

Radiological manifestations of COVID-19: key points for the physician

Rachel J Gravell¹

Mark D Theodoreson²

Danilo Buonsenso³

John Curtis¹

Author details can be found
at the end of this article

Correspondence to:
Rachel J Gravell; rjgravell@
doctors.org.uk

Abstract

The emergence of the SARS-CoV-2 virus at the end of 2019 has led to unprecedented demand on healthcare systems around the world. Healthcare workers, including doctors, have found themselves having to work in unfamiliar environments in the effort to control this pandemic. This article gives the hospital physician an overview of the radiological manifestations of COVID-19 disease, to improve knowledge and increase familiarity when reviewing radiographic images.

Key words: Radiology; Respiratory medicine; COVID-19

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Introduction

Radiology plays a key role in the assessment of COVID-19 disease and its complications. Manifestations of the viral disease on chest radiography and computed tomography are described as classical but not specific, nevertheless they are pivotal resources within healthcare systems. Ongoing research and observation has led to a better understanding of the evolution of COVID-19 on chest imaging. Because of this, countries are publishing individualised radiological guidelines pertaining to the disease, its diagnosis, monitoring and follow up. Continuously emerging evidence calls for succinct educational resources to equip frontline healthcare staff.

Pathophysiology

Understanding the pathology behind the radiological image is very useful when learning to recognise patterns of disease. Owing to the emergence of this new disease, the evidence of how and why symptoms develop is rapidly evolving. This article therefore summarises the best current available evidence but acknowledges that this may be superseded in the future.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes coronavirus disease (COVID-19), resulting in a viral pneumonia (Zhou et al, 2020a). Droplet spread enables the virus to enter the body via the mucous membranes and the lungs directly through the respiratory tract (Lin et al, 2020). SARS-CoV-2 enters host cells through the angiotensin-converting enzyme 2 receptors, which are expressed largely in the lungs and heart (Zheng et al, 2020a). The systemic effect of SARS-CoV-2 leads to the depletion of T and B cell lymphocytes and an increase in inflammatory cytokines such as interleukin (IL)-6 (Lin et al, 2020; Wan et al, 2020), IL-1 and tumour necrosis factor- α (Levi et al, 2020). There is evidence emerging of patients developing a severe hypercoagulable state, leading to venous thromboembolism and disseminated intravascular coagulopathy. It is these same inflammatory cytokines that initiate the formation of a pro-coagulopathic state (Levi et al, 2020). This cascading effect may explain why Li et al (2020a) found an increase in pulmonary embolism rates in those who are critically ill with COVID-19 disease. There is also evidence of perfusion defects as a result of pulmonary microthrombi (Fogarty et al, 2020), described as a 'pulmonary vasculopathy'. It is hypothesised that this is the cause of the profound hypoxia that has been observed, despite preservation of lung compliance (Ranucci et al, 2020).

Within the lungs, SARS-CoV-2 preferentially affects type II pneumocytes situated peripherally and subpleurally. Apoptosis of the pneumocytes results in a release of viral matter to neighbouring pneumocytes, propagating the disease (Mason, 2020), and in some patients causing a cytokine storm (Qian et al, 2013). This suggested chain of events leads

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to oedema, proteinaceous exudates, vascular congestion and inflammatory clusters within the respiratory system (Tian et al, 2020), across a spectrum of intensities. The disease can lead to a number of complications, with the most frequently reported being sepsis, respiratory failure, acute respiratory distress syndrome, heart failure and septic shock (Zhou et al, 2020b).

Symptomatology and diagnosis

Fever, dry cough and fatigue are commonly described symptoms (Rothan and Byrareddy, 2020). However, as time progresses an array of symptoms is coming to light such as ageusia and anosmia. With an incubation period of approximately 5.2 days (Li et al, 2020b) and evidence of asymptomatic transmission (Mizumoto et al, 2020), early testing and detection of the virus is imperative to prevent person-to-person transmission and aid recovery. Diagnosis is made with a reverse transcriptase-polymerase chain reaction assay, although its sensitivity has been questioned, with reported false negatives (Rubin et al, 2020). A study of 213 patients by Yang et al (2020b) showed, depending on time taken since symptoms started, a sensitivity of 11.1–61% for throat swabs and 50–73.3% for nasal swabs. Patients who underwent radiological investigations have shown respiratory manifestations of coronavirus despite testing negative, thus an ability to interpret these images in the acute setting is important. Using radiological modalities can help ensure appropriate isolation and reduce transmission from those who returned false negative swab results.

Radiographic manifestations

COVID-19 viral pneumonia has a classic appearance on chest radiography (Figure 1). It manifests as patchy consolidation (Figure 2), which may occupy an extensive geographical distribution. However, it is predominantly bilateral, peripheral and basal in nature (Kanne et al, 2020). Consolidation occurs when air in the alveolar air spaces is replaced with exudate or a product of disease (Hansell et al, 2008); in COVID-19 patients this is inflammatory exudate and oedema. This renders the lung solid (Hansell et al, 2008). As consolidation is radiographically denser than air, this results in a ‘whiter’ projection on the chest radiograph in a characteristic distribution. Notwithstanding, it is important to appreciate its widespread pulmonary involvement in some patients, demonstrating a variable and non-specific pattern.

Progression of this disease may result in areas of haziness on radiography known as ground-glass opacities, which cause increased density within the lung parenchyma while still

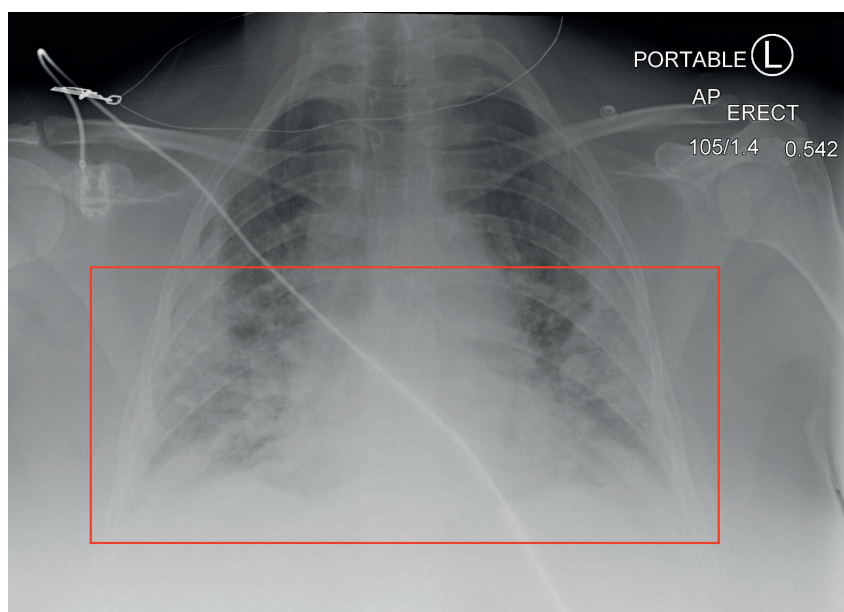


Figure 1. Classical manifestations of COVID-19. Patchy consolidation in a bilateral, peripheral and basal distribution.

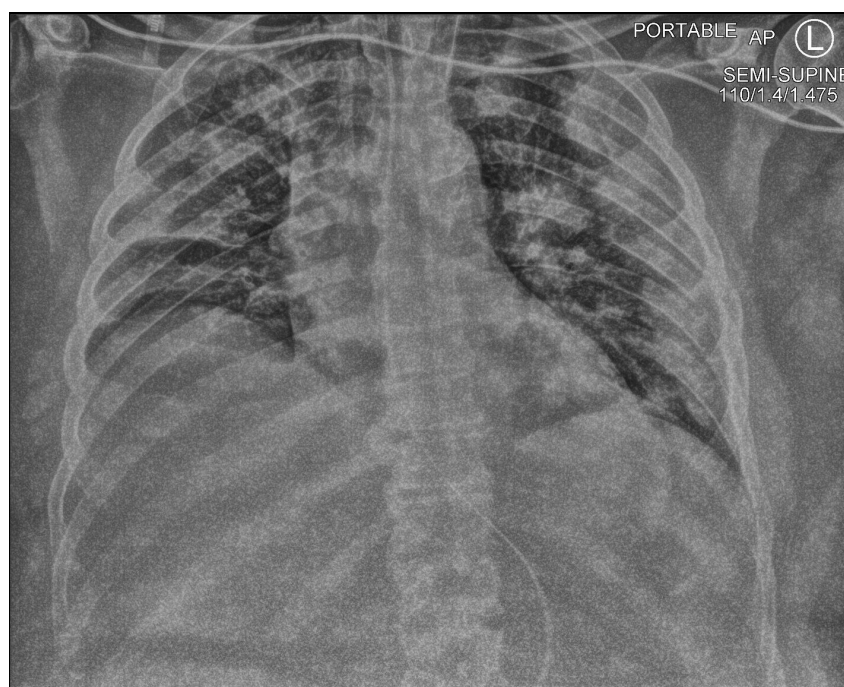


Figure 2. Patchy consolidation seen throughout both lungs and not confined to the bases or peripheries. The film is displayed with 'edge enhancement' in order to identify the lines and tubes.



Figure 3. a. Chest radiograph, (b) coronal and (c) axial corresponding computed tomography of the chest demonstrate subtle COVID-19 changes. The red box demonstrates an example of ground-glass opacity vs consolidation shown with the red arrow.

preserving visibility of the pulmonary vessels. The term ground-glass opacity is frequently used in radiology to describe a haziness that does not obscure underlying bronchial and vascular anatomy (Kobayashi and Mitsudomi, 2013). It can be caused by a number of things such as partial airspace filling, interstitial thickening, partial alveoli collapse or increased capillary blood volume (Hansell et al, 2008). Consolidation looks similar to ground-glass shadowing but tends to be more dense and renders the blood vessels invisible. Computed tomography can help better clarify these abnormalities (Kanne et al, 2020) (Figure 3).

Ground-glass opacities and consolidation tends to progress over the course of the disease on chest radiography (Figure 4). Severe cases may demonstrate extensive consolidation throughout the lung and in some cases pleural effusions (Yang et al, 2020a).

Lung nodules and lymphadenopathy are rarely seen on chest imaging in COVID-19 patients. However, if present, these findings are generally secondary to superimposed bacterial infection (Kanne et al, 2020). Pleural effusions present as blunting of the hemidiaphragms at the costophrenic angles. Although unusual, if lymphadenopathy is present, it is usually observed in the perihilar region and is seen as a fullness of the hila and with a loss of the aorto-pulmonary window.

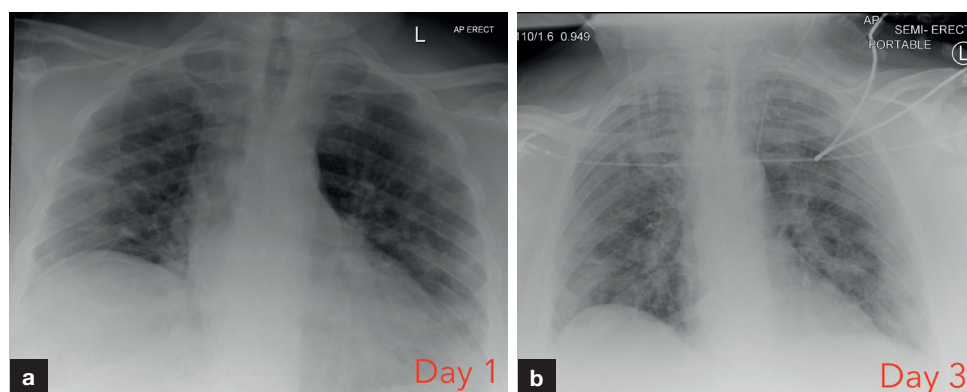


Figure 4. a. Day 1 and (b) day 3 plain film showing progression of disease in a patient with COVID-19. An increase in patchy consolidation is evident, particularly in the periphery.

Learning to recognise common patterns of COVID-19 disease is fundamental to good patient care. Although COVID-19 should not be solely diagnosed on a chest radiograph, it can be an important part of the diagnostic algorithm, along with a reverse transcriptase-polymerase chain reaction swab. Furthermore, it can aid in monitoring progression and complications of the disease (Rubin et al, 2020).

Computed tomography manifestations of COVID-19

Computed tomography is sensitive at detecting early disease as well as subtle changes that may not be evident on chest radiography (Yang et al, 2020a). It aids monitoring the interval progression and resolution of the disease. Recent studies suggest that evidence of progression on computed tomography chest imaging correlates with worsening of clinical symptoms and, equally, clinical improvements correlate with resolution on imaging (Yang et al, 2020a). It is important to appreciate that 50% of patients exhibiting symptoms of COVID-19 disease may have a normal chest computed tomography scan in the first days after symptoms present (Kanne et al, 2020). Conversely, those without symptoms can also present with COVID-19 lung changes on computed tomography (Inui et al, 2020), often found incidentally.

The characteristic computed tomography manifestations of COVID-19 have been reported in the literature as consolidation, ground-glass opacities and bronchovascular thickening (Zheng et al, 2020b) (Figures 5 and 6). These findings mimic those seen on chest radiography, preferentially adopting a peripheral, bilateral and multifocal distribution (Bai et al, 2020; Kanne et al, 2020). However, changes may also be unilateral, isolated or asymmetrical.

Many radiological reports also refer to a ‘crazy paving’ appearance, described as a classical appearance of the emerging COVID-19 pneumonia on computed tomography (Figure 7). This term refers to a ground-glass appearance together with superimposing

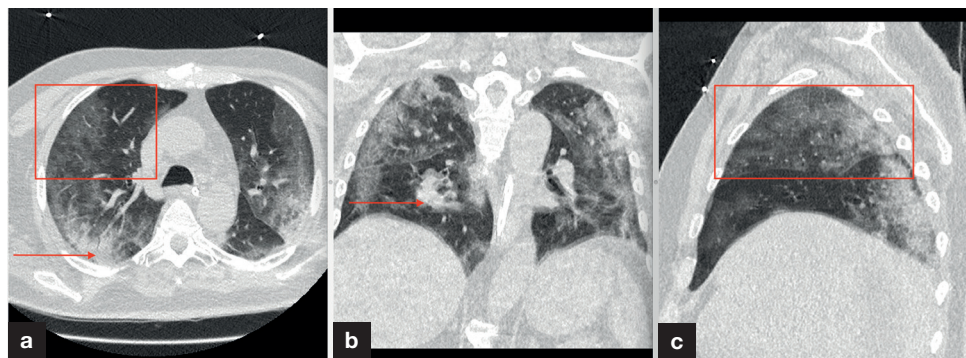


Figure 5. a. Axial, (b) coronal and (c) sagittal computed tomography of the chest demonstrating bilateral, multiple patchy changes, predominantly peripheral in location. Red boxes demonstrate areas of ground-glass changes and red arrows demonstrate consolidation.

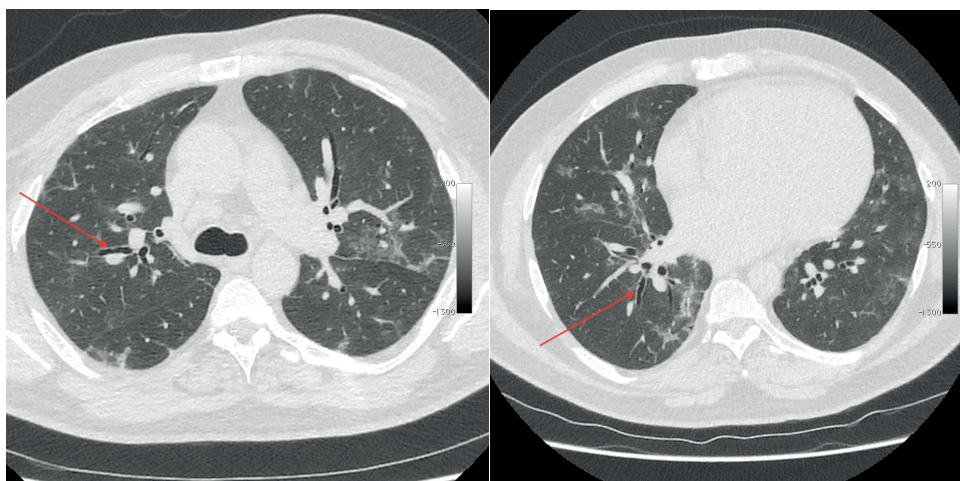


Figure 6. Axial computed tomography of the chest demonstrating bronchial wall thickening (red arrows) in a patient with COVID-19.

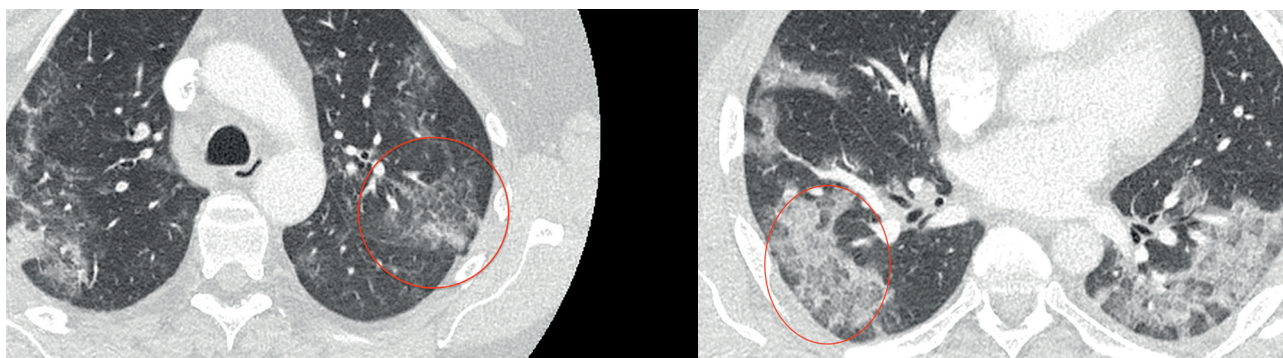


Figure 7. Axial computed tomography chest images demonstrating the 'crazy paving' sign in patients with COVID-19.

aseptal thickening and lines. It is thought to resemble irregularly shaped paving stones (Hansell et al, 2008). This is a later manifestation of the disease.

Disease progression and its associated radiological changes can be broken down into four stages (Pan et al, 2020):

1. The early stage occurs in the first 4 days, demonstrating ground-glass opacities on computed tomography scan of the chest in a bilateral or unilateral, subpleural pattern
2. Days 5–8 lead into a progressive stage exhibiting inflammatory changes. These changes result in the classical crazy paving sign in addition to lung consolidation
3. The peak stage up until day 13 describes a progression of consolidation, ground-glass opacities and crazy paving appearances, highlighted to be denser in nature with residual parenchymal bands
4. Two weeks after symptoms present the absorption stage occurs, exhibiting improvement in computed tomography manifestations (**Figure 8**).

The computed tomography chest findings of patients who were severely or critically ill demonstrate significant consolidation, ground-glass opacities and bronchial wall thickening (Li et al, 2020c). In addition, pleural and pericardial effusions have been reported (Li et al, 2020c; Yang et al, 2020a). As described above, patients with severe infection who are critically ill have a greater incidence of pulmonary emboli secondary to a hypercoagulable state (**Figure 9**). A study by Klok et al (2020), of 184 patients with confirmed COVID-19 who were admitted to the intensive care unit, found a high incidence of thrombotic complications (31%), of which pulmonary embolism was the most common. They found patients who had a thromboembolic complication had a fivefold increased risk of all-cause mortality compared to those who did not. This would suggest that there should be a low threshold for performing a computed tomography pulmonary angiogram where contrast can be tolerated.

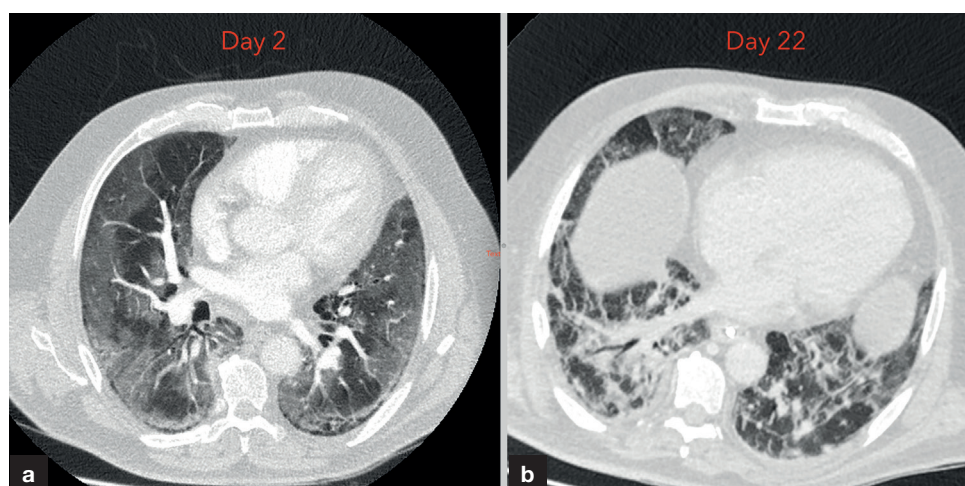


Figure 8. Axial computed tomography of the chest demonstrating progression in lung manifestations of COVID-19 over a 21-day period. a. Day 2. b. Day 22.

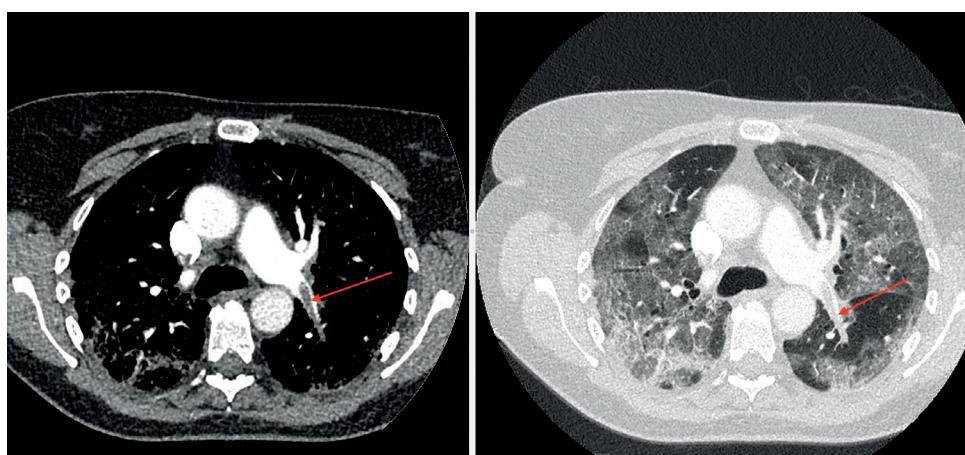


Figure 9. Axial computed tomography of the chest demonstrating a pulmonary embolism in the left lower lobe pulmonary artery in a patient with COVID-19.

Differential diagnoses

It is important to note that there are wide-ranging differential diagnoses that need to be considered when reviewing scans. Similar images can be seen in other infectious pathologies such as H1N1 influenza, adenovirus, avian influenza, atypical pneumonias including chlamydia and mycoplasma (Yang et al, 2020a), and cytomegalovirus (Kooraki et al, 2020). For example, Middle East respiratory syndrome (MERS) pneumonia caused by a similar viridae demonstrates ground-glass opacities in a subpleural and basal distribution. Adenovirus pneumonia shows patchy consolidation with bilateral ground-glass opacities (Yang et al, 2020a).

In addition, there are several non-infectious pathologies that can be included in the differential diagnosis including cryptogenic organising pneumonia, acute interstitial pneumonia and vasculitis (Yang et al, 2020a). Therefore, although changes are classical, they lack absolute specificity for COVID-19, emphasising the importance of reverse transcriptase-polymerase chain reaction and clinical findings. Furthermore, it is important to reiterate that chest radiography may be normal in patients with COVID-19.

Like any respiratory pathology, chest imaging must be interpreted in the light of the clinical and laboratory findings and not solely on the radiological findings.

Best choice advice

As cases rise exponentially, it is vital to question the best radiological modality for patients. Chest radiography is commonly used in the work up of COVID-19 patients, but the benefits of computed tomography of the chest continue to be refined. This must be weighed up

against the economy of resources, and safety of staff and patients in performing the scan from a viral transmission perspective.

Personal protective equipment and staff protection in the department, safety of transport to and from the department, and subsequent decontamination must all be considered (Mossa-Basha et al, 2020). The Centers for Disease Control and Prevention recommend that computed tomography or plain film chest radiograph cannot solely be relied upon for diagnosis, emphasising that reverse transcriptase-polymerase chain reaction is still needed regardless of evidence of COVID-19 on imaging (American College of Radiology, 2020). It must be stressed, however, that negative radiology can never exclude COVID-19 disease (Royal College of Radiologists, 2020).

There are no agreed international radiological guidelines to date. Countries and societies continue to publish best choice advice which is updated regularly, thus attention to the literature in this fast-paced pandemic is pivotal.

The British Society of Thoracic Imaging (2020), in collaboration with NHS England, has developed a radiology decision tool for clinicians to refer to when COVID-19 is suspected. Chest radiographs should be performed first line in patients with suspected COVID-19 who are severely unwell (oxygen saturation $<94\%$ or National Early Warning Score (NEWS) ≥ 3), or when clinically indicated in those who are stable. In patients who meet criteria for the severely unwell category, where chest radiographs are normal or indeterminate, a computed tomography scan of the chest is advised (British Society of Thoracic Imaging, 2020).

The American College of Radiology agrees that although computed tomography imaging is currently not indicated as a first-line modality for diagnosis, it is recommended for symptomatic patients with specific clinical indications (American College of Radiology, 2020). The Fleischner Society (a multidisciplinary, international group of experts in chest radiology) highlights the importance of imaging in cases of worsening respiratory failure and for monitoring the progression of disease (Rubin et al, 2020).

There is a wealth of advice on best choice imaging in the literature although there is no common consensus at present. While this can be frustrating when faced with the decision, a joint discussion between the clinical team and radiologist is encouraged if there is any concern.

Is there a role for ultrasound in COVID-19?

Ultrasound can be a useful tool in the diagnosis of respiratory pathology. It is quick, available at the bedside and does not involve ionising radiation. Although not routinely used to investigate COVID-19 in the UK, recognising ultrasound findings of the virus may be helpful in specialities such as acute medicine and emergency medicine.

Characteristic patterns of COVID-19 on ultrasound of the chest include irregular pleural lines (Figure 10), subpleural consolidation and the presence of B-lines (Buonsenso

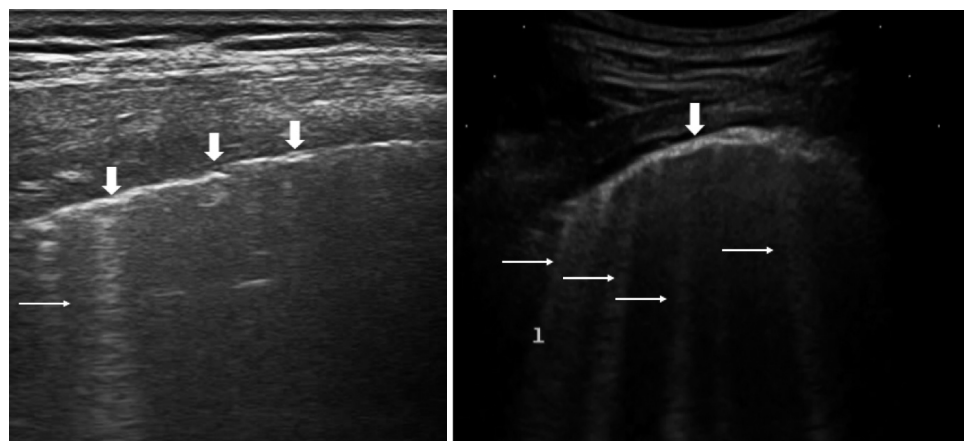


Figure 10. Lung ultrasound in patient with COVID-19 demonstrating non-confluent vertical artefacts known as B-lines (thin white arrow) and irregularities of the pleural line (thick white arrow).

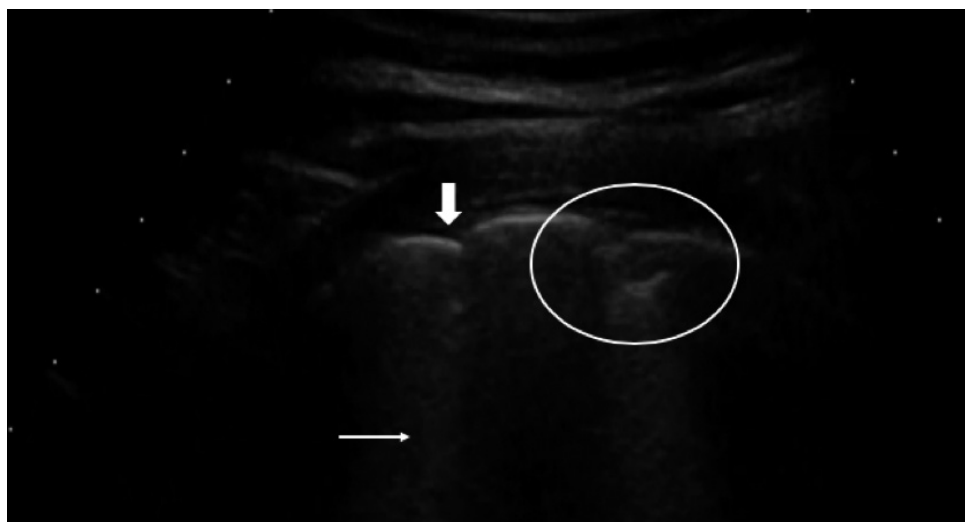


Figure 11. Lung ultrasound in patient with COVID-19 demonstrating non-confluent vertical artefact known as B-lines (thin white arrow), irregular pleural line (thick white arrow) and subpleural consolidation (white circle).

et al, 2020a) (**Figure 11**). B-lines are artefacts generated by ultrasound secondary to thickening of interlobular septa, and are present in a number of locations and angles within the lungs.

Since COVID-19 pneumonia has a patchy distribution, it is important to scan the whole thorax. Soldati et al (2020) propose a scanning procedure evaluating 14 lung areas and outline a classification system grouping ultrasound pattern findings into four groups (score 0 to 3). Score 0 is given to a normal well-aerated lung characterised by A-lines. A score of 1 is used when the pleural line is indented, suggesting infiltration of fluid into air spaces. A score of 2 is given when the pleural line is broken, with apparent areas of consolidation and associated areas of white below this. A score of 3 is given to the progression of image findings with a large, dense white lung with consolidation (Soldati et al, 2020).

On recovery, the presence of A-lines has been reported (Peng et al, 2020) (**Figure 12**). A-lines are secondary to artefacts produced in normal aerated lung signifying improvement.

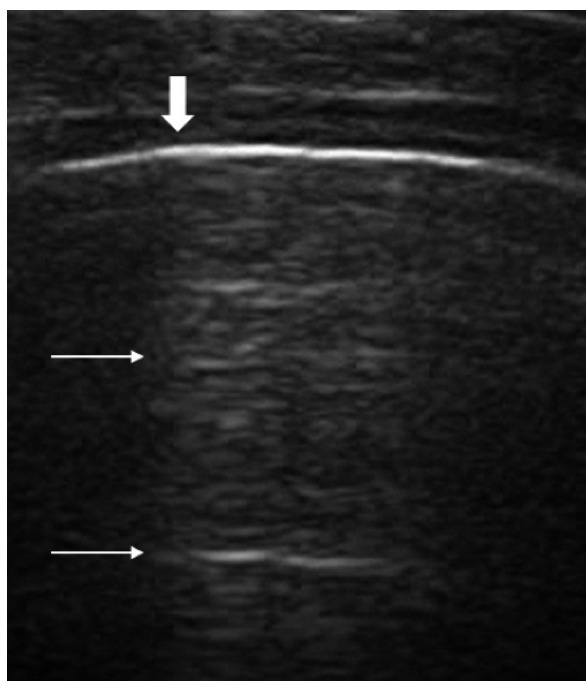


Figure 12. Ultrasound lung of patient with COVID-19 demonstrating a regular pleural line (thick white arrow) with horizontal A-lines (thin white arrows).

Key points

- Recognising the manifestations of COVID-19 on chest radiographs is likely to become commonplace for hospital physicians, especially as usual services begin to resume putting stress on radiology departments.
- COVID-19 classically appears as a bilateral, peripheral and patchy consolidation on imaging.
- It is important to remember that those with COVID-19 may not have radiological changes. Reverse transcriptase-polymerase chain reaction is needed for a diagnosis.
- Clinicians using ultrasonography in non-respiratory settings may, where appropriate, consider opportunistically scanning the thorax.

As discussed in negative findings earlier, pleural effusions were rarely seen but their presence can be suggestive of either bacterial co-infection or alternative pathology.

Ultrasound may be useful in more remote and resource-poor locations and is an emerging technique for evaluating lung disease. It may be possible to quickly train other physician groups in the use of this modality. For example, Buonsenso et al (2020b) report a preliminary study that showed how a fast lung ultrasound teaching programme for non-respiratory doctors was effective in training gynaecologists and obstetricians in evaluating pregnant women with COVID-19.

Conclusions

In the fast-changing landscape of the COVID-19 pandemic it can be difficult to keep up to date with latest guidelines and information. This article should give frontline physicians greater confidence when reviewing radiological images of COVID-19. It highlights that although the radiological changes can be dramatic, it is not clinically necessary to image all patients with suspected or confirmed COVID-19. Decisions must be made on a clinical need basis as well as considering the infection control implications.

Author details

¹Department of Radiology, Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK

²Department of Medicine, Countess of Chester Hospital NHS Foundation Trust, Chester, UK

³Department of Woman and Child Health and Public Health, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; Istituto di Microbiologia, Università Cattolica del Sacro Cuore, Roma, Italia

Conflicts of interest

The authors declare no conflicts of interest.

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