Review Article

Evolving Role of Radiology in COVID-19 Pandemic: A Review

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Abstract

Background: This worldwide outbreak has disrupted a steady world of healthcare. Until now, diagnostic radiology and laboratory tests had been reasonably accurate in confirmed disease.

Methods: The review article used data bases, published literature, radiological guidelines issued from societies related to COVID-19 and large number of research journals to find out the latest evidence for the evolving role of radiology in COVID-19 pandemic.

Results: Computed Tomography scanning of the lungs demonstrated ground glass grounded opacities (34%) alone or in combination with consolidations (41%). In the first 5 days following exposure the false-negative rate of the RT-PCR testing is as much as 76 % dropping to 21% on day 8 after exposure and CT findings are non-specific, overlapping with other types of pneumonias. Pulmonary embolism has been reported in 23-30 % of hospitalized patients with COVID-19.

Conclusions: This review attempts to clear the confusion about the application and imaging presentation of COVID-19 infection CT scanning of the lungs. Findings of glass grounded opacities and pulmonary embolism has been reported in patients with COVID-19. The evidence based practices required to deal with severity based clinical scenarios taking into account available resources in the high-, middle- and low-income countries.

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Introduction

In December 2019, China began to report cases of severe acute respiratory disease of unknown etiology clustered in the Hubei Province. A few weeks later, the outbreaks had spread to 18 other countries. The World Health Organization (WHO) announced that a novel coronavirus, SARS-CoV-2 was responsible. The designated Corona Virus Disease of 2019 later became commonly known as COVID-19. As the disease continued to spread, WHO declared a pandemic on March 11, 2020.[1] This worldwide outbreak has disrupted a steady world of healthcare. Until now, diagnostic radiology and laboratory tests had been reasonably accurate in confirming or excluding disease. But for the COVID-19, a highly sensitive test has been unavailable so far. While the test sensitivity and specificity are technically independent of disease prevalence, in practice, the sensitivity and specificity vary with prevalence. Bayesian statistics and pre-and-posttest probability assessments are often implemented to calculate conditional probability.[2] Conditional probability is the chance of an event occurring (sensitivity) in the background of another event (prevalence) that has occurred.

The uncertain prevalence of COVID-19 disease in a

community at any given time has precluded a confident assessment of pre-test probability. This is compounded by the fast changing "facts"regarding the clinical presentation, diagnosis and treatment of this novel Coronavirus infection. Since the beginning of 2020,hundreds of articles and news reports on of COVID-19 have highlighted the changing profile of the disease, making COVID-19 related conditions elusive for prompt and accurate diagnosis, containment and management.[3] Claims made on early papers were later amended as new evidence emerged.[4]

This review attempts to clear the confusion about the application and imaging presentation of COVID-19 infection. A few basic recommendations on infection control and safety will be discussed.

Testing in COVID-19

In the early days of COVID-19 pandemic, radiology articles from China endorsed chest CT as the screening test of choice. Authors reported 98 percent sensitivity for CT chest compared with 71 percent for RT-PCR (Reverse Transcription-Polymerase Chain Reaction).[3,5] Early adoption of CT for diagnosis was also due to ready availability and almost instant turn around of positive results versus hours or days wait for the RT-PCRT that was only available in specialized laboratories. Subsequently, it became clear that more than half the symptomatic patients with COVID-19 had normal lungs on CT scanning and many asymptomatic patients had positive lung findings on studies done for other indications. RT-PCR test is now widely available and may be performed at the point of care with faster turnaround time. Accepted guidelines no longer include CT chest as a modality of COVID-19 initial diagnosis.[6,7,8]

Researchers are aware that the scientific journals have a lead time of at least 8 weeks from submission to publication. Responding to the 2.3-3.3 days doubling time of the number of infected cases early in the pandemic, hundreds of articles have been published online, ahead of print, on a daily basis.[9,10] These have helped the public and the healthcare workers continually adaptto the evolving knowledge. Containment of highly contagious conditions requires a perfect binary test with100 percent sensitivity and specificity as even a single false negative test may result in large outbreaks. COVID-19 has a contagious factor also called " R naught" of up to 3 (range 1.4 - 3.9) and has the potential to infect 59,000individuals through 10 cycles of disease spread. Neither RT-PCR nor CT chest are accurate enough for the control of the pandemic.[10] In the first 5 days following exposure the false-negative rate of the RT-PCR testing is as much as 76 % dropping to 21% on day 8 after exposure and CT findings are non-specific, overlapping with other types of pneumonias.[11]

Role of Radiology in COVID-19

CT Lung Findings

CT scanning of the lungs demonstrate ground glass rounded opacities (GGO) (34%) alone or in combination with consolidations (41%) (Fig 1). By day 10 most, COVID-19 positive cases demonstrate these lung abnormalities. Opacities are predominantly peripheral, with lower lung predominance involving more than one lobe at a time. As the disease progresses, by 2 weeks or later from the onset of symptoms, lungs demonstrate diffuse ground-glass attenuation with superimposed interlobular septal thickening and intralobular lines. This geometric shaped appearance is commonly known, among radiologists and pulmonologists as "Crazy Paving pattern".Clearing starts after about 2 weeks from onset and is gradual[(4)]. Pleural effusions, nodules and cavitation should point to alternative diagnoses.[12,13,14] Mediastinal and hilar lymphadenopathy has been reported from France and China in about one third patients with severe COVID-19 pneumonia.[15,16] As the disease progresses, the GGO become confluent consolidations and exhibit reticular pattern or are verse (Atoll) sign. Following clinical recovery, a majority of patients discharged from the hospital will continue to show residual lung opacities on CT [(4, 17,18)]. The lungs may also show CT appearance of fibrosis. But in these cases, pulmonary fibrosis has neither been confirmed by long term follow up nor on histopathology.

Pulmonary Embolism (PE) and Chest CT:

PE has been reported in 23-30 % of hospitalized patients with COVID-19 (Fig 2). Obesity is a risk factor, patients with BMI > 30 kg/m^2 are 2.7 times more susceptible to PE. Contrary to the usual occurrence, the incidence of PE was higher with 52/72 patients (72 %) who did not require ICU care or intubation for acute pulmonary embolism in the

settings of COVID-19.[19] The pathogenesis of PE is not known. It has been hypothesized that COVID-19 elicitsan inflammatory thromboembolic state that results in intravascular coagulation, particularly in immobilized patients.[19]

Figure 1: *CT Chest of a Confirmed Case of COVID-19. Lungs Demonstrate Peripheral Ground Glass Opacities (GGO). Involvement was Multi-lobar.*

Some of the other uncommon presentations of COVID-19 infection in adults include deep venous thrombosis, ischemic strokes, leuko encephalopathy, myocardial infarction, and bowel ischemia. In children, it has also presented as a Kawasaki type syndromeas well as other multisystem diseases.[20-23]

COVID-19 versus Influenza (H1N1) Pneumoniaon Chest CT: Authors have reported many common imaging findings regarding the two viral infections on chest CT. For example, a report comparing CT findings in 30 patients with COVID-19 pneumonia compared to30 cases of influenza (H1N1) pneumonia showed many overlapping findings, including GGO, peripheral distribution, confluent pneumonia and vascular enlargement. Nevertheless, COVID-19 infection showed more lobar involvement, linear opacities and crazy paving. Influenza (H1N1) pneumonia showed statistically significant differences, including positive pertinent findings of bronchiectasis, pleural effusion and pericardial effusion compared with COVID-19.[24]

CT Chest as a Diagnostic Tool

CT chest is not a tool of initial diagnosis in suspected COVID-19. But during the current pandemic,GGO's atlung bases on CT studies, performed for other indications, may point to undiagnosed COVID-19 infection. Further, CT chest is used to support the diagnosis in suspected cases, determine severity, guide treatment, manage complications and assess treatment response.

Plain Chest Radiography

Chest radiography has low sensitivity for the diagnosis of COVID-19 infection at 25-69 %[(4)]. This variation is due to the severity of disease at the time of chest radiography. In a study of 636 urgent care patients with COVID-19, 58 % of chest radiographs were normal. Of the abnormal cases, 74% showed mild diseaseas faint GGO, in 25 % moderate disease showed areas of interstitial lung markings with GGO's. Only 5 (2 %) patients had severe abnormalities, where patches of confluent pneumonia were observed. Disease distribution was similar to CT findings, namely lower lobe predominance and multi-lobar involvement. Overall, 89 % of all patients either had a normal or mildly abnormal chest radiograph.[25] In another report of 388 patients, authors divided each lung into 3 horizontal zones, upper, middle and lower for a total of 6 zones for both lungs. Results revealed that disease in 2 zones required hospitalization while involvement of 3 or more zones was independent predictor of patients requiring intubation.[26]

The real value of chest radiography lies in treatment planning, detecting complications, and assessing progress in radiographically positive cases.

Chest CT is more sensitive than CXR on COVID-19 diagnosis. But immediately following image acquisition of infected individuals, the CT scanning room requires thorough disinfection. This restricts patients' through put. Therefore, use of CT scanning for COVID-19 patients is not advisable if a facility has just one scanner. Fixed and portable chest radiography, on the other hand, are widely available in most facilities, and allow for rapid cleaning and room turn over between patient.

Ultrasound

Point of care ultrasound (US) in the diagnosis and screening of patients with acute dyspnea has been reported with encouraging results.[27] A recent study from Turkey has shown utility of thoracic US in the management of pregnant patients with COVID-19 infection.[28] Despite the known advantages of this

modality, including it's ready availability, relatively low cost, and lack of ionizing radiation exposure, the risk of spread with COVID 19 due to patient proximity during examination and need to disinfect the equipment, render it less practical for regular use in this setting. In addition, expertise in thoracic ultrasound is not widely available. Furthermore, the Fleischner society consensus statement below does not include US as a preferred modality for the diagnosis of COVID-19 in patients. Further, as pleural effusion is not a typical feature of COVID-19 infection, ultrasound guided thoracentesis is unlikely to be clinically useful.

Interventional Procedures in COVID-19 Era:

Interventional procedures increase the risk of spread of infection. As far as possible, elective cases should be postponed. For urgent cases, the following are some helpful measures to consider: test availability for COVID-19, personal protective equipment (PPE), minimizing the number of staff in patient's proximity, proper disposal of consumables and thorough disinfection of the room.[27] Going forward, such measures are likely become routine.

Consensus on Imaging Modalities

Fleischner society, a leading multidisciplinary professional body of thoracic imaging, issued a consensus statement in conjunction with experts from Western and Far Eastern countries, on the role of chest imaging in patients management during COVID-19 pandemic. Importantly, the statement deals with severity based clinical scenarios taking into account available resources in the high-, middle- and low-income countries.[26] Several work-up pathways have been summarized in this document. Figure 4 depicts the limited resource scenario relevant to Pakistan. This figure provides a general guideline. Every society should develop their own in consensus with recommendations from professional societies and healthcare leaders. Radiological society of Pakistan has endorsed the statement displaying the key elements on its website www.radiologypakistan.org. pk.

Patient Triage and Disease Management

There are no standard recommendations for patient triage. Triage guidelines must be developed based on the available resources, facility, equipment and staff skills. This should include telemedicine services to minimize the number of patients physically coming to the hospital when possible. Based on the current data only 3-17 per 100,000 of confirmed cases of COVID-19 patients require hospitalization.[28] Imaging is not required for patients treated at home for COVID-19. Patients are admitted to hospital based on clinical assessment. Imaging may offer clinicians additional data for treatment planning and outcome forecasting. Radiography covers the whole lungs and can be performed without patient proximity. It is also suited for follow up exams. Even though 30 % of chest radiographs are normal at the time of admission, a base line study may be useful to evaluate the evolution of the disease.[4] In patients with COVID-19 pneumonia, plain chest film findings may predict the need for hospital and ICU admission.[26] In resource constraint environments, routine CT scanning of the chest is not feasible. CT may be reserved for patients with suspected pulmonary embolus, who have extrathoracic manifestations of COVID-19 or who require interventional procedures. Ultrasound is inexpensive, offers portability. US can be a useful adjunct to radiography and CT. US scanning should only be performed in full PPE by staff comfortable with thoracic scanning.

Best Practices: Infection Control and Safety

Much has been written about practical measures to minimize risk of infection spread. Staff and patients' protection from COVID-19 should be based on update recommendations. Going forward two critical factors important in containing the spread of infection: that persons in pre-clinical state and with a false negative COVID-19 RT-PCR test continue to be in an infectious state and that COVID-19 infection will most likely to linger on even after control of the current pandemic.

As the hospitals and departments of Radiology begin to receive more patients, the SOP's (standard operating procedures) of the "lockdown" period will require revision to accommodate a larger patient volume. Each department needs to form a committee to continually amend and implement infection control and safety guidelines for sanitizing equipment and staff and patient protection. Details of best practices for infection control can be adopted from the published guidelines issued by government

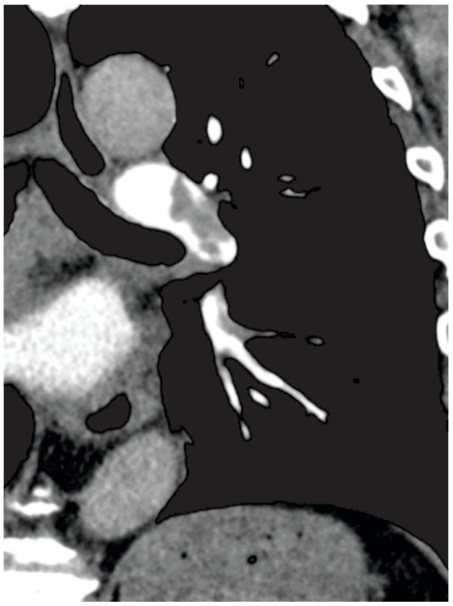

Figure 2: *CT Pulmonary Angiogram of a Confirmed Case of COVID-19 showing Pulmonary Artery Filling Defects of Emboli.*

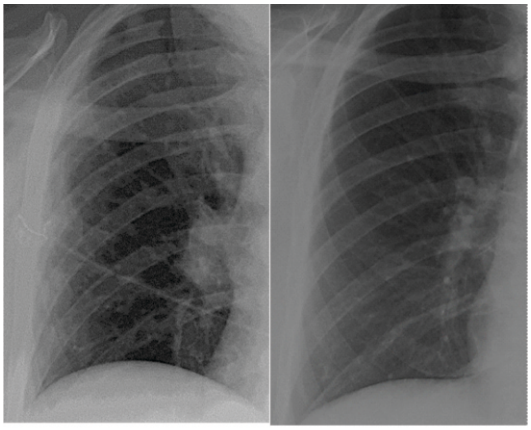

Figure 3: *Right Lung on Chest Radiographs.*

Image A: COVID-19 ground glass opacities in the periphery of mid and lower lung zones on the left image.

Image B: Compared with clear lungs with in the same patient of an earlier radiograph.

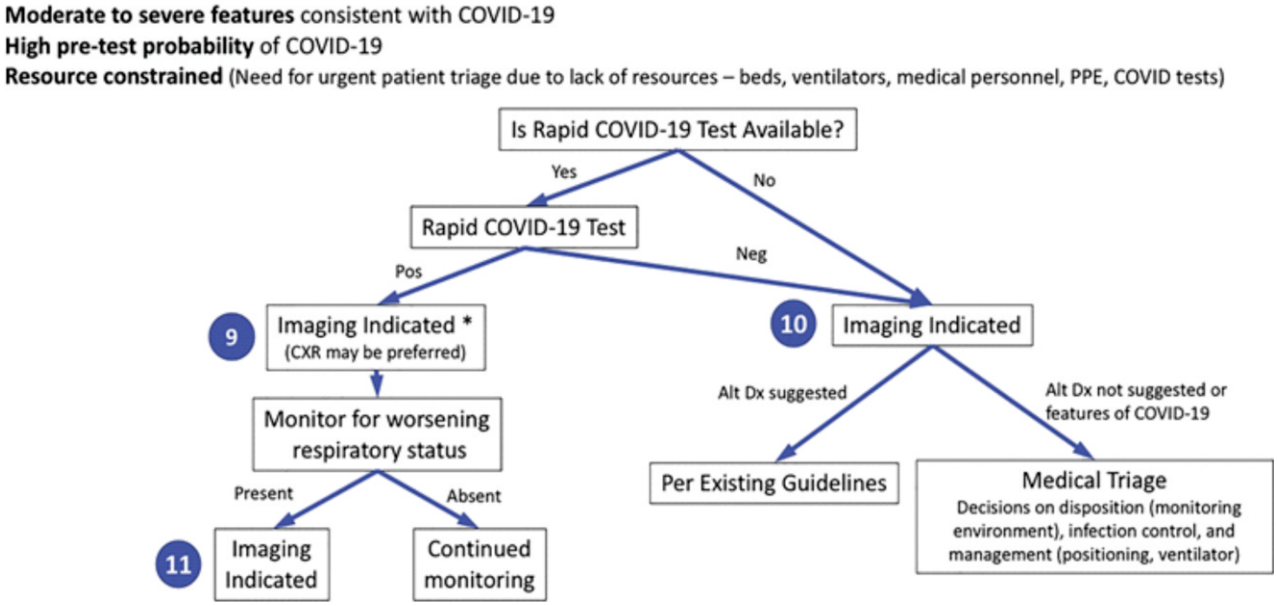

Figure 4: *Diagram illustrates the clinical scenarios for resource constraint environment relevant to Pakistan. Moderate-to-severe features refer to evidence of significant pulmonary dysfunction or damage. High pretest probability is based on high background prevalence of disease associated with community transmission. Rapid coronavirus disease 2019 (COVID-19) test is a point-of-care test with a turnaround time of less than 1 hour. Numbers in blue circles indicate the following questions:*

9 = In a resource constrained environment, is imaging indicated in a patient who presents with moderate-severe features and positive COVID-19 test?

10 = in the resource-constrained environment without a PoC COVID-19 test available, is imaging indicated in the medical triage of patients who presented to the emergency room with moderate-severe features consistent with COVID-19?

11 = in the resource-constrained environment, is imaging indicated in hospitalized patients with positive-19 test who subsequently has clinical worsening?

Contextual detail and considerations for imaging with chest radiography (CXR) versus CT are presented in the text. ⋆ = Lower priority if severely resource constrained, relative to question 10 or 11. Alt Dx = alternate diagnosis; Neg = negative; Pos = positive; PPE = personal protection equipment.

agencies, professional organizations and local institutions. Copy pasting SOP's is strongly discouraged as ownership is key to implementation. Seven critical factorsfor achieving compliance with infection control and safety SOP's (Table I)

Hand Hygiene

Frequent hand washing with soap and water is the hall mark of infection control and is a pivotal measure in Pandemic control. All staff must wash hands several times a day using the correct technique as below. Correct hand washing is well known, but it is important enough to be reproduced here (table II), and must be displayed over every hand washing facility.[27]

Hand sanitizer can be produced very inexpensively using the following ingredients: Active ingredients: Ethanol 80% volume/volume (v/v) in aqueous solution OR Isopropyl Alcohol 75% v/v in aqueous solution. Inactive ingredients: Glycerol 1.45% v/v, Hydrogen peroxide 0.125% v/v, distilled or boiled water.[28]

Table 1: *Seven Critical Factors for Achieving Compliance with Infection Control and Safety*

1.	Need based provision of protective material and sanitizing chemicals.
2.	Members of the implementing teams must participate in the developing SOP's.
3.	Policies must be in synch with local socio -economic imperatives.
4.	SOP's must be published in local language(s) and prominently displayed.
5.	Education, training and implementation.
6.	Every policy must have a verification and audit component.
7.	Compliance audit report must be shared with the staff.

Table 2: *The Correct Technique for Hand Washing*

1	Wet your hands with clean, running water (warm or cold), turn off the tap, and apply soap.
2	Lather your hands by rubbing them together with the soap. Lather the backs of your hands, between your fingers, and under your nails.
3	Scrub your hands for at least 20 seconds by watch. Need a timer? Hum the "Happy Birthday" song from beginning to end twice.
4	Rinse your hands well under clean, running water.
5	Turn off water with foot pedal or using a towel.
6	Dry your hands using a clean towel or air-dry them.

Conclusion

Insummery COVID-19 is a highly contagious infection with a mortality rate of 0.5 – 1.0 %as compared with around 0.03% for H1N1 influenza (34). The body of knowledge about COVID-19 is fast evolving. The healthcare interventions and response of the public, at large, are lagging behind the disease spread, in terms of prevention and treatment. The role of medical imaging in the initial diagnosis has rapidly evolved since the declaration of the pandemic by WHO. WHO, professional societies and government agencies have published patient data, consensus statements and protocols for safe operation during the pandemic. These can be confusing even conflicting, and out of synch with ground realities in many LMIC's. Therefore, institutions and departments should only consider them as guidelines. From these, SOP's for local use must be developed. How patients are handled and care is delivered, will depend upon the lay out of the facility, availability of equipment and, consumables, and the skills of the staff. These factors can vary greatly from one country to another and between the urban and rural communities in the same country. As the lockdown eases, the SOP's must be revisited on a periodic basis to accommodate changing healthcare needs and realize opportunities. It is important to note that plain radiography alone can be enough to answer a large majority of questions encountered in the management of COVID-19 or any other similar severe viral respiratory disease.

Limitations

There are many limitations to this review, the greatest of which is about the data quoted here. Literature search will reveal many facts and figures at variance from what is described above. The data on risk stratification and outcome estimation are based on a relatively short experience in scientific terms. Multiple on-line articles, ahead of publication, have reported data that is yet to be fully validated. Data are still coming in and will be analyzed. Once it is all complete, it is possible that total picture of the Corona virus disease 2019, will emerge with a new profile.

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