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REVIEW

Current Concepts Imaging in COVID-19 and the Challenges for Low and Middle Income Countries

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Abstract

With nearly 3,800,000 cases and 270,000 deaths reported worldwide, COVID-19 is a global pandemic unlike any we have seen in our lifetimes (1). As early as 1995, the WHO was warning of a global infectious disease crisis, citing 30 new infectious diseases emerging in the past 20 years, loss of antibiotic effectiveness, low rates of immunization, poverty, and inadequate investment in public health contributing to the more than 17 million people dying each year from infectious diseases, principally in Low and Middle Income countries (LMIC) (2). Unlike previous infectious diseases, at the time of this writing over 63% of the total reported cases of COVID-19 are in 6 High Income Countries (HIC): USA, Italy, Spain, France, Germany and the UK.

Information concerning the imaging findings in COVID-19 has been rapidly disseminated from the centers first affected by the pandemic. This article attempts to summarize the current state of knowledge regarding the imaging findings in COVID-19, focusing on pulmonary findings, and offer recommendation for the use of imaging for diagnosis and surveillance of COVID-19, particularly in LMIC.

Imaging findings

Regardless of modality, imaging is not able to distinguish COVID from other viral pneumonias. Nevertheless, for patients with the appropriate clinical presentation, during the current COVID pandemic the imaging findings described below point towards COVID causation. The high positive predictive values for imaging findings reported in many recently published papers is directly related to the high prevalence and pretest probability of COVID infection during this pandemic. For readers unfamiliar with the current terminology for chest radiography, chest CT, and pulmonary ultrasound in COVID, modality-specific terminology is listed in Addendum 1.

Chest radiography

The reported sensitivity of chest radiography (CXR) for COVID-19 varies widely from 25-69% (3). One report of high sensitivity (95%) included only patients admitted to the ICU and therefore with severe symptoms (4). In the subset of symptomatic patients with a negative RT-PCR test, only 9% of patients are reported to have CXR findings consistent with COVID-19 (3).

Initial findings on CXR are characterized as bilateral (50%), peripheral (41%), lower lobe (50%), with either ground glass opacities [GGO] (33%; Figure 1) or consolidation (47%; Figure 2) (3,5,6). Effusion is rarely present. Chest X-ray is less sensitive than CT, particularly in early disease. In a quantitative comparison with CT, radiography underestimated the extent and size of pulmonary findings (6).

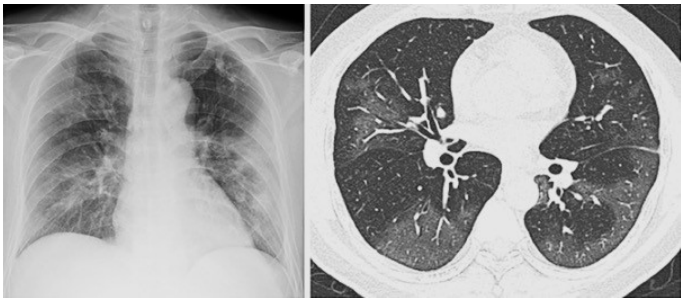

Figure 1. Ground glass opacities as observed on CXR (left) and CT (right). (Yoon et al., licensed under CC BY-NC 4.0)

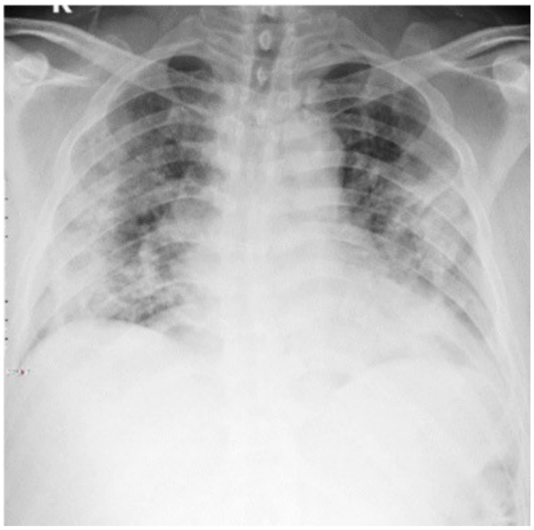

Figure 2. Multiple peripheral consolidations bilaterally. (Choi et al., used with permission)

The frequency of CXR findings increased with time and were most prominent and extensive 10 to 12 days from symptom onset (3,7,8). While Young et al. report that some patients' chest X-rays remained normal during their course of hospitalization, two thirds of their population had either mild or moderate disease not requiring supplemental oxygen.

Chest CT

Chest CT was initially touted for use in the diagnosis of COVID-19 with a report from China of sensitivity exceeding RT-PCR testing (98% vs. 71%) and the authors suggesting using CT to screen patients for COVID-19 (9). While CT does have some role in COVID-19 infection, more recent reports have found that CT findings increase during the course of the disease (Figure 3) with up to 56% of patients having a normal CT at presentation (10).

The principle findings on CT are ground glass opacities (GGO; Figures 1, 4) and consolidation (Figure 5) (5,11,12). GGO, the most common finding, occurs either alone (34%) or in association with consolidation (41%). Pulmonary involvement is variable but most often bilateral, multilobar, peripheral, and with a mild lower lobe predominance (3,5,7,10,11,13–15). Certain findings occur rarely and should prompt consideration of alternative or secondary diagnoses including: consolidation without ground glass opacity, pulmonary nodules, cavitation, mucoid impaction, and pleural effusion (13,15–17). While lymphadenopathy was initially viewed as rare with COVID-19 infection, recent reports from France and China suggest that in patients with moderate or severe disease, hilar or mediastinal lymphadenopathy (Figure 6) may be present in more than 30% of this subset of patients (18,19).

At initial presentation, early disease may manifest as GGO and/or crazy-paving (GGO with septal thickening; Figure 7) (12,13,15,20). Within one to three weeks, these opacities often progress into a more extensive mixed pattern of ground glass and consolidation (Figure 8 A-B) (11,12,15,20). Irregular septal thickening, reticular pattern, reverse halo (atoll sign) morphology (Figure 9), and linear/curvilinear opacities (Figure 10) have all been reported (10,11,15,16). With time, initial ground glass opacities and consolidation regress but the majority of patients have residual ground glass opacities upon hospital discharge (Figure 8 C-D) (12,20). CT findings progress and evolve in many patients with moderate or severe disease with reports showing consolidation developing into patterns of perilobular organizing pneumonia (Figure 11), suggesting possible progression to fibrosis—although these findings have not been evaluated long-term and fibrosis has not yet been histopathologically confirmed (11,12,15,17,21).

The clinical significance and management implications of CT findings remain uncertain. Positive CT findings have been reported in asymptomatic patients (15). In a study of RT-PCR positive passengers from an infected cruise ship, over half of asymptomatic patients had a positive CT with a strong predominance of GGO over consolidation (83%); symptomatic patients had a higher rate of CT positivity (79% vs. 54%) and a predominance of consolidation over GGO (22). One group reported CT mixed patterns of ground glass opacities and consolidation were more common in patients outside the ICU and consolidation predominated in ICU patients (23). This higher-than-expected prevalence of abnormal CT findings in infected patients, regardless of symptomology, reinforces the judicious use of CT imaging in guiding treatment and patient disposition.

Artificial intelligence (AI) has been demonstrated, in a retrospective trial, to improve radiologists' performance on CT in distinguishing between pneumonia from COVID-19 compared to other infections but the clinical impact of such technology is yet to be determined (24).

A detailed description of non-pulmonary COVID-19 related imaging findings is beyond the scope of this article. CT scanning, and MRI, if available, is being for neurodiagnosis in those COVID-19 patients who have been reported to experience cerebrovascular events and encephalitis.

Ultrasound

A standardized acquisition protocol, using 14 designated landmarks, has been proposed by Soldati and colleagues

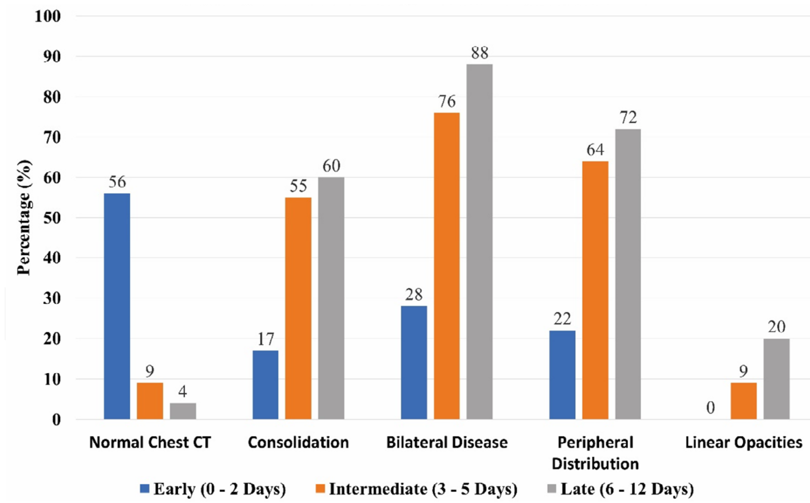

Figure 3. Frequency of selected chest CT findings as a finding of time course from symptom onset. (Bernheim et al., used with permission)

and is recommended to allow for serial comparison (25). Scoring of abnormalities can be performed using a 3-point scale (Figure 12).

Ultrasound findings are notable for pleural and septal thickening (25-27), indicating subpleural interstitial fluid or consolidation extending to the pleural edge. As with CT and radiography, pleural effusions are rarely observed on ultrasound (26).

Ultrasound can also be used for cardiac assessment in patients with COVID-associated cardiomyopathy and heart failure. The American College of Cardiology recommends limiting ultrasound to those cases requiring medical decision-making and suggests the use of point-of-care ultrasound (POCUS) as an initial evaluation with focused echocardiography reserved for patients with more severe disease (28).

Modality-based challenges with COVID

Infection control and staff safety

The COVID-19 pandemic has strained the resources and capacity of many HIC. Details concerning the best practices for infection control have previously been published in this journal and are available online (29). In addition, there are a few considerations, specific to radiology including:

- Clustering of all COVID patients requiring imaging into a single block of time to streamline efficiency and avoid the need for equipment decontamination after each patient, allowing staff to use a single set of personal protective equipment (PPE) for multiple patients.
- In rooms with adequate ventilation (6 air exchanges per hour) after a patient with COVID is imaged, it is recommended to wait one hour, including cleaning time, before imaging a non-COVID patient.
- Some sites in HIC are using a "double wipe-down" procedure—cleaning the ultrasound units first in the patient space and repeating, after a 2-minute drying time, outside of the isolation area.

Chest radiography

In LMIC, radiography and ultrasound are much more available than CT (30). In many sites in LMIC, portable radiography is not available and transportation of critically ill patients or even patients requiring oxygen, can be extremely challenging, restricting access to radiography.

Challenges with CXR include the requirement for technologists to don PPE and decontamination of the portable radiography unit after being used in the COVID isolation area. Novel approaches have been recommended to minimize both the risks of staff exposure as well as the need to decontamination including obtaining exposures through the glass doors or windows in isolation rooms and/or using a greater than routine FFD (film-focus distance) of up to 3-4.5 meters to allow the mobile radiography unit to stay outside of the room antechamber (31). The University of Utah, Department of Radiology has online instructions [https://medicine.utah.edu/radiology/news/images/through-glass-cxr-instructions.pdf] detailing the steps required to minimize staff exposure by safely performing through-glass chest X-ray.

Computed tomography

CTs role in various diagnostic protocols varies widely. According to our Italian colleagues, initial imaging for COVID-19 suspected patients is a CXR. If the CXR is positive, the diagnosis is made. If the CXR is negative, ultrasound is performed and if more than 3 B-lines are noted, CT is then performed. On the other hand, French, Russian, and Kenyan radiologists report using CT preferentially both for diagnosis and to monitor clinical improvement. In the United States, the American College of Radiology does not recommend either chest X-ray or CT for diagnosis (32). Their guidelines express concern about the use of CT given that findings overlap with those of influenza and other viral pneumonias. As mentioned above, in locations with a high prevalence of COVID-19, this issue has less significance and with the continued uncertainty concerning RT-PCR testing in both timeliness and accuracy, CT is being selectively used in the U.S. to aid in patient care decisions.

What emerges from all sides in this debate is that the ability to minimize contamination of staff and equipment, as well as the availability or scarcity of PPE, have overarching effects on selecting an imaging modality. We find that disparate decisions are being made on the ground by similar institutions in the same country.

Ultrasound

The potential of pulmonary ultrasound in suspected or confirmed COVID-19 patients has been reported but no blinded studies exist concerning its utility. In our informal survey of clinicians and radiologists from multiple countries, divergent views of ultrasound emerged. Proponents cite the

Figure 4. Peripheral lobe ground glass opacities with new areas of consolidation on CT (arrows), observed five days following initial presentation with fever, cough, and productive sputum. Additional CT images demonstrated bilateral disease involvement. (Kong et al., used with permission)

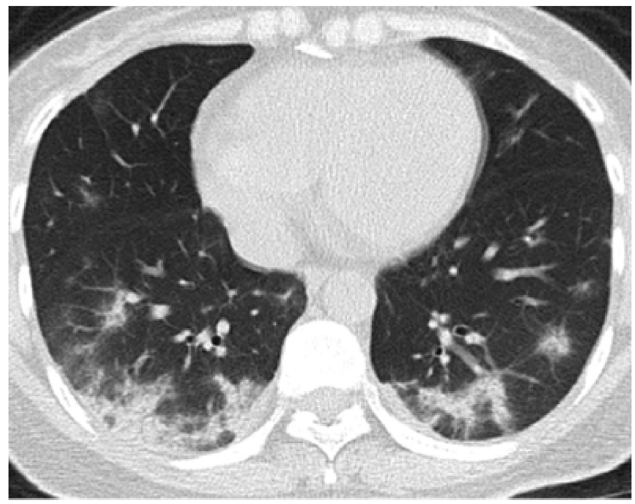

Figure 5. Consolidation in bilateral lower lobes on CT, observed on day 13 of illness. (Wang et al., used with permission)

Figure 6. CT chest showing enlarged mediastinal and right hilar lymph nodes. In this patient, timing related to disease onset or disease severity is unclear. (Li et al., used with permission)

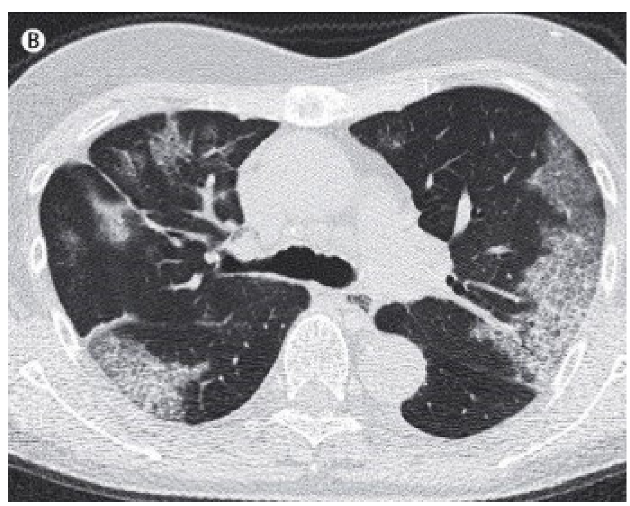

Figure 7. CT demonstrating crazy-paving in the periphery bilaterally, consisting of thickened interlobular and intralobular septa atop a background of ground glass opacity. Observed on day 10 after symptom onset. (Shi et al., used with permission)

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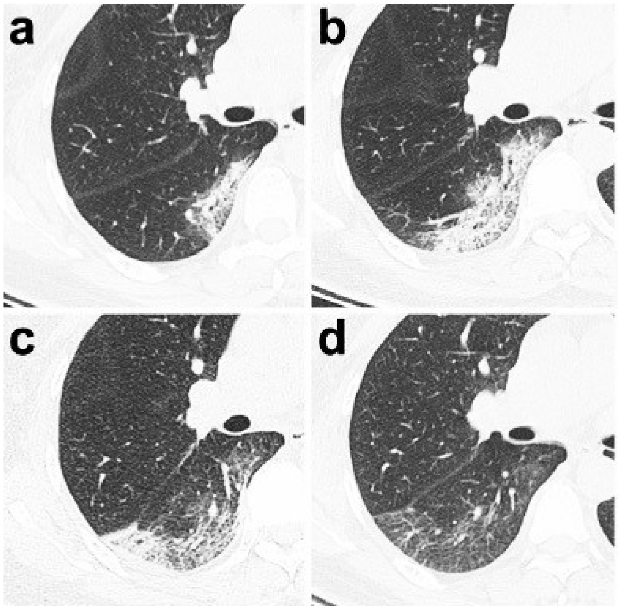

Figure 8 (A-D). On presentation or day 3 of illness, CT demonstrated ground glass opacity (A) with progression to crazy paving pattern and partial consolidation (B) by day 7. Follow-up CT on days 11 (C) and 20 (D) showed continued resolution of initial GGO. (Pan et al., used with permission)

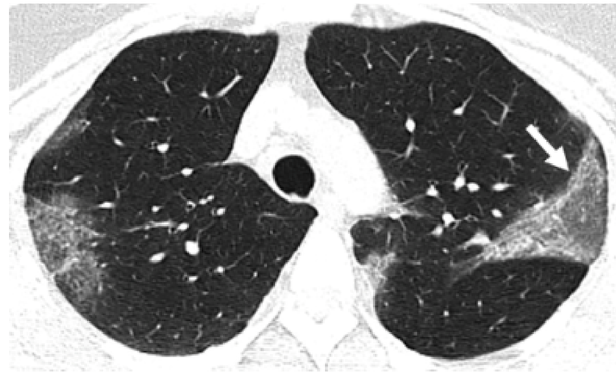

Figure 9. Left upper lobe peripheral opacities with reversed halo pattern (arrow). Timeframe from symptom onset unclear; however this was noted to progress to organizing changes on follow-up CT two days later, as observed in Figure 10. (Kong et al., used with permission)

Figure 10. Subpleural curvilinear opacities observed on CT, two days following initial presentation with fever and chills (arrows). (Kong et al., used with permission)

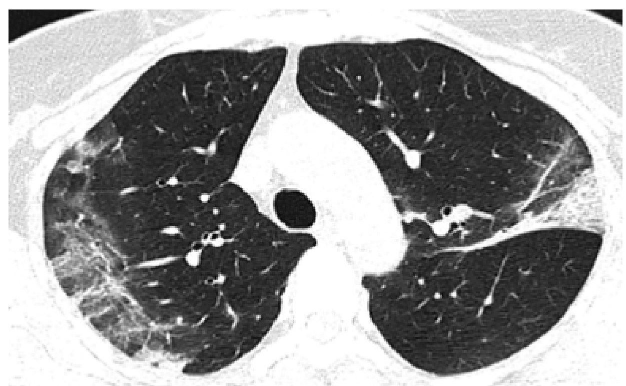

Figure 11. Follow-up CT with organizing changes. Timing from symptom onset unclear. (Kong et al., used with permission)

lack of radiation, wide availability, often inexpensive devices, relative ease of machine cleaning, and the ability to perform serial examinations at the bedside. Detractors note that the risk of radiation, even from serial chest X-rays, is minimal in this setting, and that ultrasound risks prolonged proximity to the patient, is subject to operator dependency, and many sites lack experience with acquiring and interpreting pulmonary ultrasound images.

Even within Europe, while we see many reports from Italy suggesting that ultrasound has much promise, at the same time, radiologists and several French radiologic societies have cautioned for sparing use of ultrasound due to the required close proximity to patients. Sites in Iran and Pakistan report that pulmonary ultrasound is not being used. We have anecdotal reports, from Russia, of handheld ultrasound being used for quick home assessment.

The Fleischner Society recently released their COVID guidelines. While their fundamental recommendations are important, ultrasound is explicitly not considered in these guidelines because of a paucity of experience and “infection control issues” (33). In the coorresponding author’s experience, tablet-based POCUS, with its paucity of knobs and keys, is easier to disinfect in most environments than either portable radiography equipment or standard

Score 0	Score 1	Score 2	Score 3
Pleural line (red arrow) is continuous, with "A-line" horizontal artifacts (blue arrow) visible	Indented pleural line (red arrows), with vertical areas of white (blue arrows) representing "B lines"	Broken pleural line (orange arrows) with small darker consolidated areas (red arrows) and areas of white lung (blue arrows)	Large, dense consolidations (darker areas, red arrows) with generalized white lung (orange arrow)

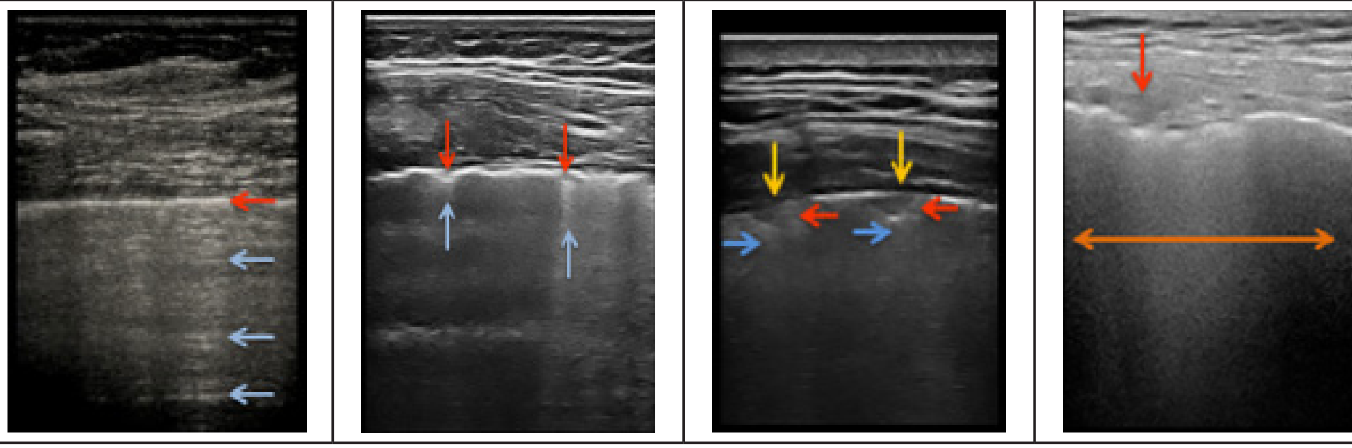

Figure 12. Lung ultrasound Score 0 through 3, as observed with linear transducer. (Adapted from Soldati et al., used with permission)

ultrasound units.

Decision making

What lessons can we garner from the divergent use of imaging when attempting to offer guidance on imaging COVID-19 patients in LMIC? Obviously, local conditions, including the availability of PPE, CT, and skill at performing pulmonary ultrasound are major drivers.

In choosing between chest X-ray and ultrasound in both sporadic and serial patient evaluation, local capabilities, availability of PPE and cleaning equipment, and the need to assess the entire chest (e.g. endotracheal tubes) will be the prominent drivers. In terms of decision-making, we have divided decision-making in imaging into three arenas: screening, triage, and management (Figures 13, 14).

Screening

Despite early, optimistic reports concerning CT, imaging currently plays no primary role in screening patients for COVID-19. Selective use of imaging can be considered in patients with typical COVID-19 symptoms and a negative or pending RT-PCR test. Since patients with mild symptoms are typically sent home to self-isolate and not hospitalized, imaging should only rarely be performed in this population. Patients with mild symptoms but with an atypical clinical presentation may benefit from chest X-ray as a method for ruling out alternative cardiopulmonary diagnoses as well as documenting findings suggestive of COVID-19. No definitive data exists about the clinical utility of ultrasound for screening.

Triage

Decisions about disposition in patients with at least moderate disease are primarily driven by the clinical assessment including symptom severity, vital signs, pulse oximetry, etc. Imaging assessment of pulmonary involvement can offer clinicians an additional data point, especially in the situations in which hospital capacity is strained and the baseline extent of disease, particularly on CT, has been reported to predict both ICU admission and mortality (34). Ultrasound, chest X-rays, and CT can all be used in triage. Chest X-ray offers the advantage of familiarity, reproducibility, complete coverage of the thorax, and does not require the clinician time typically required to perform lung ultrasound. However, chest X-rays have been reported to be normal in ~30% of COVID-19 positive patients requiring hospitalization (3). In experienced hands and with appropriate PPE, ultrasound can be performed and offers portability. Although ultrasound is reported to be positive prior to chest X-ray abnormalities, the false negative rate of ultrasound for significant pulmonary pathology is currently unknown (35). In many LMIC settings there is limited availability of CT scanners, trained technologists, and radiologists capable of interpreting chest CT. CT should therefore be reserved for patients in whom other imaging is incongruent with the clinical assessment, or in whom occult cardiopulmonary disease, such as pulmonary emboli, is suspected.

Management

In hospitalized patients, imaging can assist in evaluation of disease severity, progression, and the detection of acute respiratory distress syndrome (ARDS), bacterial co-

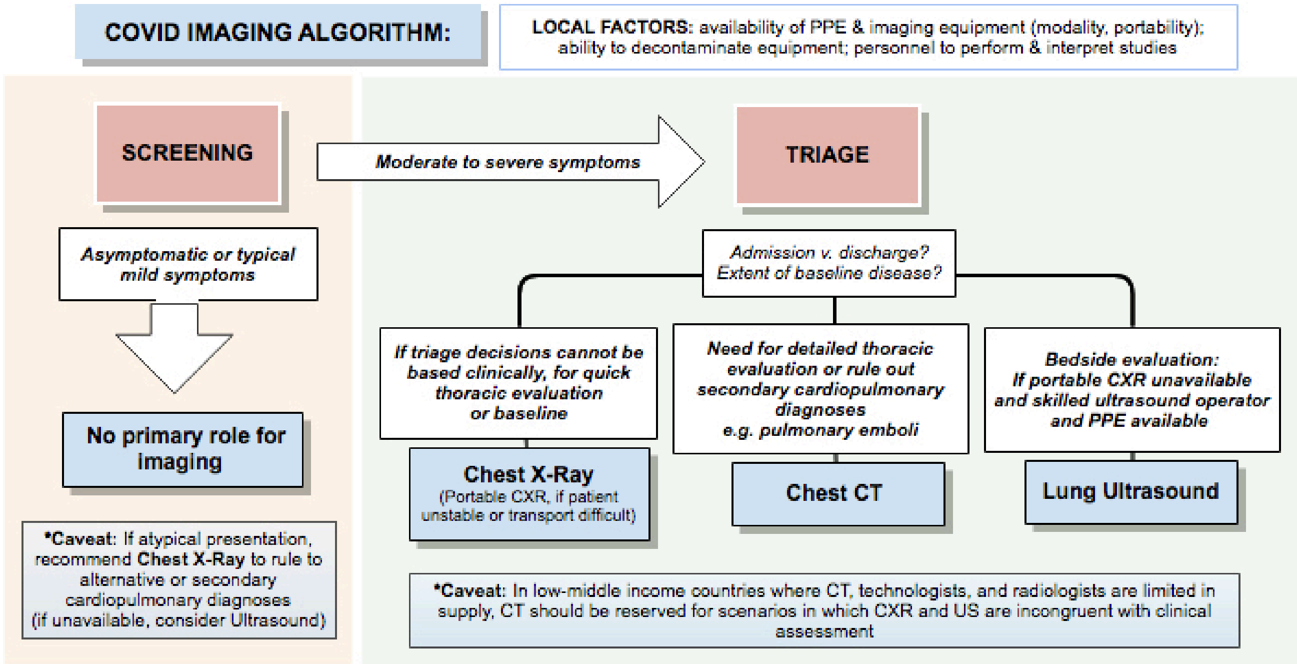

Figure 13. Decision-making in screening and triage.

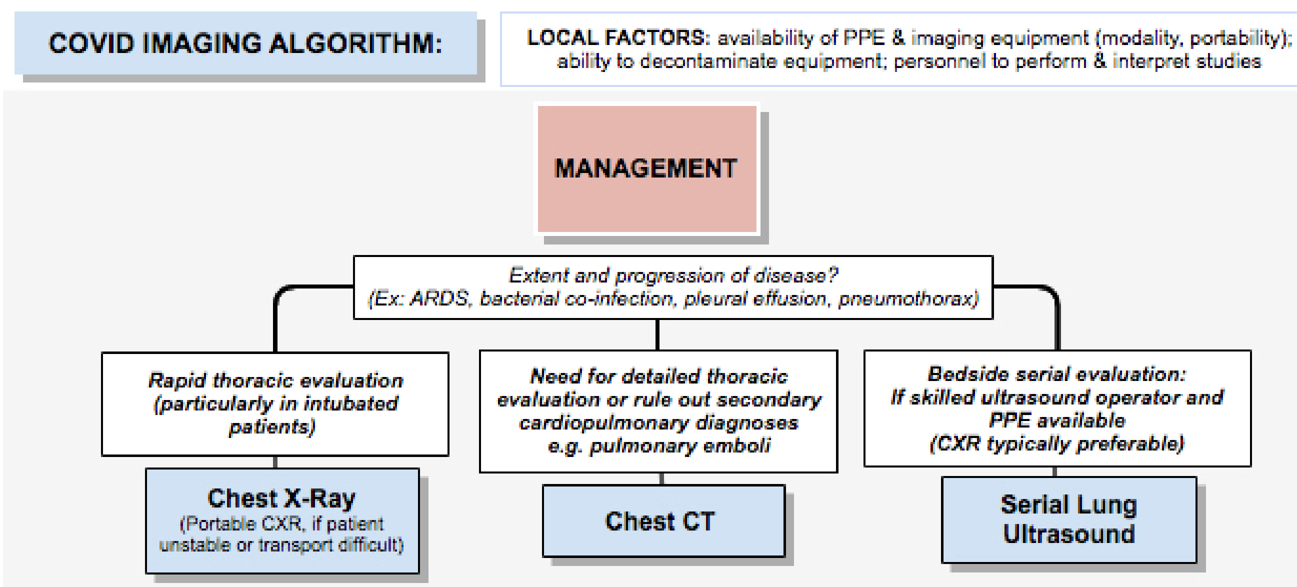

Figure 14. Decision-making in management.

infection, pleural effusion, and pneumothorax. Although serial ultrasound by experienced practitioners is showing promise as a low-cost method to assess disease progression, chest X-ray is preferred for severely ill patients who require assessment of support tubes, such as endotracheal tubes. While the pulmonary physiology of ARDS in COVID-19 may have unique characteristics, the radiological appearance is similar to ARDS from other causes, including SARS (SARS-CoV), with imaging playing a similar role in management.

Limitations

The greatest limitations in writing this article are the novel nature of this virus, the rapid evolution of the pandemic, and the absence of empirical data comparing the effect of different imaging modalities on patient outcome. In determining which modalities might be most effective, we are limited by the absence of recent data in LMIC on access to ultrasound and the relative availability of ultrasound (commonly POCUS) versus CXR, in small and medium-sized healthcare facilities. Also unknown is the capability of local clinicians to perform and interpret chest ultrasound. A survey, published in 2015, identifies lack of training as a primary barrier to regular use of ultrasound in LMICs (36). Despite the availability of online educational materials, this barrier will continue to be formidable for this novel use of ultrasound.

'Resource constrained' is often used in published articles, specifically with reference to LMIC. As we witness Italy, Spain, and New York City suddenly become resource constrained, COVID has taught us that resource constraints are not defined solely by a nation's economics. Most LMIC have pockets of advanced radiology resources which coexist with large segments of the population lacking basic imaging (30). Although data only gradually became public, rates of illness and death are higher in communities of color than in the white population of the United States (37), highlighting that local economic and medical conditions constrain efforts to prevent and mitigate the spread of COVID by social distancing and self-quarantine. In this dystopic, pandemic-enveloped world, segmenting global radiology and constrained resources by country may be arcane. The environmental and medical resource limitations in LMIC clearly have homologues in areas of HIC. Perhaps the focus should be low-income areas (LIA) regardless of the country in which they exist?

Conclusion

In summary, we are living though a pandemic over a century beyond the devastation wrought by The Spanish Flu. We have a great amount of information about how imaging can potentially help diagnose and manage patients with COVID-19 but there is an absence of empirical data about which imaging modalities would be most appropriate in specific clinical situations. Radiologists and clinicians will need to continue making these decisions based on the evolving knowledge of COVID and the published anecdotal data. Those working in LMIC can be reassured that even in the absence of high-tech imaging, such as CT, the two basic imaging modalities of radiography and ultrasound can answer the vast majority of questions raised in the management of COVID-19 patients.

Addendum 1: Terminology

Chest X-ray: (As defined by Fleischner Society; Hansell et al.) (38)

- Ground glass opacities: Hazy increase in lung opacity without obscuration of pulmonary vessels.
- Consolidation: Homogenous increase in pulmonary parenchymal attenuation with obscuration of underlying vessels and airways.

Chest CT: (As defined by Fleischner Society; Hansell et al.) (38)

- Ground-glass opacity: Hazy increased opacity of lung and preservation of bronchial, vascular margins. Refers to partial filling of airspaces, partial collapse of alveoli, and interstitial thickening.
- Consolidation: Homogenous increase in pulmonary parenchymal attenuation that obscures bronchovascular margins. Refers to exudate or other product of disease that replaces alveolar air.
- Crazy-paving pattern: Thickened interlobular septa and intralobular lines superimposed on a background of ground-glass opacity.
- Reverse halo (Atoll sign): Focal rounded area of ground-glass surrounded by a ring of consolidation.

Pulmonary Ultrasound: (Adapted from Lee) (35)

- A lines: Short, repetitive equidistant horizontal lines that fade with increasing depth; an artifact of the pleural line.
- B lines: Strong, narrow vertical artifact comprising of short horizontal lines that do not fade with depth; indicative of thickened pleura and or lung interstitium.

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