity compared to computed tomography (CT), but can be a quick and inexpensive tool to establish a baseline in patients with moderate to severe disease. CT must be limited to selected patients with other justified indications. The radiology community must continue to share knowledge and direct research to further define the role of imaging in containing this pandemic.

Keywords

Coronavirus, COVID-19, Imaging, Radiology, Chest radiology, Computed tomography

Background

The most significant health-related crisis to impact the world in recent times began as an outbreak of what was thought to be a respiratory illness of unknown etiology in Wuhan, Hubei, China. It was, first reported to the World Health Organization (WHO) on December 31, 2019 [1]. On January 7, 2020 the 2019 novel coronavirus (2019-nCoV; later renamed severe acute respiratory syndrome coronavirus 2 [SARSCoV-2]) was confirmed as the cause of these reported cases, and the clinical condition was called coronavirus disease 2019 (COVID-19). It was declared as a global health emergency by the WHO on January 30, 2020 and as a pandemic on March 11, 2020 [2]. As of July 28, 2020 more than 16.4 million cases have been reported across the world, with close to 654 thousand deaths [3]. In this article, we describe the clinical features and role of imaging in the management of this disease and briefly review its known imaging manifestations.

Clinical Features

The disease has an incubation period of 3-7 days, and usually no longer than 14 days. The most common presenting features are fever (89-98%) and dry cough (68-76%) followed by shortness of breath and myalgia or fatigue. Less common symptoms are sputum production, sore throat, nasal congestion, diarrhoea, haemoptysis, conjunctival congestion and headache. The illness most commonly affects 35-60 year age group with a slight male preponderance [4, 5]. Severe illness is seen in older individuals and those with co-morbidities. Laboratory

parameters are often notable for lymphocytopenia (83%), elevated C-reactive protein (61%) and elevated D-dimer (46%). Arterial blood gas evaluation can show hypoxia in severe illnesses [5].

Although determining the fatality rate of an ongoing pandemic is challenging, a model-based prediction by Verity et al., estimates the crude case fatality ratio at 3.67% (95% confidence interval 3.56–3.80) [6]. The fatality rate is higher in older individuals reaching up to 13.4% (11.2–15.9) in those aged 80 years or older [6].

Role of Imaging

The rate of transmission of the SARS-CoV2 is much higher than that of the SARS-CoV1 outbreak of 2003, possibly due to its higher shedding in the upper respiratory tract even in asymptomatic patients [7, 8]. Quarantining and physical distancing measures remain the most effective methods of containing the spread. In this context, the perceived advantages of imaging must be weighed against the risk of transmitting the virus to both the staff involved in the process of imaging and to other patients being imaged for other illnesses.

Several articles have described greater sensitivity of computed tomography (CT) compared to reverse transcriptase polymerase chain reaction (RT-PCR) and have suggested a role for imaging as a tool to establish diagnosis [9, 10]. However, it is imperative to note that in the midst of a spreading pandemic, symptomatic individuals must be assumed to have the illness, unless definitively proven otherwise. Although CT may be more sensitive and quicker than RT-PCR, a negative study does not exclude the diagnosis and so patients suspected to have the illness must remain on isolation. Besides, imaging findings are not specific and may overlap with other respiratory infections like influenza. Therefore, the American College of Radiology (ACR) recommends that CT must not be used as a screening tool and must be reserved for patients with other indications [11].

The Fleischer Society consensus statement for chest imaging in patient management can be summarized as follows [12]:

- Chest radiography (CXR) can be used in patients with moderate to severe clinical features of COVID 19, independent of RT-PCR status or availability.
- CXR can also be used in those with mild clinical features but moderate to high pre-test probability, when RT-PCR status is negative or unavailable.
- In patients with mild features and low pre-test probability imaging is not indicated. Likewise, when RT-PCR is available to test patients with mild symptoms, imaging is not indicated.
- CT may be indicated in patients with persistent respiratory symptoms or hypoxia after clinical recovery from the illness.
- Personal protective measures must be implemented as recommended by the Radiological Society of North America (RSNA) COVID-19 task force [13] during all imaging

procedures. Even when used judiciously, a large number of thoracic imaging studies are likely to be performed during the course of this pandemic. Additionally, abdominal imaging may reveal the disease in lung bases [14] (Figure 1). Radiologists must therefore be well versed with the imaging findings of COVID-19 both to characterize them in known patients and, perhaps more importantly, to alert the referring clinician in cases detected incidentally. This review article aims to compile and stratify this data for ease of understanding of the same.

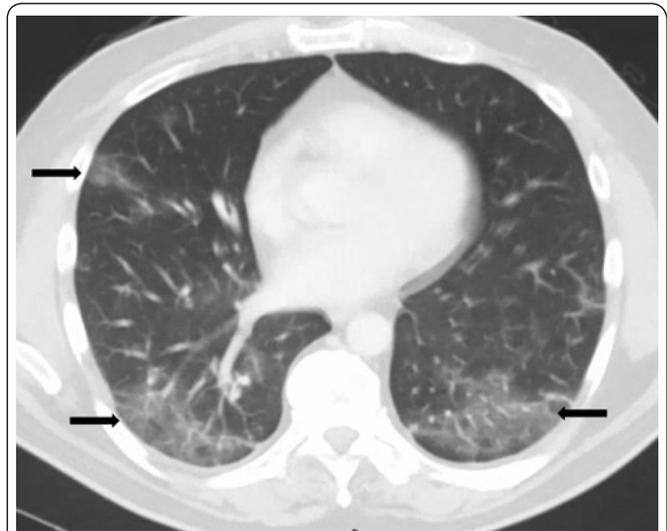


Figure 1: 61-year-old male presented with flank pain and underwent CT scan of the abdomen. CT of the lower chest incidentally detected bilateral peripheral ground glass opacities (arrows). The patient was confirmed to have COVID-19 infection with PCR test.

Chest Radiography

As is case with acute respiratory distress syndrome (ARDS) due to any cause, COVID-19 causes dysfunction of type-I and type-II pneumocytes, which lowers surfactant levels and thus leads to lung collapse [15, 16]. Extent of radiographic findings usually parallels the disease severity [17]. In a study done by Wong et al., 79% of patients demonstrated abnormalities on CXRs at some point during their illness. On baseline CXR, consolidation was the most common finding (47%), followed by ground glass opacification (GGO) with most opacities showing peripheral and lower zone distribution. About half patients showed bilateral involvement and pleural effusion was uncommon [18]. Furthermore, data from China and Korea suggests that COVID-19 infection should also be suspected in patients with nodular lung lesions and pneumothorax [18–21].

CXR has a lower sensitivity than initial RT-PCR testing (69% versus 91%). About one third of patients who have a normal baseline CXR may develop abnormalities during the course of their illness [18]. Depending on time since onset of symptoms, imaging features of CXR may be as follows [18]:

- No abnormality may be detected in the first 4–5 days since onset of symptoms
- Basal and peripheral linear or reticular opacities (Figure 2)

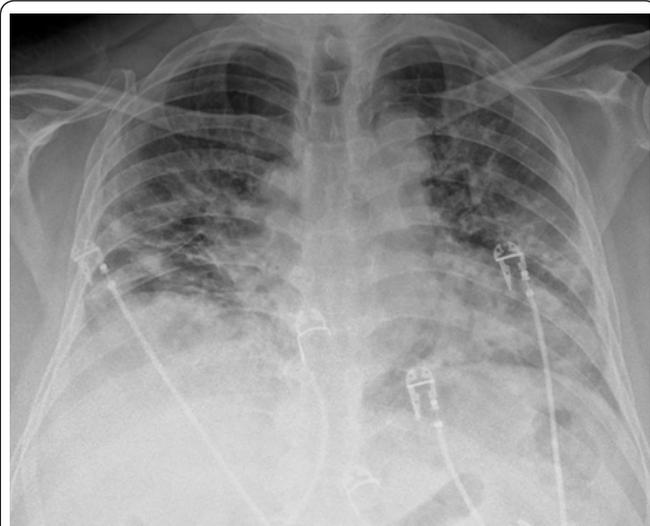


Figure 2: 42 year old male with COVID-19 infection, presented with fever and shortness of breath. Chest radiograph shows bilateral linear opacities, primarily in the lower lungs.

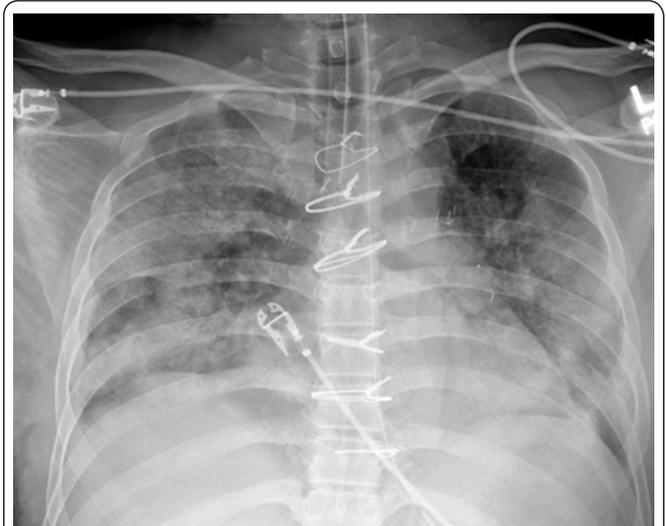


Figure 4: 59 year old male with COVID-19 infection, presented with fever, shortness of breath and cough. Chest radiograph shows extensive consolidations and ground glass opacities bilaterally.

- Bilateral consolidation and GGO which is initially predominantly peripheral (Figure 3) and increases in extent with increasing severity (Figure 4) (peaks at 10-12 days since onset of symptoms).

A similar scoring system was used by Wong et al., [18] to score lung involvement in patients with SARS-CoV-2 infection. However, this system scores each lung from 0-4 as follows:

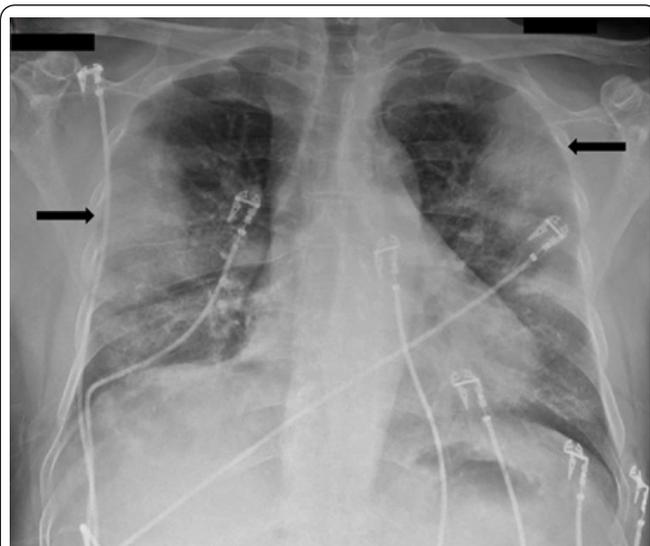


Figure 3: 54 year old male with chronic renal failure, presented with shortness of breath, cough and fever. Chest radiograph shows predominantly peripheral consolidations and ground glass opacities (arrows). Found to have COVID-19 infection on PCR test.

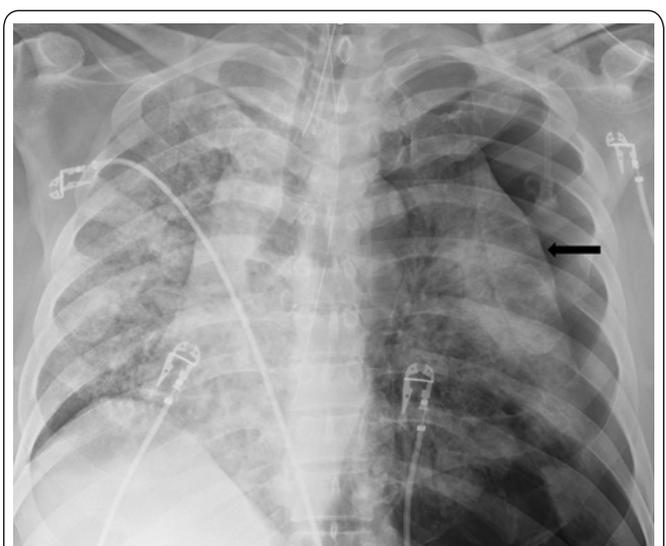


Figure 5: 55 year old male, admitted with fever and mild shortness of breath developed rapidly worsening respiratory failure requiring intubation. Chest radiograph showed left sided tension pneumothorax (arrow) and extensive consolidations and ground glass opacities in the right lung, also noticeable to a lesser extent in the atelectatic left lung. Found to have COVID-19 infection on PCR test.

- Atelectasis, pleural effusion
- Additional findings which may or may not be related to mechanical ventilation include giant bulla formation, mediastinal emphysema and pneumothorax (Figure 5) [22].

Chest Radiograph Scoring

Warren et al., described a method of scoring pulmonary edema on CXR by dividing the CXR into four quadrants and used a combination of extent and density of opacities to develop a score ranging from 0-48. Higher score correlated with worse survival [23].

0 = no involvement; 1 = < 25%; 2 = 25-50%; 3 = 50-75%; 4 = >75% involvement.

The combined score of both lungs gives the final severity score ranging from 0-8 (Figures 7 and 8). Density was not used as a criterion. In this study, there was no significant difference in mortality between the groups that had initial negative CXR from those with positive CXR. There was also no difference in time to recovery [18]. Further studies combining both density and extent of involvement may be helpful.



Figure 6: 42 year old male with COVID-19 infection, presented with fever, shortness of breath and cough. Chest CT shows multifocal peripheral ground glass opacities (arrows).

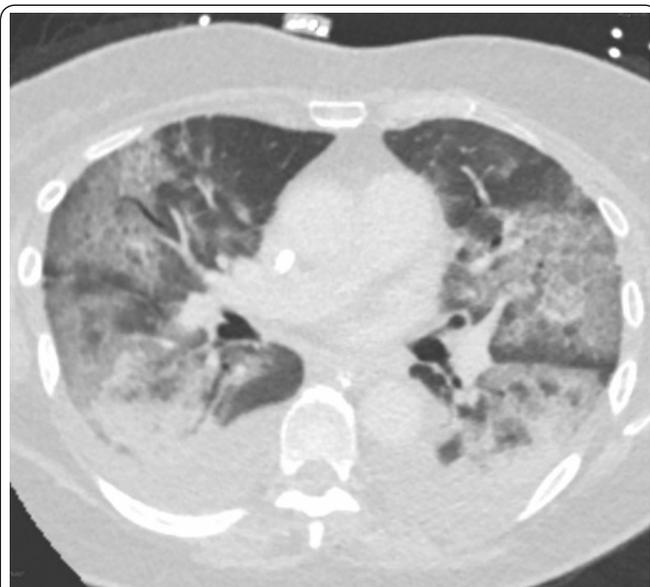


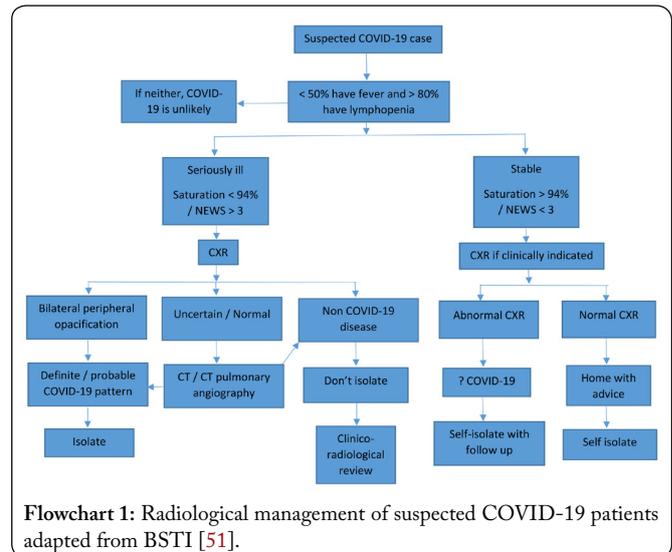
Figure 7: 71 year old Female with COVID-19 infection, presented with fever, rapidly progressive shortness of breath and cough. Chest CT shows extensive ground glass opacities, crazy paving and consolidative opacities.

Radiological management of suspected COVID-19 patients adapted from BSTI is shown in (Flowchart 1).

Chest Computed Tomography

Chest CT has been reported to have a higher sensitivity than CXR in the early stages of the disease and has also been reported to be more sensitive than RT-PCR [10]. There has been literature suggesting chest CT be used as a tool for establishing a diagnosis of COVID 19. In China, CT has been preferred over chest radiography as an early diagnostic tool for this particular reason [12]. Likewise it has been reported that well aerated lung on baseline chest CT may be predictive of a better outcome [24].

However, it is important to note that while the sensitivity



Flowchart 1: Radiological management of suspected COVID-19 patients adapted from BSTI [51].

of chest CT ranges from 79-88% in symptomatic patients [10, 25], in asymptomatic patients the sensitivity is about 54% [25]. In addition, while the positive predictive value for chest CT is around 92%, the negative predictive value is only around 42% [26]. The higher positive predictive value may be reflective of a higher prevalence during an ongoing pandemic. This, combined with the non-specific nature of the opacities mean that unnecessary utilization of chest CT would result in overburdening an already overwhelmed healthcare system, while increasing the risk of spread of the disease [27].

Chest CT findings peak at 6-11 days since onset of symptoms [28, 29]. The evolution of opacities correlates with the underlying histological findings of diffuse alveolar damage which is characterized by infiltration of inflammatory cells and exudates in the early stages, and fibrosis in the later stages [31]. Thus, Pan et al., were able to divide the time course of the opacities into 4 stages: [28]

1. Early stage (0-4 days after onset of symptoms): Negative CT or predominantly peripheral GGO (Figure 6).
2. Progressive stage (5-8 days after onset of symptoms): Opacities progress with slowly increasing crazy-paving and consolidation (Figure 7).
3. Peak stage (9-13 days after onset of symptoms): Consolidations increase with development of atelectasis and parenchymal bands.
4. Absorption stage (≥ 14 days after onset of symptoms): Decrease in density of consolidations which revert to GGO. Fibrotic bands may be seen (Figure 8).

Additional findings include perilobular and peribronchial distribution of opacities and reverse-halo sign (Figure 9), indicating organizing pneumonia. In the later stages of the disease and in patients who recover, fibrotic bands may be accompanied by architectural distortion and traction bronchiectasis, indicating the development of pulmonary fibrosis [29-31].

In a systematic review by Salehi et al., [32], the frequency and distribution of opacities were as follows: GGO (88.0%),

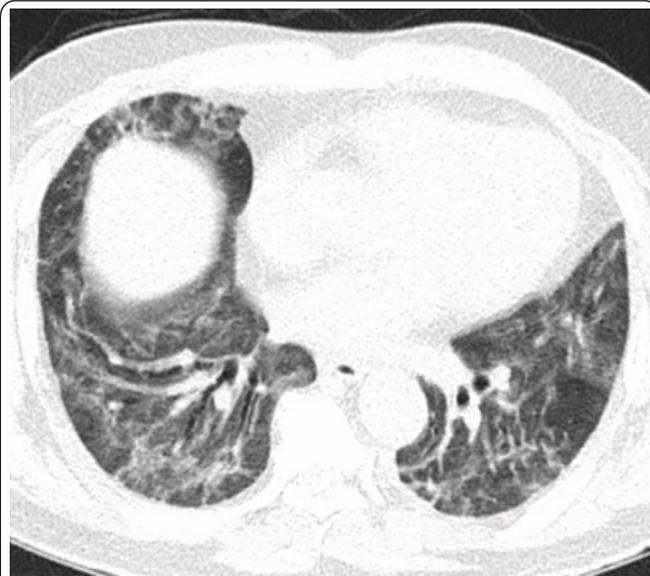


Figure 8: 72 year old male who recently travelled from China, presented with shortness of breath. He was found to have COVID-19 infection on PCR test and needed hospitalization for supportive care. CT chest done 1 week later for persistent dyspnea required linear opacities in both lungs associated with mild bronchiectasis, indicating fibrotic changes.

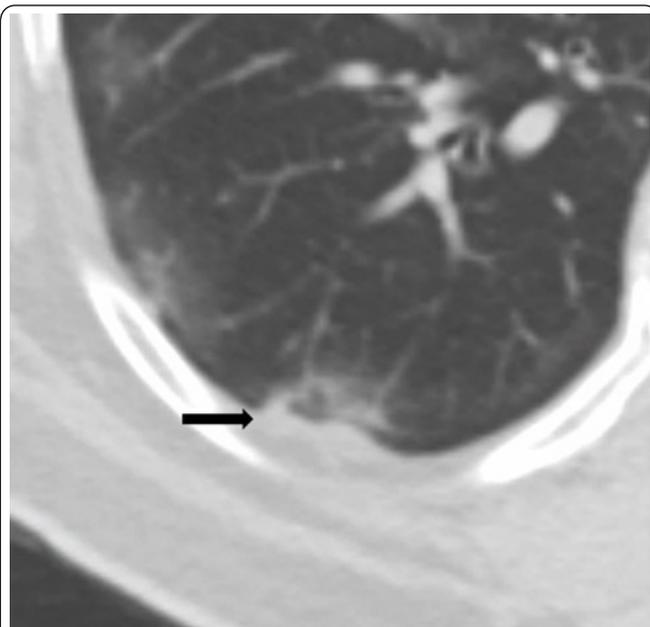


Figure 9: 83 year old male with COVID-19 infection. Axial CT of the lower chest shows a subpleural ground glass opacity in the right lower lobe with central lucency (arrow), representing a reverse halo sign.

bilateral involvement (87.5%), peripheral distribution (76.0%), multilobar (more than one lobe) involvement (78.8%) and consolidation (31.8%). Isolated GGO or a combination of GGO and consolidative opacities were the most common overall findings [32]. Pleural effusion, pleural thickening, pericardial effusion, lymphadenopathy, cavitation, CT halo sign, and pneumothorax can also occur as part of the COVID-19 spectrum, but are rare [33, 34].

CT scoring

Chung et al., and Inui et al., described a method of scoring

the extent of involvement on CT as follows [25, 35]:

Each lobe of both lungs is scored for extent of involvement as none (0%), minimal (1%-25%), mild (26%-50%), moderate (51%-75%), or severe (76%-100%) corresponding to scores of 1-4 respectively. The total score is calculated by adding the scores of each lobe (range of possible scores, 0-20) [35].

Another method of CT scoring was described by Zhou et al., [31]. In this method each lung was divided into three zones using the carina and the inferior pulmonary vein as the upper and lower landmarks respectively. Further, each lung was divided into an anterior and posterior part by a plane passing through the midpoint of the diaphragm on the sagittal plane. The 12 zones thus obtained were scored from 1-4 using a similar method of extent of involvement as described by Chung et al and [35].

A higher total score is seen in the lower lobes and symptomatic patients compared to asymptomatic patients and in the lower lobes [25]. However, its value in predicting outcome is not known. Like the CXR scoring system, the CT scoring systems have not used density of opacities as a parameter. Further studies are needed to determine if CT score has a prognostic significance with or without including density as a parameter.

Structured Reporting

The rationale of structured reporting is to help radiologists recognize findings, decrease variability in reporting, reduce uncertainty in reporting findings and to enhance the referring clinician's understanding of the findings. The Radiological Society of North America (RSNA) has released a consensus statement endorsed by the Society of Thoracic Radiology (STR) and the American College of Radiology (ACR). It proposes 4 categories for reporting CT imaging findings attributable to COVID-19, each with standardized terminologies [36]. This has been summarized in table 1.

CO-RADS

The CO-RADS classification is a standardised reporting system proposed by the Dutch Radiological Society, for suspected COVID-19 patients [37]. Based on CT findings, the suspicion for COVID-19 is graded from very low (CO-RADS 1) to very high (CO-RADS 5) (Table 2). While this system is a helpful tool for reporting findings, interpretation of imaging must never be independent of clinical data.

Other Imaging Manifestations and Complications of COVID 19

COVID-19 is known to predispose patients to thrombotic events in both the venous and arterial systems, due to the systemic inflammatory response leading to platelet activation, endothelial dysfunction, stasis and cytokine storm. However, more data is needed to learn how COVID-19 and thrombotic diseases interact. Such data could help to differentiate between pre-existing and new-outcome thromboembolic disease in

Table 1: A summary of the consensus statement on structured reporting for COVID-19 pneumonia, released by the Radiological Society of North America (RSNA) [33].

COVID-19 pneumonia imaging classification	CT findings	Suggested Reporting Language
Typical appearance	Peripheral, bilateral, multifocal GGO of rounded morphology with or without consolidation or visible intralobular lines (“crazy-paving”). Reverse halo sign or other findings of organising pneumonia.	Commonly reported imaging features of COVID-19 pneumonia are present. Other processes such as influenza pneumonia and organising pneumonia, as can be seen with drug toxicity and connective tissue disease, can cause a similar imaging pattern.
Indeterminate appearance	Absence of typical features and presence of: Multifocal, diffuse, perihilar or unilateral, non-rounded, non-peripheral GGO with or without consolidation	Imaging features can be seen with COVID-19 pneumonia, though are nonspecific and can occur with a variety of infectious and non-infectious processes.
Atypical appearance	Absence of typical or indeterminate features and presence of: Isolated lobar or segmental consolidation without GGO Discrete small centrilobular nodules (“tree in bud”). Cavitary opacities. Smooth interlobular septal thickening with pleural effusion	Imaging features are atypical or uncommonly reported for COVID-19 pneumonia. Alternative diagnoses should be considered.
Negative for pneumonia	No CT features to suggest pneumonia	No CT findings present to indicate pneumonia.

COVID-19 patients, and identify optimal treatment strategies for the same [38].

In a study done by Li et al [39], out of 221 patients admitted with COVID-19, 5% developed acute ischemic stroke, 0.5% developed cerebral venous sinus thrombosis and 0.5% developed cerebral haemorrhage. COVID-19 positive patients who manifested with new onset cerebrovascular disease were significantly older and were more likely to have cardiovascular risk factors [39]. Additionally, they were more likely to have increased inflammatory response and hypercoagulable state as indicated by the C-reactive protein and D-dimer levels. However, the association between large vessel stroke and COVID-19 disease however needs further evaluation [40].

COVID-19 may enter the CNS via the bloodstream or by the retrograde neuronal route route to cause meningitis and encephalitis [41]. A recent study has suggested that

COVID-19 can involve the CNS via a spread through the cribriform plate, causing complications such as anosmia and hyposmia [42, 43]. Another recent study has also reported COVID-19 associated acute hemorrhagic necrotizing encephalopathy in a patient with altered mental status, in whom CT showed symmetric hypoattenuation within the bilateral medial thalami and MRI showed hemorrhagic rim enhancing lesions within the bilateral thalami, medial temporal lobes, and sub-insular regions [44].

A study done by Grillet et al., [45], pointed to a high prevalence of acute pulmonary embolism (PE) in patients

Table 2: CO-RADS system described by the Dutch Radiological Society [34].

	Level of suspicion of COVID-19 infection	CT findings
CO-RADS 1	None	Normal or non-infectious abnormalities
CO-RADS 2	Low	Abnormalities consistent with infections other than COVID-19
CO-RADS 3	Indeterminate	Unclear whether COVID-19 is present
CO-RADS 4	High	Abnormalities suspicious for COVID-19
CO-RADS 5	Very high	Typical COVID-19
CO-RADS 6	Known RT-PCR positive status	



Figure 10: 69 year old female with COVID-19 infection admitted for supportive care, developed acute worsening of dyspnea. Axial CT pulmonary angiogram shows a small filling defect in the medial segmental branch of right lower lobe (arrow) indicating pulmonary embolism.

with COVID-19 (Figure 10) presenting at a mean of 12 days since onset of symptoms. CT pulmonary angiograms done in patients suspected to have acute PE may reveal both findings of COVID-19 pneumonia and the pulmonary emboli. Patients with superimposed acute PE are more likely to require critical care and mechanical ventilation [45].

Lushina et al., in their case report have described an 84 year old COVID-19 positive hypertensive with multifocal pulmonary, cerebral and renal thromboembolic disease, who succumbed to the disease despite low molecular weight heparin and mechanical thrombectomy for stroke [46].

Perini et al., and Bellosta et al., have described acute limb ischemia in COVID-19 positive patients, including young patients with no underlying atherosclerotic disease [47, 48].

When objective imaging for thromboembolic phenomena is not possible due to lack of resources, high risk of spread of infection or the patient's unstable conditions, clinicians must rely on clinical assessment to rule out the same [49]. Likelihood of PE is higher in case of known deep vein thrombosis, unexplained hypotension, tachycardia, unexplained worsening of respiratory status and having risk factors for thrombosis [49]. A normal D-dimer can effectively rule out a pulmonary embolism [49].

Abnormalities in the abdomen have been recently described in patients with COVID-19 [50]. These include bowel wall abnormalities in patients with 31% patients consisting of bowel wall thickening, pneumatosis and portal vein gas, attributed to ischemic enteritis and arteriolar fibrin thrombi. Additionally, cholestasis was noted in nearly 54 % of patients in whom a right upper quadrant ultrasound was performed, in the form of a sludge filled gall bladder [50].

Acute necrotizing encephalopathy (ANE) is usually a rare complication of influenza infections. It has been attributed to intracranial cytokine storms, which break down the blood-brain-barrier, rather than viral encephalitis [51]. While it is predominantly described in children, ANE is known to occur in adults as well. A case report by Poyiadji et al., described COVID-19-associated hemorrhagic ANE, seen as symmetric rim-enhancing hemorrhagic lesions in bilateral thalami, medial temporal lobes and subinsular regions [52].

Recent reports have suggested that gastrointestinal manifestations are present in a significant number of patients [41]. A recent study has also given the suggestion that gastrointestinal manifestations could be the only presenting symptom, in the absence of respiratory manifestations [53, 54]. The radiological manifestations include distended and fluid filled small and large bowel loops with mural post contrast enhancement and surrounding fat stranding [41].

Compared to adults, pediatric patients with COVID-19 illness showed milder clinical symptoms, fewer CT findings and lesser extent of the disease in the lungs. Although CT findings are similar, they are typically less severe than that of the adult population. Peri-bronchial distribution and bronchial wall thickening which are less frequently encountered in adult patients with the disease are commonly seen in children with

COVID-19 [55].

Role of Artificial Intelligence

CORADS-AI, an artificial intelligence algorithm developed by Lessmann et al., scores chest CTs of suspected COVID-19 patients according to CO-RADS and the results were found to be comparable to that of radiological observers [56]. A three level decision-tree classifier based on deep learning was developed by Yoo et al., which was used to detect TB vs non-TB diseases, including COVID-19. These studies may allow for quick decision making and pre-screening in COVID-19 suspects prior to RT-PCR results [57].

Conclusion

Radiologists must be well versed with the known imaging manifestations of the COVID-19 disease. The benefit of imaging must be weighed carefully against the risk of inadvertently transmitting the virus by the procedure. As the knowledge and understanding of the disease evolves, radiologists must strive to identify emerging imaging manifestations and further define the role of imaging in the management of the disease. Institutions must follow current guidelines on appropriate usage of imaging resources, mandatory safety precautions and recommended reporting terminology.

Conflict of Interest

The authors declare no conflict of interest.

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