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Role of Imaging in the COVID-19 Pandemic

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Abstract

In the last 2 years, we have seen the most unprecedented times of our lives. The pandemic appears to be petering off and hopefully will become endemic. These 2 years have been a significant learning experience with many new imaging techniques, medical and social concepts introduced. Also, along the pandemic course, numerous articles and editorials were penned on new learnings, as well as new thoughts on controlling and mitigating the suffering of those afflicted. From a collection of editorials and articles in *The Indian Journal of Radiology and Imaging* (IJRI) on the pandemic, this review is constructed to put imaging-related facts in a perspective.[1–11] Even though the pandemic may have petered off, this will serve as a memory, as well as repository of information for future pandemics.

Keywords

- COVID-19 pandemic
- radiology
- imaging
- HRCT

Introduction

In December 2019, an outbreak of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection occurred in Wuhan, Hubei province China. On February 12, 2020, the World Health Organization (WHO) named the disease as novel coronavirus disease 2019 (COVID-19). With international air travel, the disease spread across the globe infecting nearly every country on the planet. On March 12, WHO notified COVID-19 as a pandemic in view of its global spread.

SARS-CoV-2 is a single-stranded RNA virus which results in a lower respiratory tract pneumonia termed as COVID-19 pneumonia. The clinical symptoms of the disease are non-specific presenting with influenza-like illness (ILI) with fever >38°C, cough associated with malaise, generalized myalgia, headache, and breathlessness.

Corona viruses are characterized by spike proteins which are optimized to engage human angiotensin-converting enzyme-2 (ACE-2) receptors. Gaining entry into the cell via proteolytic action and membrane fusion. ACE-2 receptors are in abundance in type -2 alveolar epithelial cells, gastrointestinal tract (GI) tract, heart, endothelium, and kidney. The lungs are the most vulnerable because of their large surface area, as well as type-2 alveolar cells act as a reservoir for viral replication. After gaining entry into the cell, viral genome replication occurs triggering apoptosis, release of proinflammatory cytokines, and exudation into alveolar space with associated diffuse alveolar damage[11–13]

High-Resolution Computed Tomography Appearances

The COVID-19 pneumonia causes diffused alveolar damage. This passes through three stages, an initial exudative phase where there is minimal exudation of fluid into the alveoli. As a result, imaging appearances will be negative or subtle abnormalities of ground glass will be seen.[1,2,5,14–18]

Subsequently, with increased exudation into the alveoli, it passes into the next stage, an inflammatory stage. Depending on the extent of alveolar exudation, the appearances on imaging are ground glass densities, consolidation, or a combination of these[6,18–20] (►**Fig. 1–4**).

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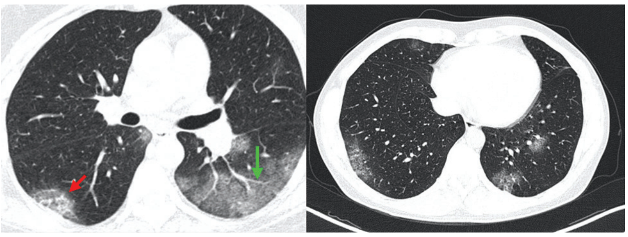

Fig. 1 HRCT chest demonstrates bilateral subpleural ground glass opacities typical of viral pneumonia. HRCT, high-resolution computed tomography.

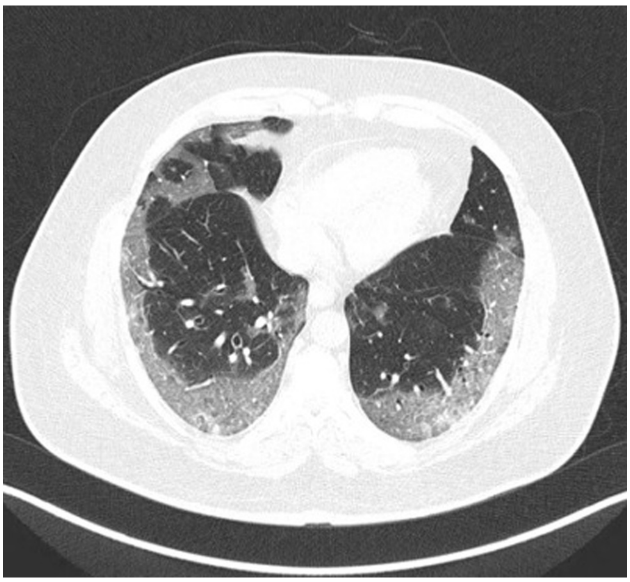

Fig. 2 HRCT chest of COVID-19 pneumonia patient with positive RT-PCR showing bilateral subpleural ground glass densities. Patient went on to require a maximum of 10 L of oxygen during his hospital admission and was discharged subsequently. COVID-19, novel coronavirus disease 2019; HRCT, high-resolution computed tomography; RT-PCR, reverse-transcription polymerase chain reaction.

The distribution maybe anterior, posterior, upper lobe, lower lobe, or multilobar.[21] The most common appearance is ground glass densities in a subpleural posterior basal distribution.

As the infectious process and body mount varying responses, different features of progression and regression may be visualized, resulting in a variety of internal appearances on imaging. The internal contents may be visualized, such as central clearing of ground glass, known as Atoll's sign.[2,22,23]

Progression of inflammation along the periphery of consolidation is seen as ground glass on the periphery of consolidation, the Halo sign[17] (►**Figs. 5** and **6**). Presence of ACE-2 receptors in endothelium result in inflammation of the vessels that appear prominent in the affected areas[11] (►**Fig. 7**). There may be intravascular thrombosis with resultant hemorrhagic infarction. There may be interlobular septal thickening due to prominence off lymphatics superimposed on ground glass densities, appearing as a crazy paving appearance[14,24,25] (►**Figs. 8** and **9**).

In a small percentage, the alveolar cell damage progresses to acute respiratory distress syndrome resulting in a white out appearance to the lungs.[12]

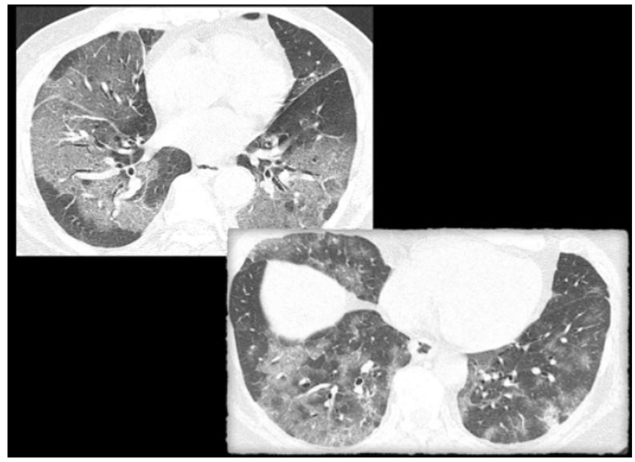

Fig. 3 HRCT demonstrates diffuse ground glass densities in both lung fields with a few areas of denser consolidation in the left base due to COVID 19 Pneumonia. COVID-19, novel coronavirus disease 2019; HRCT, high-resolution computed tomography.

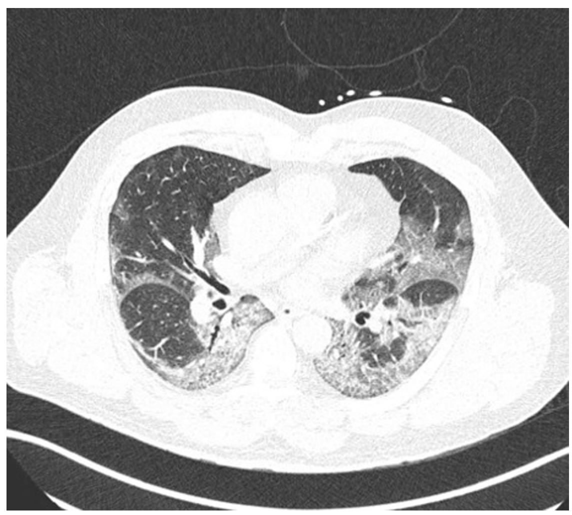

Fig. 4 HRCT chest revealing diffuse peribronchovascular and subpleural ground glass densities with few pleural bands. HRCT, high-resolution computed tomography.

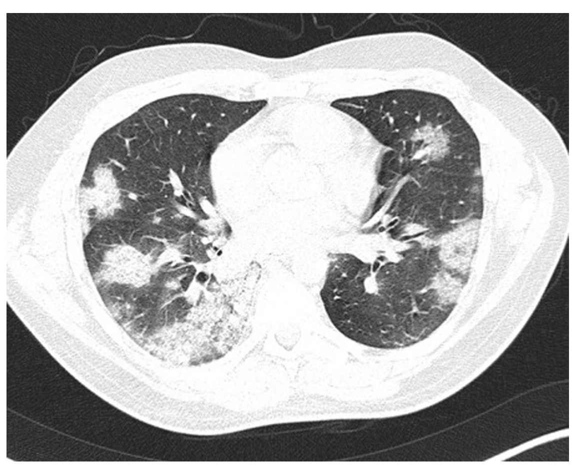

Fig. 5 HRCT chest images reveal central ground glass opacity surrounded by a ring of denser consolidation defined as the "Atoll/Reverse Halo" sign. HRCT, high-resolution computed tomography.

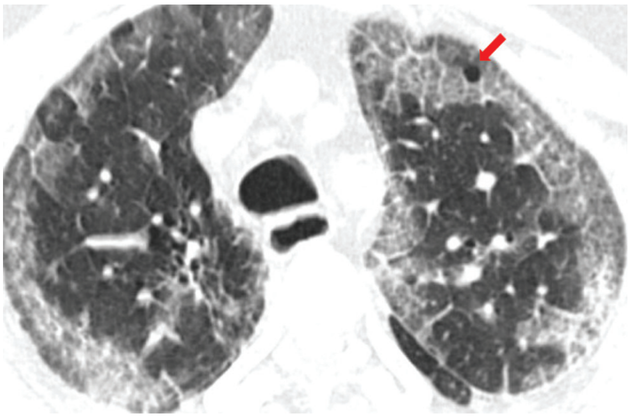

Fig. 6 "Air Bubble Sign" (vacuolar sign) small air-containing space <5 mm in length within the lung lesion.

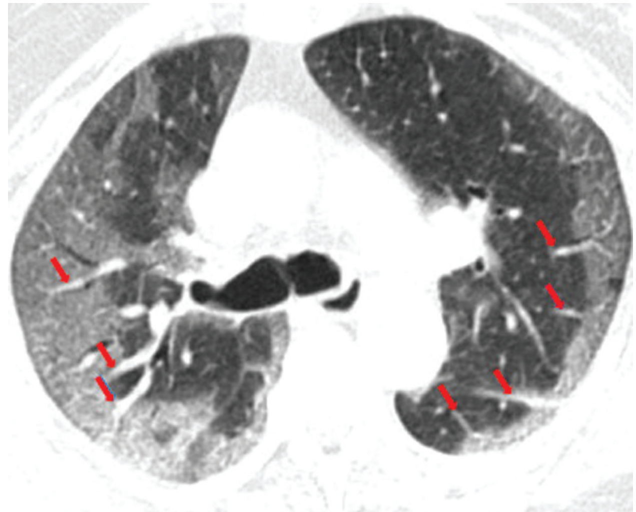

Fig. 7 HRCT chest reveals prominent vessels in the region of ground glass opacities described as the "Vessel Enlargement sign." HRCT, high-resolution computed tomography.

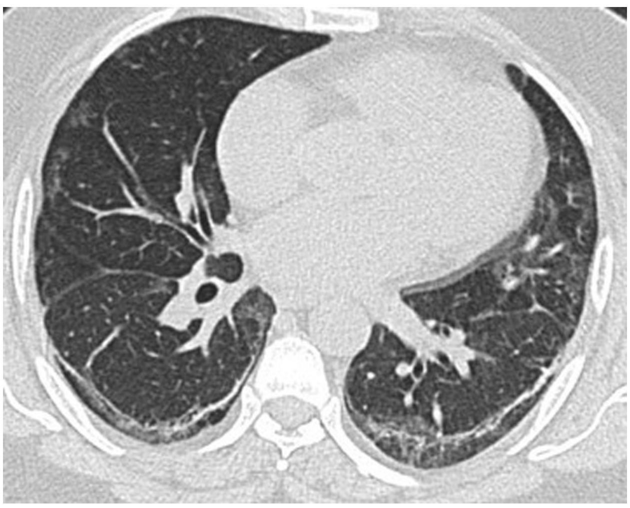

Fig. 8 HRCT chest reveals subpleural curvilinear opacities "Subpleural Parenchymal Bands" involving both lung fields usually seen extending to pleura. HRCT, high-resolution computed tomography.

Fig. 9 HRCT chest reveals areas of interlobular and intralobular septal thickening in background of ground glass opacities described as the "Crazy Pavement pattern." HRCT, high-resolution computed tomography.

In most cases, the diffuse alveolar damage passes into a final reparative phase where there is proliferation of epithelial cells and fibroblasts with collagen deposition. On imaging, the appearances in this stage are off an organizing pneumonia.[6,26] The brunt of the disease process of COVID-19 is in the interstitium, therefore location of lesions is in the peripheral subpleural and peribronchovascular regions.[24]

Subsequently the organizing pneumonia clears, resulting in well-aerated lung parenchyma or reticular opacities. The reticular opacities in the interstitium (peribronchovascular and hilar) from resolution of organizing pneumonia may resemble fibrosis seen in ILD. A common appearance is a thin subpleural curvilinear line.[6,16]

Often with time, sometimes 4 to 6 months, these tend to totally clear up, even the subpleural curvilinear lines have been seen to clear up. Only in very few cases, persistent reticular abnormalities have been seen. When these persist long term, possibly a year or more, they may be termed as COVID-19-related ILD (►**Figs. 10–18**).

The main consideration is whether these reticular opacities should be reported as fibrosis. This is important as fibrosis is irreversible. Time will tell whether these are also really fibrosis or slow resolving, organizing pneumonia, since these may clear with time. To call this fibrosis before a year of follow-up may be a little premature.[6]

Previous coronavirus epidemics, SARS (2002), Middle East respiratory syndrome (MERS; 2012), and Influenza A subtype (H1N1) 2009, have demonstrated relatively similar and characteristic imaging findings.[5]

The Novel Coronavirus Disease 2019 Reporting and Data System

The COVID-19 computed tomography (CT) features may partially overlap with those of other diseases, mainly viral

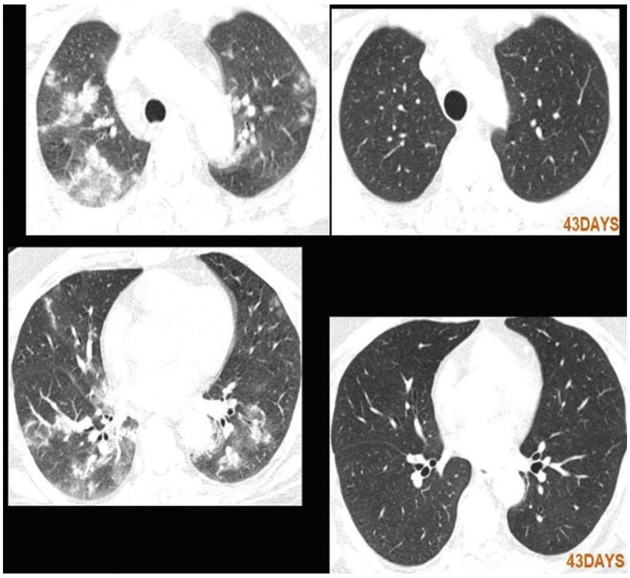

Fig. 10 Follow-up HRCT shows complete resolution of ground glass opacities. HRCT, high-resolution computed tomography.

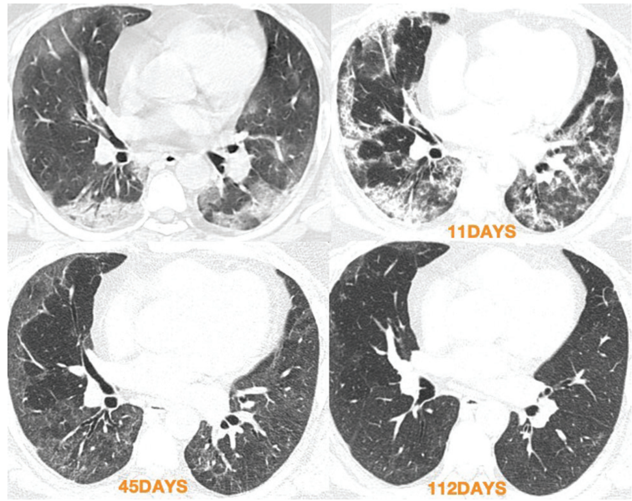

Fig. 11 Follow-up HRCT reveals initial progression of subpleural ground glass opacities on initial HRCT , to areas of patchy consolidation on day 11 to resolution with complete regression on day 112. HRCT, high-resolution computed tomography.

Fig. 12 Follow-up HRCT showing initial progression of patchy subpleural ground glass opacities to patchy areas of consolidation and subsequent resolution. HRCT, high-resolution computed tomography.

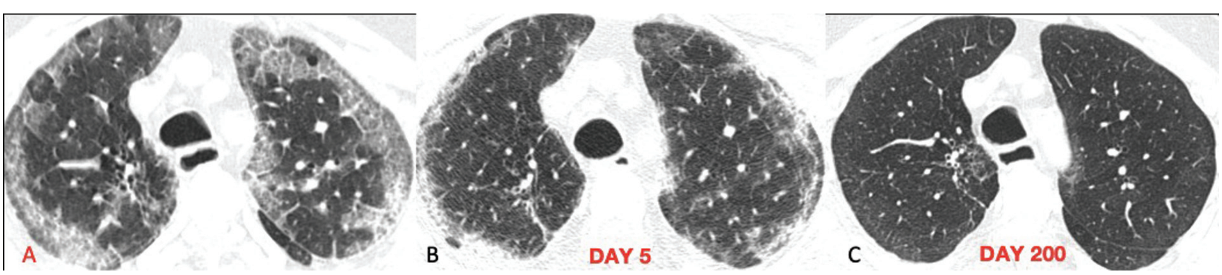

Fig. 13 Follow-up HRCT showing initial progression of subpleural ground glass opacities to consolidation and subsequent near complete resolution with formation of few subpleural bands. HRCT, high-resolution computed tomography.

infections, but also has characteristic features that may also be frequently seen in other settings. In view of the sheer volume of cases, a standardized communication format was devised to assess the suspicion of pulmonary involvement on CT known as COVID-19 Reporting and Data System (CORADS).[27]

The Novel Coronavirus Disease 2019 Reporting and Data System-1

Very Low Level of Suspicion

Normal CT or noninfectious findings on pulmonary CT such as emphysema, interstitial fibrosis, neoplasm were conducted.

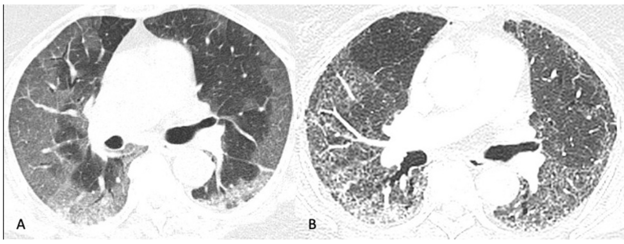

Fig. 14 (**A**) Follow-up HRCT showing subpleural ground glass opacities with areas of septal thickening, few vacuoles. (**B**) Progression to subpleural consolidation. (**C**) Followed by complete regression except for an atelectatic band in the right upper lobe. HRCT, high-resolution computed tomography.

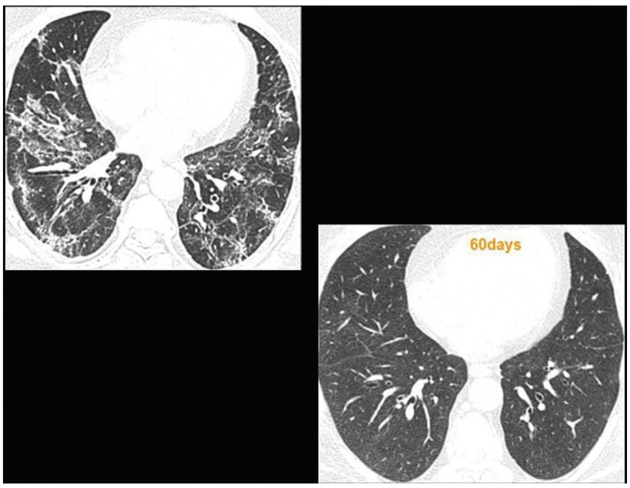

Fig. 16 Follow-up HRCT showing initial progression to diffuse patchy subpleural and peribronchovascular consolidation with complete resolution on day 98. HRCT, high-resolution computed tomography.

The Novel Coronavirus Disease 2019 Reporting and Data System- 2

Low level of suspicion for pulmonary involvement, infectious but not compatible with COVID-19 such as -infectious bronchiolitis, bronchopneumonia, lobar pneumonia, smooth interlobular septal thickening, pleural effusion.

The Novel Coronavirus Disease 2019 Reporting and Data System- 3

Presence of perihilar ground-glass densities and septal thickening is suggestive of pulmonary edema and consolidation is compatible with organizing pneumonia.

The Novel Coronavirus Disease 2019 Reporting and Data System- 4

High level of suspicion: CT findings are typical but show some overlap with other viral pneumonias.

The Novel Coronavirus Disease 2019 Reporting and Data System- 5

Very high level of suspicion: typical CT findings such as peripleural/subpleural ground-glass opacities.

Two variants of CORADS are also added as listed below:

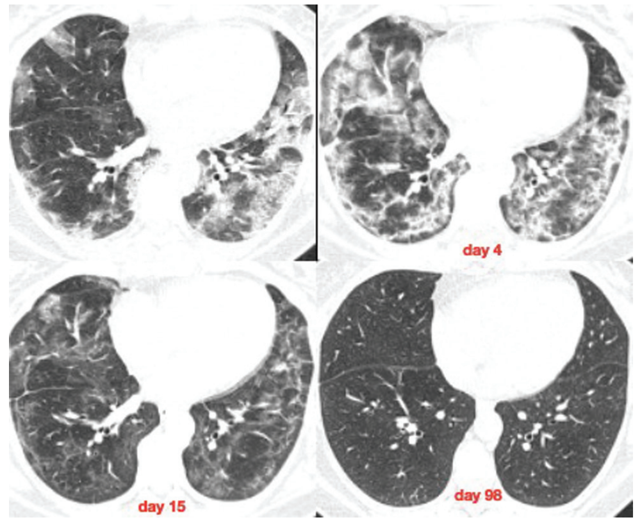

Fig. 15 (**A**) HRCT chest showing bilateral subpleural ground glass densities. (**B**) Follow-up HRCT reveals progressive diffuse fibrosis. HRCT, high-resolution computed tomography.

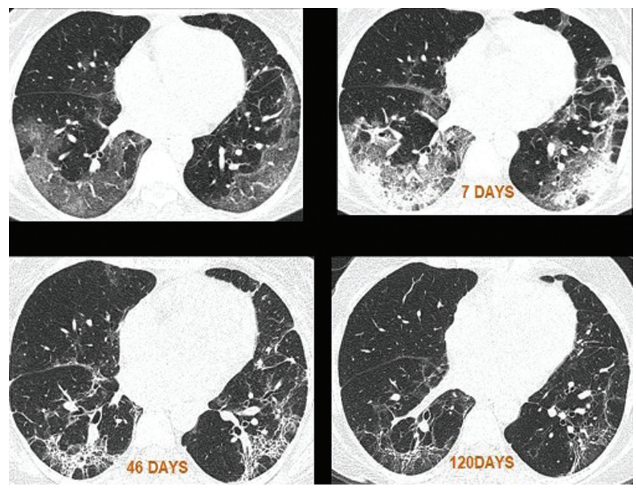

Fig. 17 RT-PCR proven COVID-19 pneumonia, after 6 days of fever onset shows GGO, consolidations associated with parenchymal bands and interlobular septal thickening on initial CT. Follow-up study after 60 days shows complete resolution of the disease process. There are subtle areas of mosaic attenuation on follow-up study. COVID-19, novel coronavirus disease 2019; CT, computed tomography; RT-PCR, reverse-transcription polymerase chain reaction.

- CORADS 0: when scan is not readable due to breathing artifacts.
- CORADS 6: reverse-transcription polymerase chain reaction (RT-PCR) positive, and, irrespective of high-resolution computed tomography (HRCT) findings, the scan is positive.

Role of High-Resolution Computed Tomography as a Public Health Tool to Assist in Containment of Infection

The COVID-19 is a highly infectious disease caused by a single-stranded RNA corona virus, that is, SARS-CoV-2.[28]

The main routes of spread are human to human via droplets, as well as surface contamination. The key to control

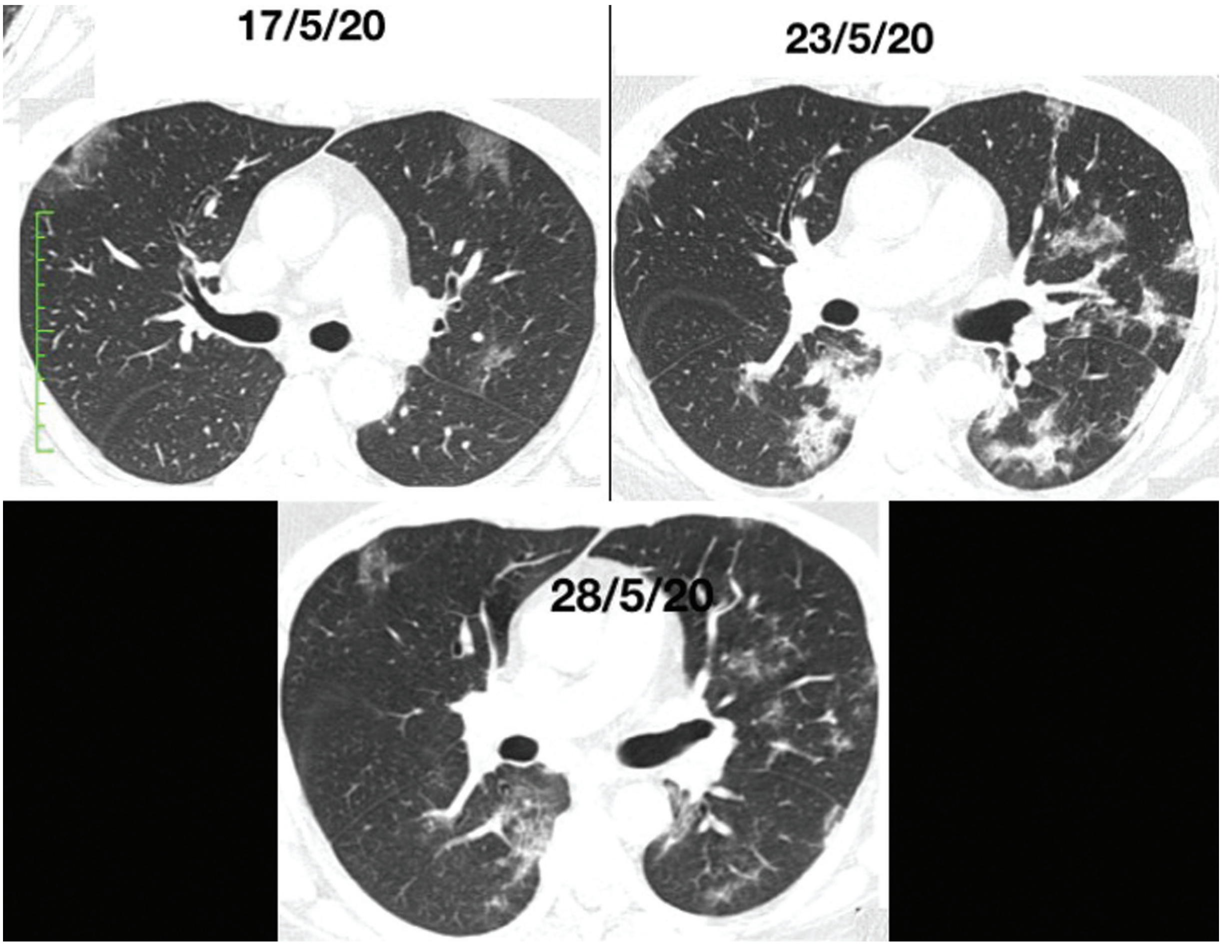

Fig. 18 Initial CT shows pure GGO lesions diffusely involving both lung fields. Follow-up study after 1 week shows focal superimposed consolidation. Follow-up study after 46 days shows resolving GGO with interlobular thickening. CT, computed tomography.

of COVID-19 is to break the human-to-human contact chain. To achieve this, early detection and prompt isolation is imperative. RT-PCR is the current gold standard to detect SARS-CoV-2; however, the false-negative rate ranges from 30 to 40%.[2,11,12]

There are numerous reasons for this high false-negative rate, these are related to sampling, transportation, and processing errors. RT-PCR may also be negative if the viral load is low, a second/third or fourth RT-PCR may be required to demonstrate positivity.[2,14,29]

Sensitivity of RT-PCR is maximum between days 5 and 7, lower before day 5, and peters off after day 7 of contracting the infection.[19,30]

Though in the third wave, as the infectiousness of the virus increased, the sensitivity of RT-PCR increased, as well as positivity was seen on day 2 or 3. In addition to false-negative rate of RT-PCR, in resource-constrained regions, RT-PCR may not be freely available or available with a significant turnaround time spanning from 24 to 48 hours. The accuracy may be improved in certain centers with better training and facilities; however, COVID-19 being a global pandemic, it is difficult to ensure uniform quality. Thus, the main concerns are the high false-negative rate, lack of freely available RT-PCR in resource-constrained environments, and long turnaround times. Undetected individuals are infectious and, unless isolated, will be mediums for transmission of SARS-CoV-2, thus perpetuating the pandemic.[31–33]

Symptomatology is also not a criterion. Numerous studies have documented asymptomatic individuals, as well as symptomatic patients in the presymptomatic phase are known to transmit the infection.[34]

CT screening of asymptomatic RT-PCR-positive individuals on the diamond princess cruise ship showed findings of pneumonia in 54%.[35] Numerous other studies have also supported this finding of asymptomatic with positive CT features.[36] In view of these limitations of RT-PCR, there is a need to increase the accuracy of RT-PCR or supplement with another diagnostic technique to reduce the false-negative rate, thus increasing the accuracy of detection of SARS-CoV-2.

HRCT is very sensitive in demonstrating alveolar pathology. HRCT appearances may appear at the onset of disease, occasionally, before the real-time RT-PCR is positive or 3 to 5 days after symptomatology onset. In fact, a large study that conducted early in the pandemic demonstrated HRCT to be positive in 88% of cases, compared with RT-PCR which was positive in 59% of cases,[11] indicating the specificity of CT features for COVID-19 during the pandemic, as well as the positivity of CT in the setting of negative RT-PCR.[37] This is not surprising as RT-PCR and CT scan evaluate different aspects of COVID-19.

In view of this significant high predictive value of HRCT and relative false-negative rate of RT-PCR, it had been aggressively suggested to utilize HRCT in surveillance for COVID-19. Considering the only means to control the pandemic was by identifying positive cases, isolating them, and quarantining their contacts during incubation and infectious phases, the recommendation to use HRCT for surveillance may not be aggressive at all. In fact, it may have turned the tide in the pandemic.

A Head-to-Head Comparison between High-Resolution Computed Tomography and Reverse-Transcription Polymerase Chain Reaction

HRCT is easily available in India and across the world. There are more than 3,000 CT scanners in India. Nearly every district has one or multiple CT scanners. Time taken to obtain nasal swab and HRCT is relatively similar as just a breath hold scan required. Turnaround time of result HRCT is instantaneous; RT-PCR is 6 hours. HRCT also has additional advantages, as it helps assess the extent of pulmonary involvement and disease severity, thus helping to guide clinical management.

Then why is CT not used to reduce the false negative rate in helping curb the spread of SARS-CoV-2.

Numerous guidelines including American College of Radiology (ACR) advised against utilization of HRCT as a first-line tool with a logic that RT-PCR testing is the definitive diagnosis and will be required to establish the diagnosis.[38]

Other reasons cited for not advocating CT were as follows:[39–41]

(1) low specificity of CT; (2) advocacy of CT may overwhelm existing resources, as well as may reduce access of non-COVID patients to imaging suites; (3) CT may act as a potential disease transmitter via surface contamination, especially exposure to imaging department staff; and (4) utilization of ionizing radiation.

Most of these guidelines were constituted in the early part of the pandemic, in fact coinciding with WHO declaration of a pandemic. The pandemic has been raging for more than 2 years. As we reflect, all these points of concern can be addressed hopefully with a fresh view for the future.

The specificity of CT has been questioned, especially in its ability to differentiate from other viral pneumonias and other chronic lung diseases, such as small airway disease, chronic eosinophilic pneumonia, and hypersensitivity pneumonitis. There are numerous publications which have helped differentiate between these different pathological processes.[42,43]

SARS, H1N1, and COVID-19 have similar specific appearances of multifocal areas of ground glass density in a subpleural location with lower lobe preponderance. Differentiation between these is difficult as the appearances overlap.[44–50]

However, in a pandemic due to the sheer propensity of several cases, these typical, as well as atypical, patterns point toward COVID-19, other diseases recede into the background due to sheer numbers. Sensitivity is the key, not specificity.[41]

Social distancing has been advocated extensively through every possible medium and health care establishments are perceived as hotspots for COVID-19. This has resulted in significant drop in non-COVID-19 imaging volumes, thus lack of access to imaging suites for non-COVID-19 patients does not really arise. In fact, imaging facilities are extremely underutilized; in a recent study, imaging volumes plummeted at 75 to 90%. Imaging studies done for emergency medical conditions. such as stroke, also reduced significantly.[46] Furthermore, diseases disappeared in the pandemic providing health care establishments capabilities to cater to COVID-19 patients.[11,47,48]

Protocols for surface decontamination and infection control procedures are now very well documented. Personal protective equipment (PPV) and surface decontamination of CT gantry and table, as well as air exchanges, [[66], [67]] to remove any aerosolization are required to be practiced by all imaging facilities, as asymptomatic COVID-19-positive patients may be scanned for other symptoms, though COVID-19 pneumonia being incidentally detected.[49]

There are also numerous means to reduce the radiation and achieve low-dose CT studies, minimizing the utilization of ionizing radiation. Modulating tube current to body habitus, increasing the slice thickness to 1.5 mm, increasing the pitch to 1.5, collimating scan to cover apices to bases helps to reduce scan time and MA, thus reducing MAs. The kV may be reduced in thinner individuals to 100 kV. Iterative reconstructions further help to reduce radiation dose. In a recent study utilizing these parameters, the CTDI vol was reduced significantly from 3.4 to 0.4 mGy.[50,51]

Several studies from China, where the pandemic started from, have advocated the utilization of CT as a tool to detect COVID-19, as well as also have alluded the fact that CT features are independent of the RT-PCR status.[50,52]

China, the most populous country, where the pandemic started from, has reported only 100,000 infections out of a world total of 430 million with a very low level of new infections.

Extrapulmonary Manifestations of Novel Coronavirus Disease 2019

Though COVID-19 is well known for causing respiratory pathology, it can also result in multiple extrapulmonary manifestations. This is due to presence of ACE-2 receptors at multiple extrapulmonary sites, resulting in direct viral tissue damage.[53]

Though nearly every organ may be affected, the most affected extrapulmonary sites are heart, blood vessels, central nervous system, and gastrointestinal system.

Neurological Manifestations

These may be acute stroke pattern, altered mental status, epilepsy, or encephalopathy. The basic mechanism of injury is to the vascular endothelial and epithelial cells, resulting in disruption of the blood–brain barrier, hypoxic injury, and immune injury secondary to cytokine syndrome. Multifocal

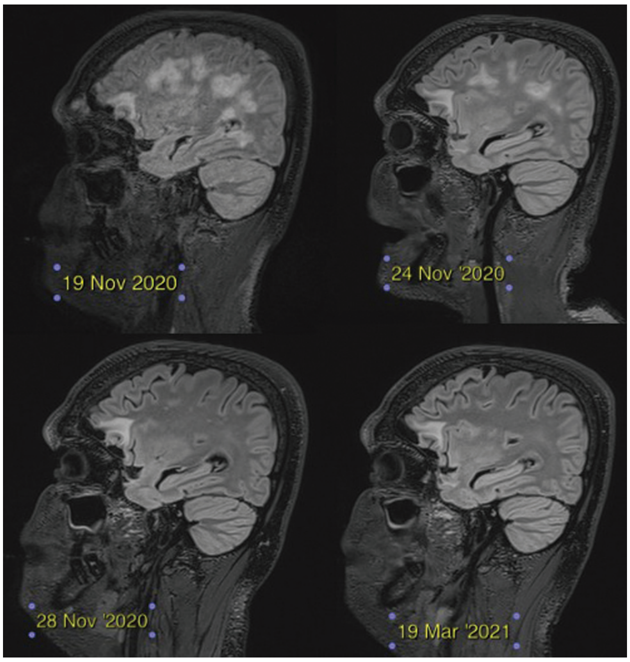

Fig. 19 Post-RT-PCR positive COVID-19 pneumonia patient presented with one episode of seizure. Sagittal FLAIR images on MRI revealed multifocal frontoparietal subcortical and periventricular white matter hyperintensities with relative sparing of the callososeptal interface suggestive of demyelination likely acute disseminated encephalomyelitis (ADEM). COVID-19, novel coronavirus disease 2019; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; RT-PCR, reverse-transcription polymerase chain reaction.

white matter abnormalities with hemorrhagic lesions, acute disseminated encephalomyelitis, acute hemorrhagic leukoencephalitis, viral encephalitis, postinfectious demyelination, and delayed post–hypoxic encephalopathy may be visualized (►**Fig. 19**). In the spinal cord Guillain–Barré syndrome associated with COVID-19 infection has also been demonstrated.[54–56] These patients present with paraparesis, acute in onset and may be associated with transient urinary incontinence with back pain. On MRI, long-segment T2 hyperintensity is seen in the spinal cord indicative of myelitis (►**Fig. 20**).

Rhinocerebral Mucormycosis

Also Termed as Black Fungus

India witnessed a devastating outbreak of mucormycosis due to the second wave of COVID-19. Prior to the pandemic, mucor was seen in immunocompromised individuals due to uncontrolled diabetes, post–organ transplantation, chemotherapy, and other diseases.

During the second wave, the outbreak of mucormycosis was attributed to rampant use of steroids to suppress severe COVID-19 inflammatory syndromes in ventilated patients.[57]

Fungal hyphae from mucor-invade blood vessels causing necrotizing vasculitis and thrombosis with consequent extensive tissue infarction. Involvement of paranasal sinuses results in invasive fungal rhinosinusitis. Progression beyond the sinuses results in rhinocerebral mucormycosis in the paranasal sinuses. The affected mucosa usually has a low T2 signal, this helps differentiate it from acute sinusitis where mucosa may reveal a bright T2 signal.

The low T2 signal is due to paramagnetic iron and magnesium present in the fungal elements. Extension beyond the paranasal sinus occurs to the orbits and/or intracranially.

Clinically, patients present with pain in the paranasal sinus or facial region, nasal congestion, serosanguinous nasal discharge, epistaxis, and maxilla facial swelling. Intraorbital extension manifests clinically with orbital symptoms, visual disturbances, proptosis, and ophthalmoplegia.

On CT, there is mucosal thickening within the cavity of paranasal sinuses along the turbinates and nasal cavities, there may be hyperdense areas due to intraluminal metal dense spots, corresponding to fungal-based products in the soft tissue in the paranasal sinuses.

There may be associated bony changes in the form of thinning, erosion of sinus walls, bony nasal septum, ethmoid trabeculae, medial wall, floor of orbit, as well as the cribriform plate. Also, there may be erosion/destruction of greater/lesser wings of sphenoid bone, pterygoid plate, hard palate, maxillary alveolar process, greater/lesser palatine foramen, floor of sella, basiocciput, and clivus. Oroantral fistula may occur due to hard palate/maxillary alveolus and septal involvement.

The disease extension beyond the sinus walls may be obvious with only alteration of periantral fat with no visible bone destruction. Air within the bony structures may be seen as mottled foci on CT.

On contrast administration, there is mucosal enhancement, though areas of nonenhancement in the mucosa may be visualized due to tissue necrosis. The classical sign is the "Black Turbinate sign," the turbinate may not enhance due to invasion of mucosa secondary to occlusion or small vessels. On MRI, the thickened mucosa appeared T2 hypointense due to presence of paramagnetic iron and magnesium in fungal elements. In acute bacterial sinusitis which may resemble clinically invasive fungal sinusitis, the mucosa is T2 hyperintense (►**Figs. 21–23**)

The proximity of structures and ethmoid veins result in spread from the sinuses to the orbital fossae.

Intraorbital extension is seen in the form of heterogeneously enhancing T2 hypointense soft tissue protruding into the orbit from the floor, roof, or medial wall depending on the site of sinus disease. The extraocular muscles may appear bulky, edematous, and heterogeneous in signal and enhancement. There may only be fat stranding of the extraocular and intraocular fat. There may be extension to the orbital apex causing mass effect on the optic nerve or optic nerve involvement which is seen as enhancement of the optic nerve sheath and/or optic nerve enhancement. There may be preseptal cellulitis, soft tissue anterior to the orbital septum, or postseptal cellulitis which involves contents of the orbit.

Diagnosis is usually made by nasal endoscopic biopsy of involved areas with confirmation by culture. Invasive fungal sinusitis can be successfully treated by a combination of

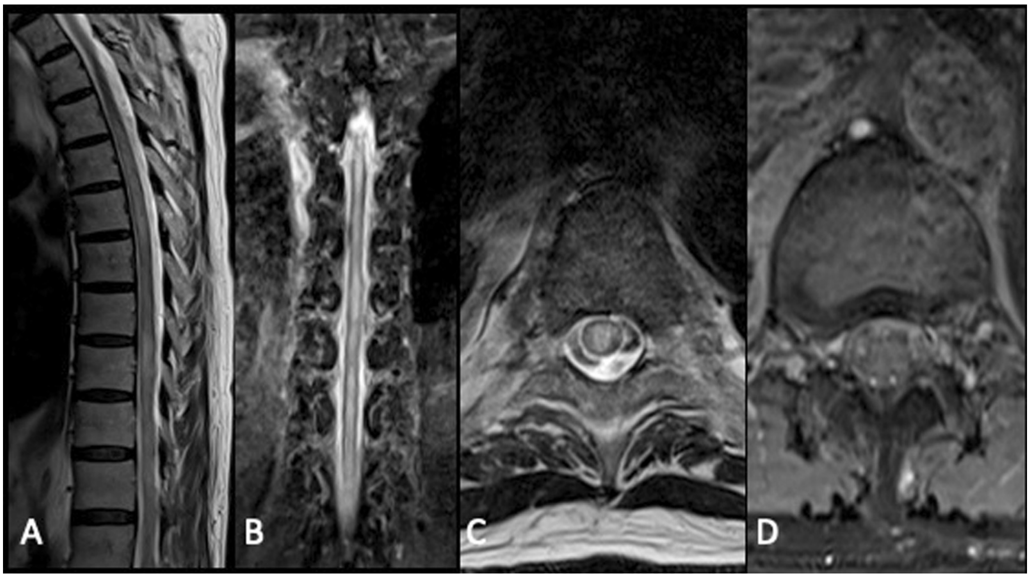

Fig. 20 MRI dorsolumbar spine in a patient with sudden bilateral lower limb weakness, 1-month postvaccination. (**A, B**) long segment T2 hyperintense signal involving the dorsal cord from the D4–L1 level on sagittal and coronal images. (**C**) T2-weighted axial reveals cord edema. (**D**) Mild postcontrast enhancement. These features are likely to represent transverse myelitis/Guillain–Barre syndrome (GBS) postvaccination. Patient did not respond to corticosteroids. Reversal of paresis was seen post-plasmapheresis thereby favoring GBS.

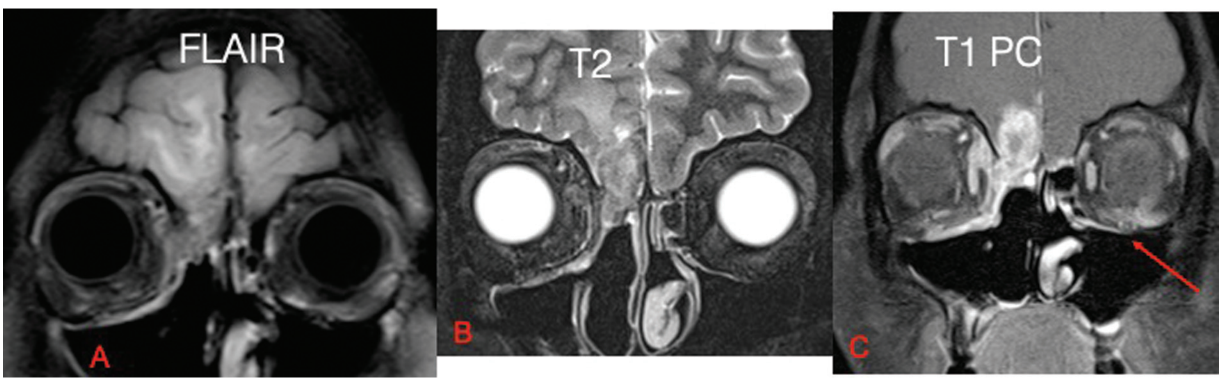

Fig. 21 Rhinocerebral mucormycosis (**A**) FLAIR, (**B**). T2-diffuse intermediate signal intensity soft tissue with right periorbital, extraconal, and intracranial extension suggestive of inflammatory soft tissue (**C**). Diffuse heterogeneous enhancement of the inflammatory soft tissue showing intracranial extension to the right frontal lobe and intraorbital extension into the right orbit with mild extraconal extension with involvement of medial rectus muscle. FLAIR, fluid-attenuated inversion recovery.

surgical debridement of affected tissues by FESS and antifungal medications.

Essentially aggressive treatment, as well as reversal of immune suppression, is effective. Even with aggressive treatment, only 50% survive. In case of intraorbital involvement, aggressive surgery and exenteration of the orbit maybe required.

The fungal hyphae tend to involve nerves and vessel wall leading to perineural spread. This may occur along the division of trigeminal nerve, Vidian nerve, or orbital nerves. On imaging, there is heterogeneous enhancement, as well as obliteration of the perineural fat. MRI is very useful in the detection of perineural spread due to the superior soft tissue contrast and excellent demonstration of neural pathways. Perineural spread can extend to the cavernous sinus. in this setting, enhancing soft tissue is seen in the orbital apex and cavernous sinus. Angioinvasive involvement has seen in the form of thrombosis, enhancement of thickened arterial wall, and tissue necrosis.

Intracranial involvement may occur via (1) direct extension via cribriform plate and superior orbital fissure; (2) perineural extension via foramens in the base of the skull (mandibular nerve, foramen ovale; ophthalmic nerve, superior orbital foramen, Vidian nerve, Vidian canal; and infraorbital nerve, pterygopalatine fossa and foramen rotundum); (3) angioinvasion; and (4) hematogenous spread.

Intracranial extension is in the form of meningeal inflammation or parenchymal involvement in the form of cerebritis/abscesses. The dural/meningeal enhancement can be the earliest and an obvious finding. Parenchymal involvement is seen as hypointensity on T1/T2 with peripheral enhancement. On diffusion-weighted imaging, restriction may be seen. There is peripheral restriction with intracavitatory projections which also demonstrate

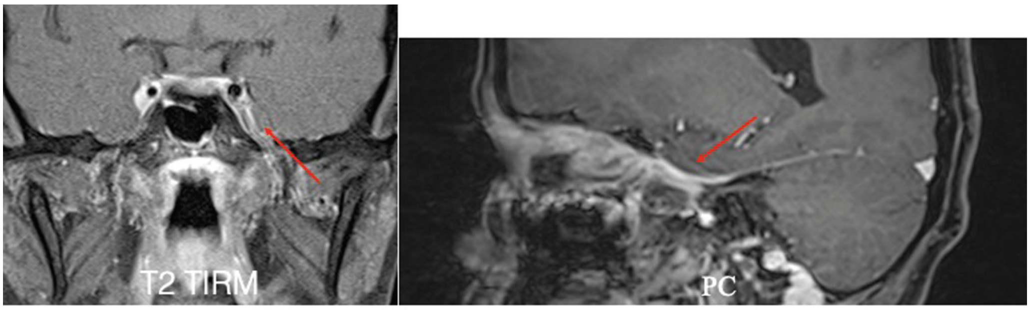

Fig. 22 Rhinocerebral mucormycosis showing left cavernous sinus involvement with thin, uniform dural enhancement.

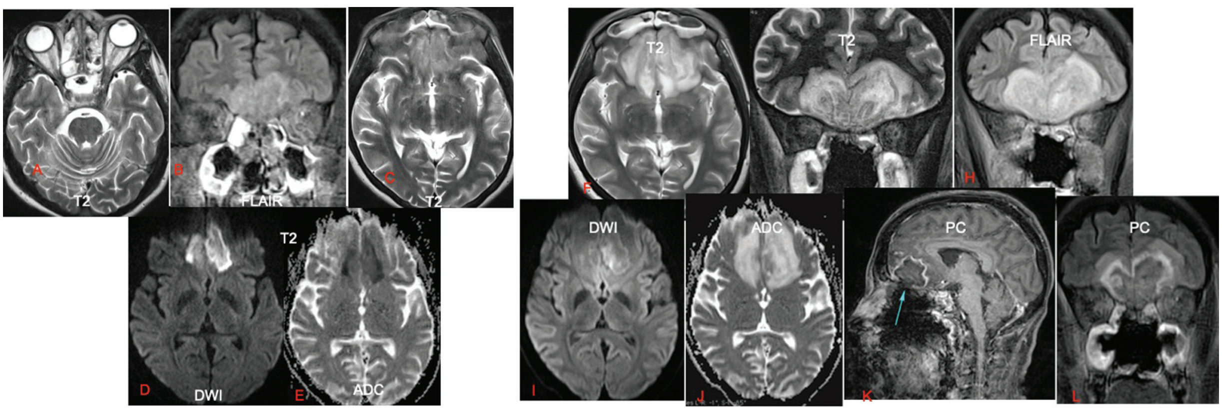

Fig. 23 (**A**) Patient with mucormycosis showing bilateral ethmoid and sphenoid sinus mucosal thickening. (**B**) Coronal FLAIR image showing intracranial extension seen as bilateral frontal hyperintensities. (**C**) Hyperintensities in bilateral parasagittal location of frontal lobes on axial T2-weighted images. (**D**) Corresponding diffusion restriction with ADC drop (**E**) representing cerebritis. (**F–H**) Follow-up imaging study after undergoing extensive paranasal sinus surgery to resect areas involved by mucormycosis—Intracranial bifrontal involvement with adjacent edema has progressed from previous study. (**I, J**) There is now significant necrosis with peripheral enhancement representing dead nonviable soft tissue. (**K, L**) Inflammation is seen along the periphery with diffusion restriction with corresponding ADC drop. Peripheral enhancement with central nonenhancing areas. DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery.

diffusion restriction; however, the core of the lesion is spared. The T2-hypointensity is due to fungal involvement or ischemic tissue necrosis secondary to angioinvasive fungal involvement. Contrast enhancement is useful in differentiation of viable from the necrotic tissue.

Imaging is extremely important, as it aids in early accurate diagnosis, as well as a guide for effective surgical management.

Cardiac Manifestations

Patients may manifest with acute coronary syndromes, myocardial dysfunction, or arrhythmias.[58]

The exact underlying mechanism causing myocardial injury is not entirely understood and is most likely due to the contributory effect of several direct and indirect mechanisms. Direct mechanism is caused by viral injury due to presence of ACE-2 receptors and indirect mechanism is caused by cytokine storm and uncontrolled immune cell activation which leads to open reduction of proinflammatory cytokines resulting in endothelial dysfunction, as well as direct cytotoxic effects on intestinal cells, macrophages, and cardiac tissue.

The myocardial injury is reflected in an activated troponin-D level, electrocardiogram (ECG) changes, and drop in ejection fraction.

Cardiac MRI is the ideal modality to evaluate this. On cardiac MRI, regional/global wall motion abnormalities are seen on steady state free precession (SSFP) imaging. A diffuse increase in T1 relaxation time on T1 mapping is seen. There is late gadolinium enhancement in a nonischemic pattern, typical subendocardial in location, along a nonvascular distribution, though it may also be midmyocardial/transmural[59] (►**Fig. 24**).

Occasionally, acute myocarditis may be seen as T2 hyperintensity on T2-weighted sequences representing cardiac edema.

Role of Chest Radiography

The chest X-ray is usually the initial and often only investigation required in the evaluation of diseases of the chest.

SARS-CoV-2 has a particular affinity for ACE-2 receptors. These are in abundance in type-2 alveolar cells. After gaining entry into the type-2 receptor cells, there is diffuse alveolar damage resulting in exudation into the alveolar spaces.[10,60,61]

This appears on chest radiographs X-rays as a diffuse haziness obscuring vascular markings, akin to the well-documented ground-glass densities seen on CT scans. With further progression in alveolar cell apoptosis, the exudation may result in denser opacities on the X-ray appearing as

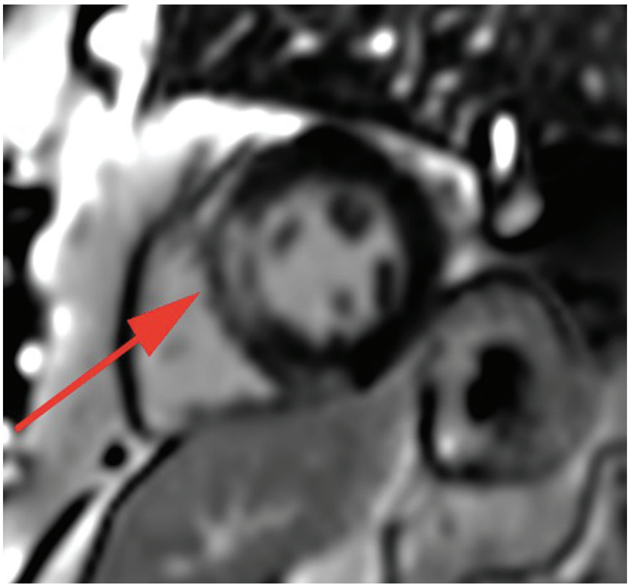

Fig. 24 Cardiac MRI: subepicardail gadolinium enhancement along septal and inferior mid-ventricular myocardial wall suggestive of myocarditis. MRI, magnetic resonance imaging.

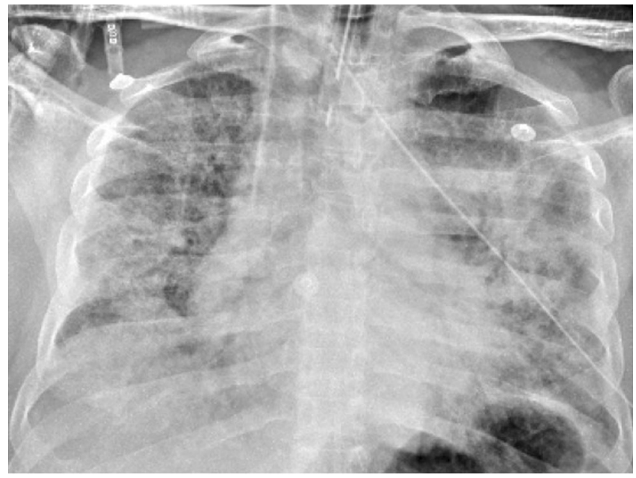

Fig. 25 Chest radiograph of COVID-19-positive patient on RT-PCR reveals diffuse airspace consolidation in bilateral mid and lower zones with relative sparing of left upper zone representing a "white out lung." COVID-19, novel coronavirus disease 2019; RT-PCR, reverse-transcription polymerase chain reaction.

consolidations. These consolidations do not incite sympathetic effusions or internal cavitation as may occur with bacterial pneumonias. Occasionally, reticular opacities may be seen on the X-ray as linear bands due to septal/alveolar thickening due to inflammation. The distribution of abnormalities is usually in the lung bases, as well as in the periphery.[62–64]

The diffuse alveolar damage evolves over 1 to 3 weeks, resulting in temporal changes on imaging. There are three stages of diffuse alveolar damage.

Stage 1 is the exudative phase which occurs in the first few days after infection, usually till day 4/5. There is limited leakage of fluid into the interstitium, as a result radiographs demonstrate essentially clear lung fields.

Stage II is an inflammatory stage where there is an alveolar capillary leak of protein and fluid, resulting in diffuse alveolar opacities predominantly in the peripheral portions of the lungs. With increasing capillary leak diffuse alveolar damage may progress with extensive lung involvement resulting in acute respiratory distress syndrome (ARDS). This results in loss of aerated lung tissue, impaired gas exchange, and hypoxia. Opacities tend to become confluent, lungs become totally opaque, and air bronchograms may be present with injury to alveolar cells, there is decreased surfactant production and decreased lung compliance. This is reflected in the radiographic findings of relatively small lung volumes and atelectasis. Rarely, there are associated pleural effusions; these are usually small if present. At this juncture, it is important to differentiate cardiogenic, overhydration edema from the alveolar edema of ARDS. The alveolar edema of ARDS is not accompanied by widening of the vascular pedicle, cardiomegaly, altered pulmonary blood flow distribution, pleural effusions, and septal lines. In fact, if the pulmonary vessels can be distinguished, they are often constricted in size. The opacities tend to be in the periphery as compared with central in cariogenic edema, as well as do not change temporally as they do in cardiogenic edema.

Stage III is a fibroproliferative phase, in this phase, there is proliferation of epithelial cells and fibroblasts with collagen deposition. A transition from alveolar to interstitial opacities is seen. The radiographic appearances are of progressive clearing of alveolar opacities which are replaced by reticular opacities. In the chronic phase, the radiograph often returns to normal, occasionally residual fibrosis or cystic changes may be present (►**Figs. 25–29**). The main complication of COVID-19 pneumonia is the development of ARDS.

The mainstay of treatment of ARDS is to recruit the alveoli in the atelectatic/consolidated portions of the lung by using high positive end expiratory pressures via mechanical ventilation. This distends the alveoli. An effort to recruit the consolidated atelectatic portions can result in over distension of these alveoli and consequently barotrauma due to rupture of alveoli. The radiologist has an extremely important role to play in the detection, prevention, and treatment of these complications.

The adverse effects of positive pressure ventilation can be classified into two groups listed below:

1. Due to physiological effects of mechanical ventilation on heart/pulmonary vasculature.
2. Direct lung injury resulting in air leak phenomena.

During the acute phase, the use of positive end expiratory pressure may result in improvement of the chest radiograph appearances, such as clearing of previously visualized opacities. This in fact is a paradox, as the positive end expiratory pressure causes over distension of the alveoli resulting in the apparent clearing of opacities on the chest X-ray. This over distension of the alveoli results in diversion of pulmonary blood flow to the poorly ventilated regions resulting in paradoxical worsening of the oxygenation (►**Fig. 30**).

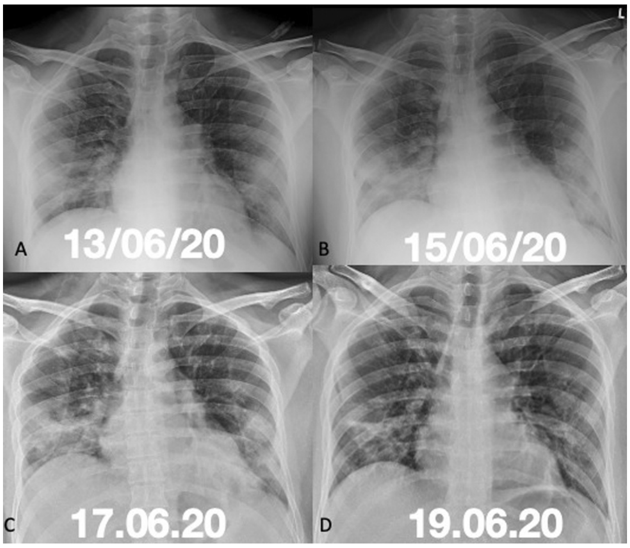

Fig. 26 (A) Subtle haziness in bilateral mid and lower zones. (B) Follow-up radiographs show progression to dense opacities. (C) Subsequent clearing with areas of bilateral lower zone opacities. (D) Near-complete regression with clearing of lungs.

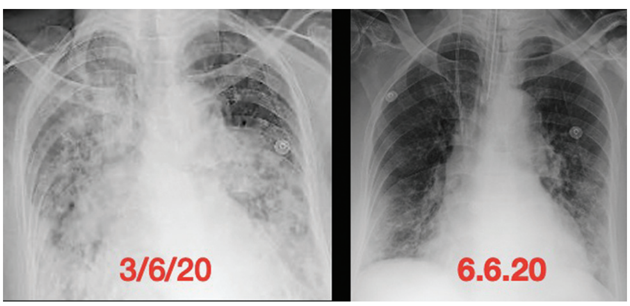

Fig. 27 Follow-up radiograph shows diffuse airspace opacities bilaterally with subsequent clearing of opacities.

Air Leak Phenomena

This is the most recognized manifestation of barotrauma, the development of extra alveolar air collections which may accumulate in the following five compartments: the pleural space, mediastinum, interstitium, pericardial sac, and subcutaneous tissues. Although each area has distinct radiological features, overlap exists and occasionally differentiation can be difficult. In our study, 40% of patients mechanically ventilated developed barotrauma.[15]

Pulmonary Interstitial Emphysema

This occurs due to rupture of alveoli with resultant leak of air into the interstitium and interstitial emphysema. This air then dissects along the vascular sheaths and interlobular septae, paths of least resistance, and centrally to the hilum, resulting in a pneumomediastinum and peripherally to the pleura resulting in a pnuemothorax. Pulmonary interstitial emphysema is difficult to observe on radiographs as the air in the interstitium is difficult to detect against the background of dark alveolar air. Pulmonary interstitial emphysema becomes much easier to detect in a consolidated lung as

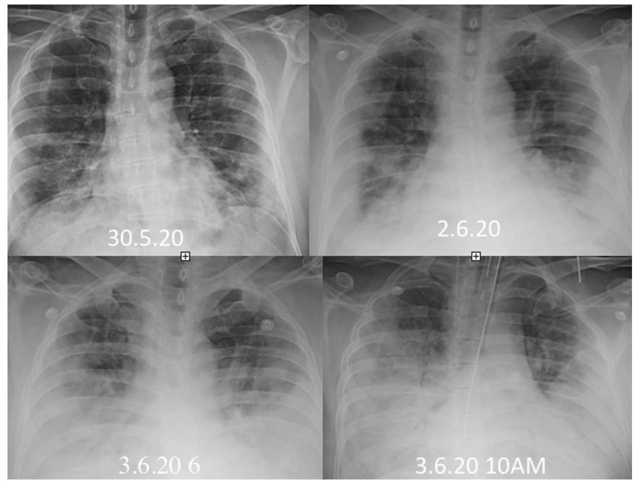

Fig. 28 Serial chest radiographs over 5 days in a case with COVID-19 pneumonia showing progression of density and area of airspace opacities. Patient was intubated on the day 5 and unfortunately expired one day later. COVID-19, novel coronavirus disease 2019.

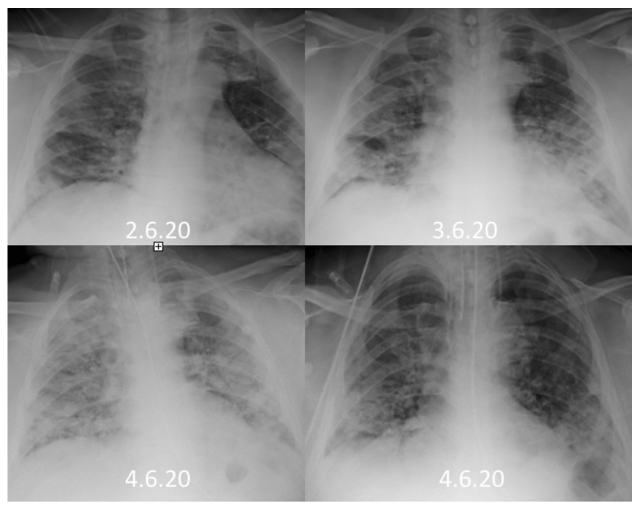

Fig. 29 Serial radiographs reveals diffuse patchy opacities in bilateral lungs with initial rapid progression to ARDS followed by resolution. ARDS, acute respiratory distress syndrome.

the consolidation contrasts the air in the interstitium (►**Fig. 31**).

The earliest radiographic signs are a mottled increase in the radiolucency of the lung anteriorly and medially around the heart, as well as the diaphragmatic surface. There may be streaky linear radiolucencies radiating from the hila to the periphery of the lung. These may resemble air bronchograms, they however differ from air bronchograms by the fact that they do not branch, nor do they taper to the periphery.[65] They may form pnuematoceles which may coalesce to form large subpleural cysts.

Pneumomediastinum

The mediastinum is anatomically defined as the space between the two lungs, it is enveloped all round by parietal pleura. It contains two air filled structures, the trachea and the esophagus. Any air outside these structures is

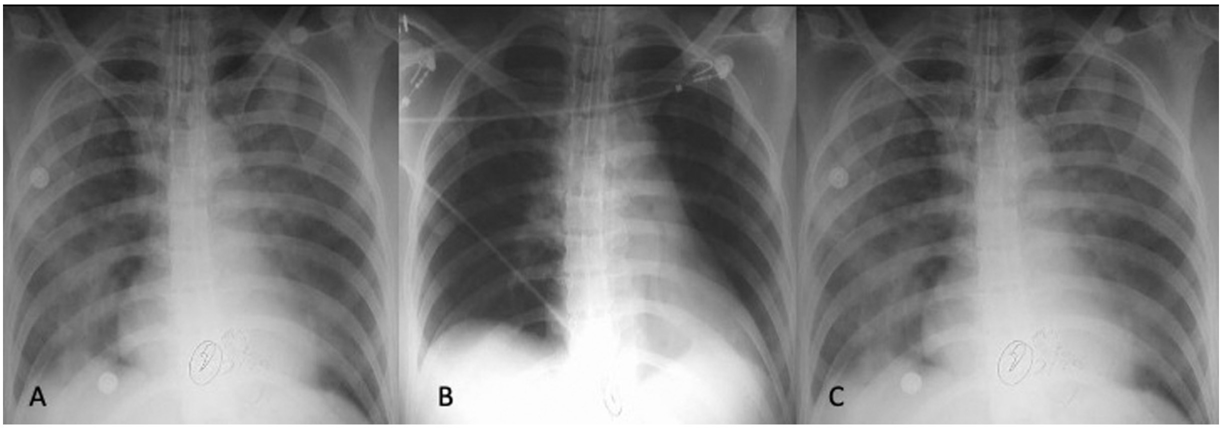

Fig. 30 PEEP effect patient was intubated. (**A**) Diffuse haziness due to airspace opacities representing ARDS seen in bilateral lungs. (**B**) After increasing PEEP there is Apparent clearing of the opacities following intubation, tubular heart. (**C**) As PPEP effect was seen, this endangers patient to barotrauma. PEEP was reduced and consequently reappearance of diffuse airspace opacities. ARDS, acute respiratory distress syndrome.

pathological. As the air collects around the mediastinal structures and great vessels, the cardiac contour is demarcated extremely well. Streaky vertically oriented opacities may be visualized extending superiorly into the neck. Normally, the infracardiac surface of the diaphragm is not visualized, this is as the density of the cardiac structures and diaphragm are similar. In a pneumomediastinum, air dissects inferiorly into the infracardiac region, separating the cardiac and diaphragmatic densities producing a continuous diaphragm sign. The diaphragm is seen in its entire extent. The mediastinal pleura may be visualized as a thin line surrounding the mediastinal air (►**Fig. 32**).

Pneumothorax

This is the most common life-threatening emergency in patients supported by mechanical ventilation. Pneumothorax usually follows the development of pneumomediastinum. The relatively thin mediastinal pleura ruptures when overdistended with air. Once a pneumothorax develops in a patient on the ventilator, it may rapidly increases in size to become a tension pneumothorax.[50,52]

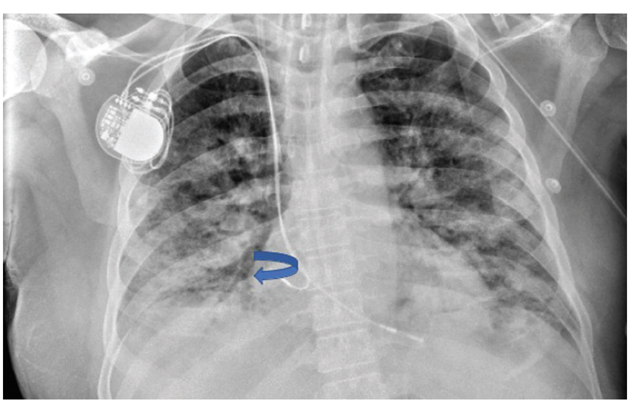

Fig. 31 Portable chest radiograph of a COVID-19 pneumonia patient with diffuse airspace opacities in bilateral lung fields with relative sparing of both upper lobes. Linear lucencies in the right lower zone (blue arrow) representing pulmonary interstitial emphysema. COVID-19, novel coronavirus disease 2019.

The most important radiographic feature of a pneumothorax is the presence of a thin white line representing the visceral pleura with air on both sides of this white line, air in the pleural space and air in the lung parenchyma. Other signs are absence of lung markings beyond the visceral pleural line and hypertranslucency of the pleural space. Unfortunately, in most patients with suspected barotrauma, only supine X-rays are possible. In these situations, detection of a pneumothorax may be difficult, and the signs are different. The principles are the same, air collects in a nondependent location such as the anteriomedial or subpulmonary location, when the air leak is large and air may collect in the apicolateral location. The displaced visceral pleural line is difficult to demonstrate on a supine radiograph X-ray. In the absence of this specific sign, secondary signs to demonstrate the collection of extra pleural air is important. As air collects

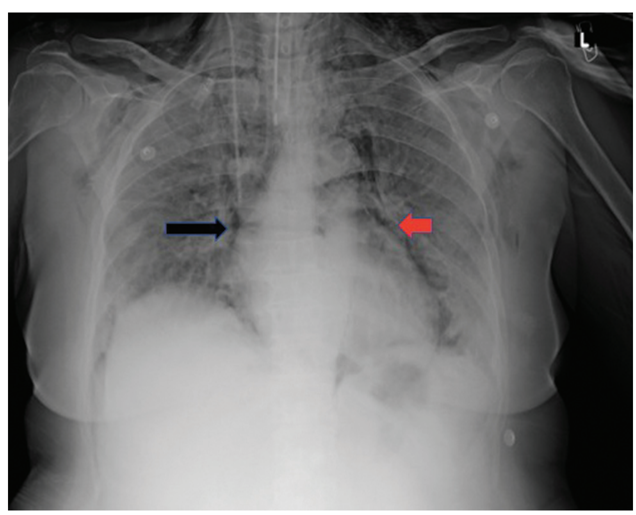

Fig. 32 Portable chest radiograph in a COVID-19 pneumonia patient on mechanical ventilation developed mediastinal emphysema (red arrow) and diffuse subcutaneous emphysema as a result of barotrauma . Linear lucencies noted in the right mid zone representing pulmonary interstitial emphysema (black arrow). COVID-19, novel coronavirus disease 2019.

in the anterior costophrenic sulcus, there is transradiancy in the hypochondrial region overlying the diaphragm. There is increased sharpness of adjacent mediastinal margin and diaphragm. The costophrenic sulcus becomes deep with a well-defined margin. The inferior edge of collapsed lung becomes visible. Ipsilateral hemidiaphragm is depressed. Cardiac margins become sharp and pericardial fat pads become well outlined. A pneumothorax suspected on a supine film can be confirmed on a cross-table lateral view or lateral decubitus with suspect side uppermost. If there is any doubt, CT chest is very useful as it would be confirmatory.

Skin folds may mimic the white line of displaced pleura. Skin folds are often in pairs, as well as often cross the midline, diaphragm, or chest wall. Lines or tubes projecting over the lung may also simulate the white visceral pleural line. In these cases, the other signs of a pneumothorax are absent, and the appliances can be seen exiting the confines of the thoracic cage.

A pneumothorax is considered under tension when the pressure in the pleural space exceeds atmospheric pressure. The ipsilateral lung collapses with mediastinal shift, especially displacement of the azygoesophageal recess. There may also be evidence of inversion of the diaphragm and flattening of the heart especially the inferior vena cava (IVC) and superior vena cava (SVC) ,impairing normal venous return to the right heart (►**Figs. 33** and **34**).

Pneumothorax is treated by placing a thoracic tube. If there is only air in the pleural space, the thoracic tube is placed anteriorly in the second intercostal space, if there is a mixture of air and fluid, then the tube is placed in the sixth or seventh interspace in the mid axillary line.

Subcutaneous Emphysema

Air can dissect along the fascial planes of the neck, chest, and abdominal walls from the mediastinum or pleura. Often, the presence of air in the chest wall in a patient on mechanical ventilation is the first sign of barotrauma. Due to the presence of subcutaneous emphysema, pneumothorax or underlying parenchymal abnormalities may not be detected on the chest radiograph. Rarely subcutaneous emphysema may be due to a necrotizing soft tissue infection. Radiographically, multiple lucencies of varying configurations may be seen within the soft tissues of the neck and thorax. Subcutaneous emphysema present is of little clinical significance.

Ventilator-Associated Pneumonia

Due to the immunosuppressed state of critically ill patients, bacteria colonize in the endotracheal/tracheostomy tube. The endotracheal or tracheostomy tube allows free passage of bacteria into the lower segments of the lung, thus these maybe imbibed into the lungs with each breath, also they may be propelled down by suctioning and bronchoscopy.[66,67]

This results in an infectious pneumonia. The key to the diagnosis is the presence of new opacities, especially cavitation and pleural effusions. Clinical and laboratory parameters support the diagnosis. On chest X-ray, these may be difficult to demonstrate on the background of white out lung.

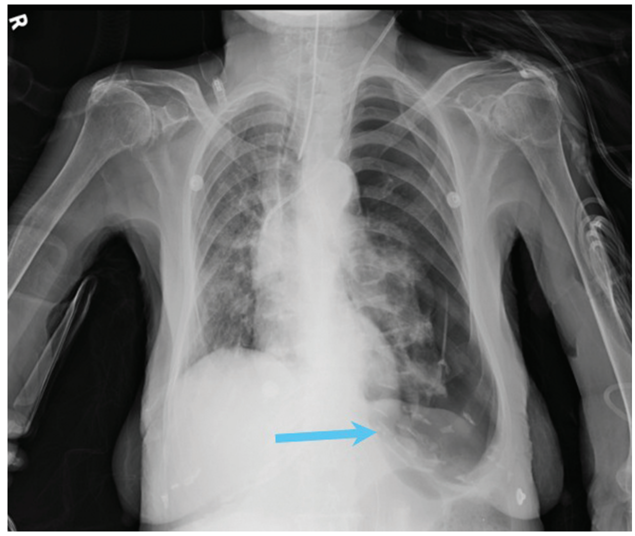

Fig. 33 Radiograph with pneumothorax due to ventilatory barotrauma causing inversion of left hemidiaphragm.

The chest X-ray is an important diagnostic tool in the detection and management of COVID-19 pneumonia. Chest X-ray is useful tool to detect changes to suggest the diagnosis, CT chest, however, has a higher sensitivity. The common CT findings of bilateral involvement and peripheral distribution, predominantly in lower zones, were also appreciated on chest X-ray which was commensurate with other studies.

Portable chest X-ray, being a bedside modality, can be used to monitor the progression, regression of lung changes, complications in the form of ARDS, barotrauma, ventilator-associated pneumonia, and misplaced tubes and lines helping reduce the morbidity and mortality (►**Figs. 35–37**).

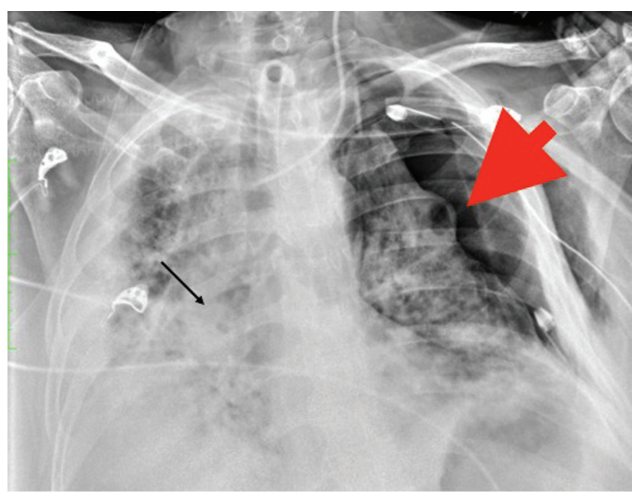

Fig. 34 Portable chest radiograph after chest tube insertion in COVID-19-positive patient with bilateral diffuse air space consolidation requiring positive pressure ventilation developed left sided pneumothorax likely due to barotrauma resulting in collapse of the underlying left lung and mediastinal shift towards right. A well-defined oval radioluceny in periphery of left-middle zone representing a pneumatocele (black arrow) with linear radiolucencies in left mid and lower zones around heart representing pulmonary interstitial emphysema. Possibility of bronchopleural fistula was considered as the pneumothorax persisted even after ICD placement. COVID-19, novel coronavirus disease 2019.

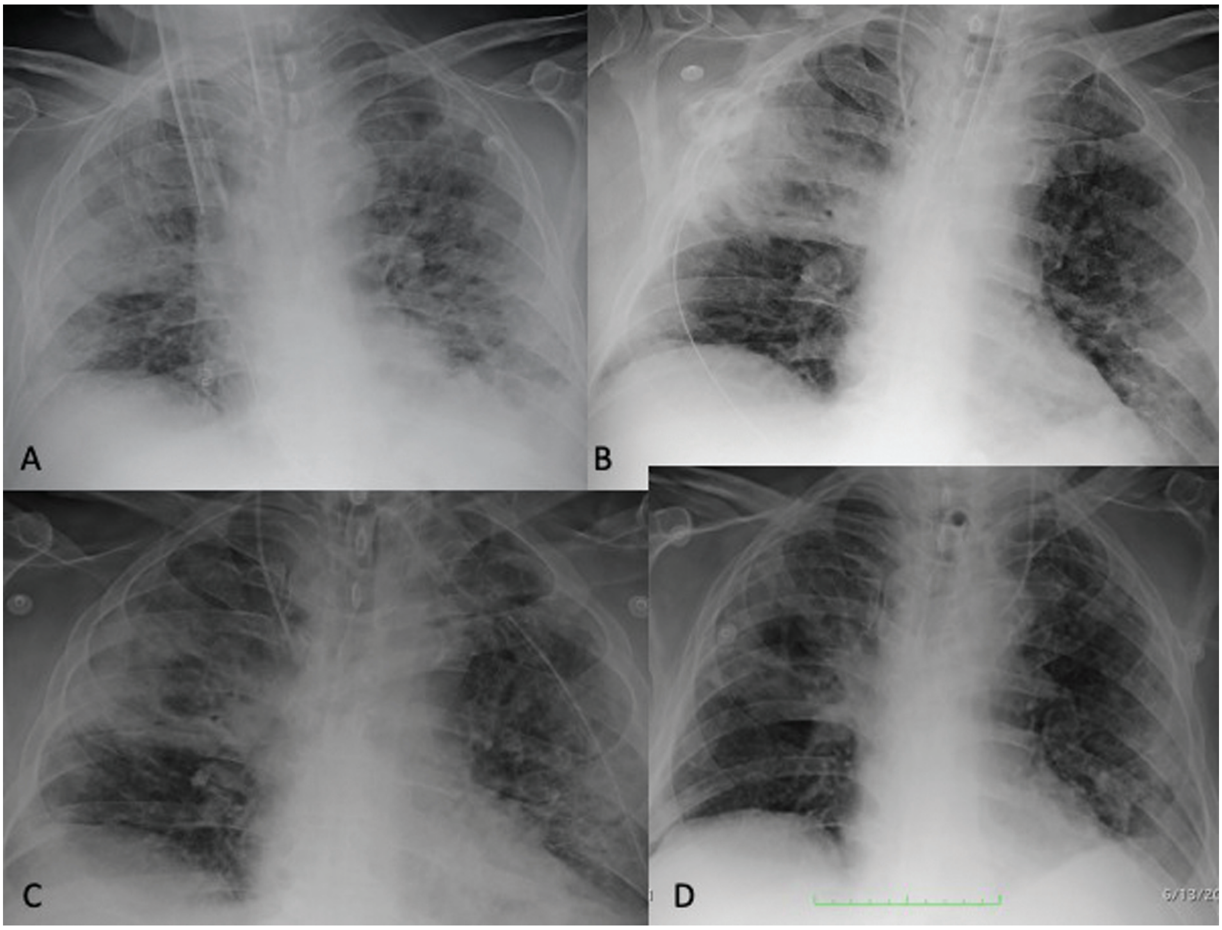

Fig. 35 Ventilator-associated pneumonia: serial portable chest radiographs in a COVID-19-positive patient requiring mechanical ventilation, showing (**A**) dense consolidation in right upper and mid zone (this was a new finding as compared to old X-rays). (**B–D**) shows cavitation in dense consolidation. Endotracheal tube swab (ETS) grew acinetobacter baumannii on culture. Pneumonia resolved on appropriate antibiotic therapy as shown in follow up chest X-rays. COVID-19, novel coronavirus disease 2019.

Value of Imaging in Triaging of Patients—Computed Tomography Severity Index

The main concern of a pandemic is the overwhelming of medical facilities due to the sheer number of patients presenting at the same time. This may also trigger panic in the general population leading to societal issues. Lockdowns are primarily to slow the number of patients presenting at the same time, allowing medical facilities to try and cope. An important component of alleviating the pressure on medical establishments is to triage patients.[3,68]

COVID-19 pneumonia has a wide spectrum of presentations and outcomes, ranging from asymptomatic to severe hypoxia which may result in death. Triage is needed to decide the order of treatment when the number of patients is large, outweighing the capacity of the available facilities. As the clinical presentation, management and outcomes of COVID-19 are so varied, triaging patients into those who require management at home, COVID-19 care facilities or those who require hospitalization is essential. Additionally, for the patients in hospital, whether they will require admission in a ward or intensive care unit (ICU), whether the oxygen requirement would be low flow, high flow, or whether they would require noninvasive ventilation (NIV) or mechanical ventilation via intubation is also important.

COVID-19 pneumonia pathologically is a diffuse alveolar damage which progresses in a temporal manner. Initially. patients may be mildly symptomatic but can rapidly progress to severe hypoxia requiring oxygen support and hospitalization. The extent of lung involvement in the second phase of diffuse alveolar damage approximately between days 7 and 10 may be a good surrogate to decide disease burden. A low percentage of aerated lung tissue corelates with a poor prognosis. For this purpose, a CT severity score has been proposed to determine the extent of lung involvement based on extent of involvement on CT scan.

Several CT severity scoring systems have been proposed. There are 20-, 25-, 40-, and 72-point scales which evaluate extent of lung involvement depending on the involvement of each lobe, expressed as percentage which is finally summed up to provide the final score.[69]

This may be done subjectively with visual interpretation of the scans or by an automated deep learning software program.[70] Opacity score was calculated by dividing the lung parenchyma into five anatomical lobes and assigning scores by adding percentage of opacity within the lobes. If the

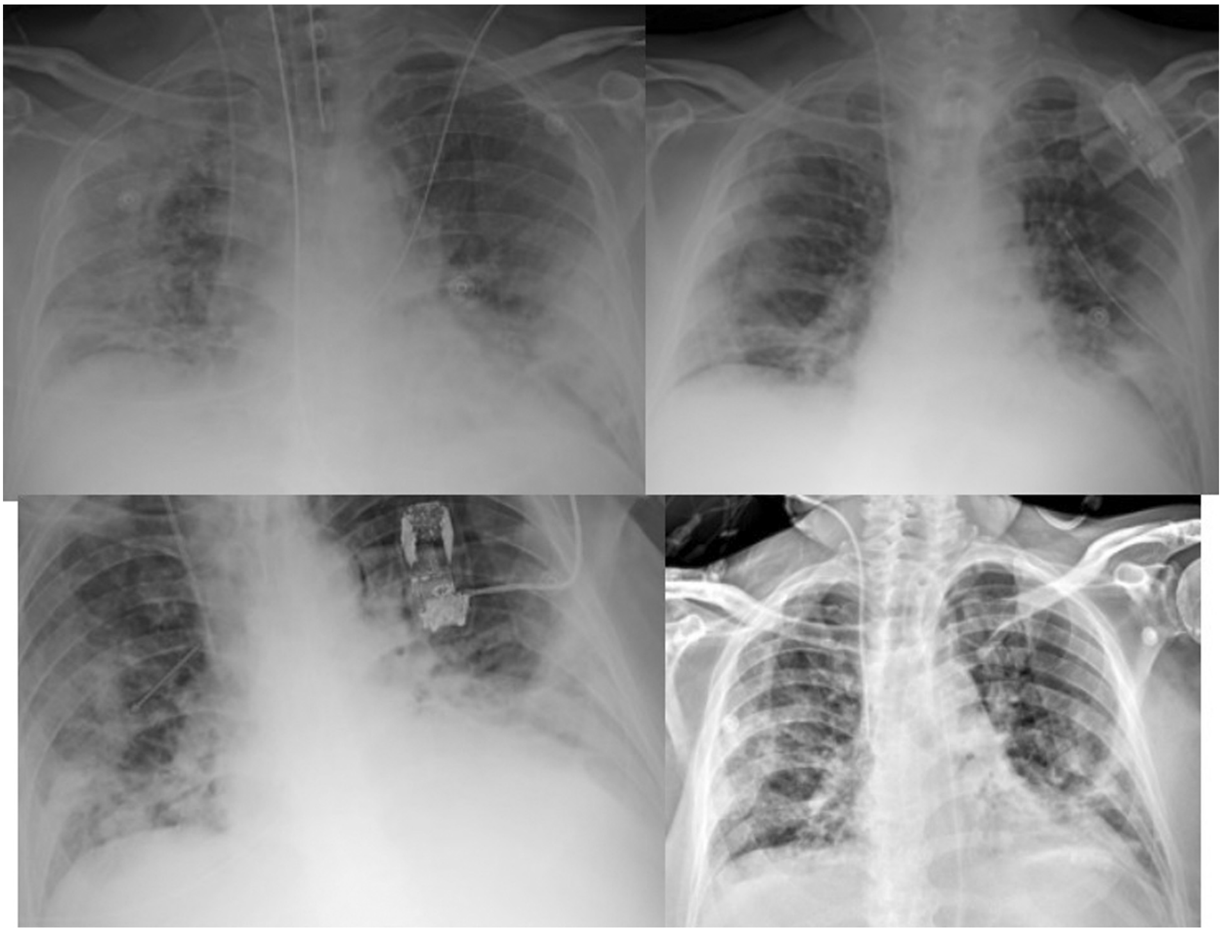

Fig. 36 Serial portable chest radiographs in a COVID-19-positive patient. (**A**) showing airspace consolidation in right lung and left mid and lower zone, (**B**) resolution in the density and extent of airspace consolidation in right lung field and left mid zone, (**C**) ill-defined consolidation in right mid and lower zone (new finding-red arrow). Microbiological investigations revealed acinetobacter baumannii on culture, (**D**) resolution of extent and density of opacities noted in right mid and lower zones after appropriate antibiotic treatment. COVID-19, novel coronavirus disease 2019.

parenchymal involvement was 0, <25%, 25 to 50%, 50 to 75%, or >75%, they were assigned a score of 0, 1, 2, 3, and 4, respectively for a 20-point scale, and involvement was 0 to 5%, 5 to 25%, 25 to 50%, 50 to 75%, and >75% while they were assigned a score of 1, 2, 3, 4, and 5, respectively, for 25-point scale. The scores for each lobe were added to provide the final CT severity score. The 25-point scale is the most popularly used scoring system (►**Fig. 38**).

The subjective visual method is fraught with numerous inter- and intraobserver errors, as it is a visual assumption,

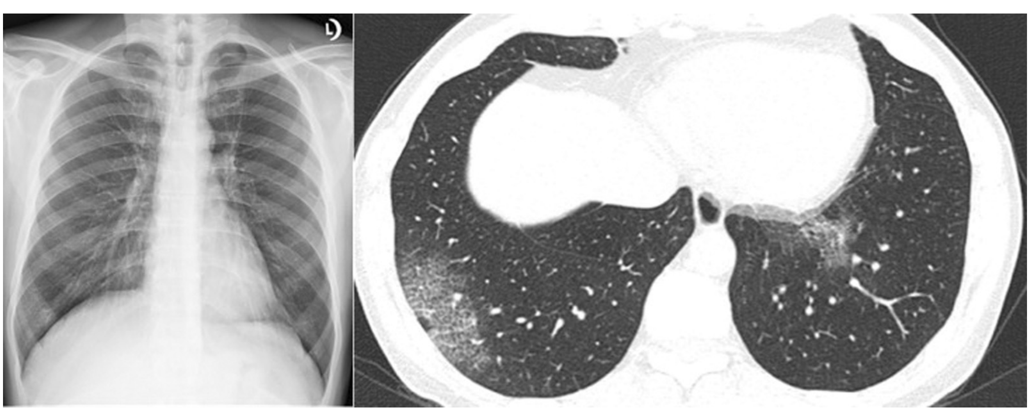

Fig. 37 (**A**) Chest radiograph of a RT-PCR proven COVID-19-positive patient shows no abnormality. (**B**) HRCT chest was done on same day as patient was symptomatic revealed patchy areas of ground glass densities with interlobular septal thickening in posterior basal segment of right lower lobe and medial basal segment of left lower lobe. COVID-19, novel coronavirus disease 2019; HRCT, high-resolution computed tomography; RT-PCR, reverse-transcription polymerase chain reaction.

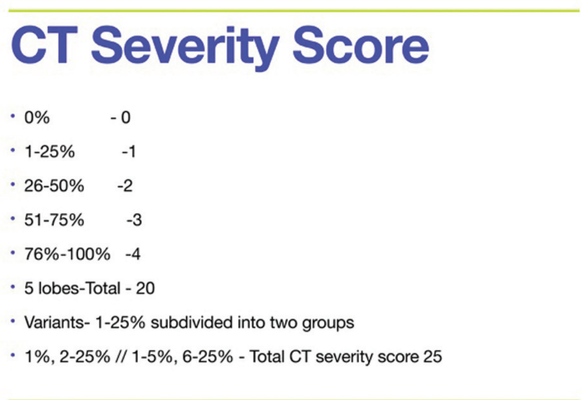

Fig. 38 CT severity score. CT, computed tomography.

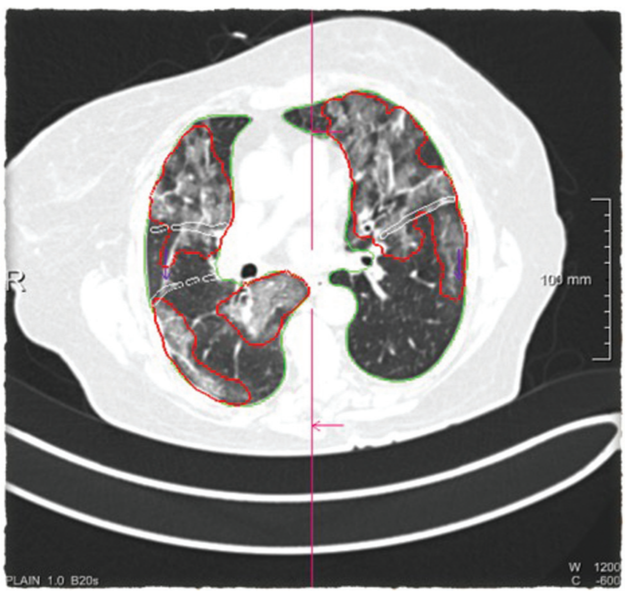

Fig. 39 CT severity index: calculated by the "CT Pneumonia Analysis Software"—Lung involvement is assessed and assigned scoring according to severity of involvement by artificial intelligence. CT, computed tomography.

resulting in significant under and over estimation. This process is manual; thus, it is extremely time consuming which does not help in a pandemic where accurate and timely information is required for triage. In view of this, we utilized an automated deep learning software, Siemens Healthcare version 2·5·2 (Erlangen, Germany). The artificial intelligence (AI) software, automatically processed CT-severity score, volume, and percentage of opacity. The software also provided a total percentage of lung involvement, representing opacity percentage of lung involvement (►**Figs. 39–41**)

A statistically significant relation was found between the severity scores and oxygen requirement, need for hospitalization, ICU admission, and mortality.

Patients were divided into three groups based on CT severity scores as follows:[3] (1) mild CT severity (25) of 1 to 7 and percentage opacity of 0 to 10%; (2) moderate CT severity (25) of 8 to 18 and percentage opacity of 11 to 30%; and (3) severe CT severity (25) of >15 and percentage opacity of >30%.

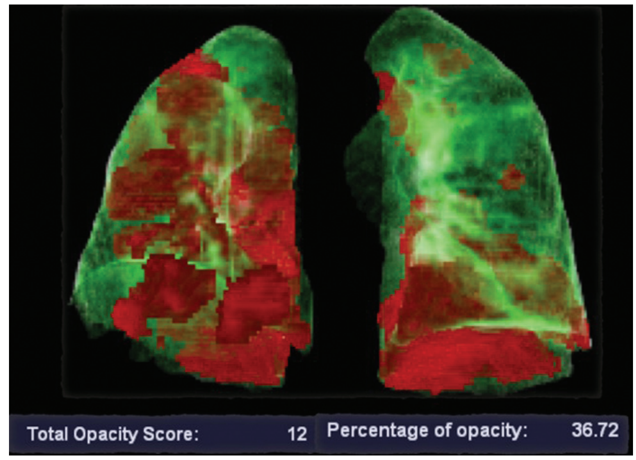

Fig. 40 CT pneumonia analysis: color coded representation; red depicts areas of involvement and green depicts normal lung parenchyma. CT, computed tomography.

Majority of the patients in the mild group were on room air and were treated on an outpatient department (OPD) basis, whereas majority of the patients in severe group were admitted in ICU and were either on NIV/high-flow nasal canula (HFNC) or were intubated. Moderate group patients overlapped both groups more often requiring room air. This finding was consistent for all the three scoring systems. Mortality was the highest in the severe group.

Statistically receiver operating characteristics (ROC) curve analysis found a cut-off of 4 for cycle threshold score (CTS) 20, 9 for CTS 25, and 12·5% for percentage opacity to be a predictor of oxygen requirement.[3]

Unlike the findings of Zhang et al, we could not find a correlation between the scoring system and the laboratory parameters.[71]

Only the early CT scans, done within 1 week of disease, were taken into consideration, this is very important as these findings can help in early triaging and prognostication of patients who are likely to deteriorate and administer early medical therapy, even if the patients clinically have mild symptoms.

In conclusion, an early CT scan in patients affected with COVID-19 is predictive of the oxygen requirement of the patient. As severity scores increase, the chances of requirement of higher oxygen and intubation increase as well. CT severity scoring using an automated deep learning software program is a great boon for determining oxygen requirement and triage.

Antibodies

The human body responds to viral infections by producing antibodies. SARS-CoV-2 is no different, as it stimulates a rapid antibody response in symptomatic and asymptomatic infected individuals. Immunoglobulin M (IgM) titers

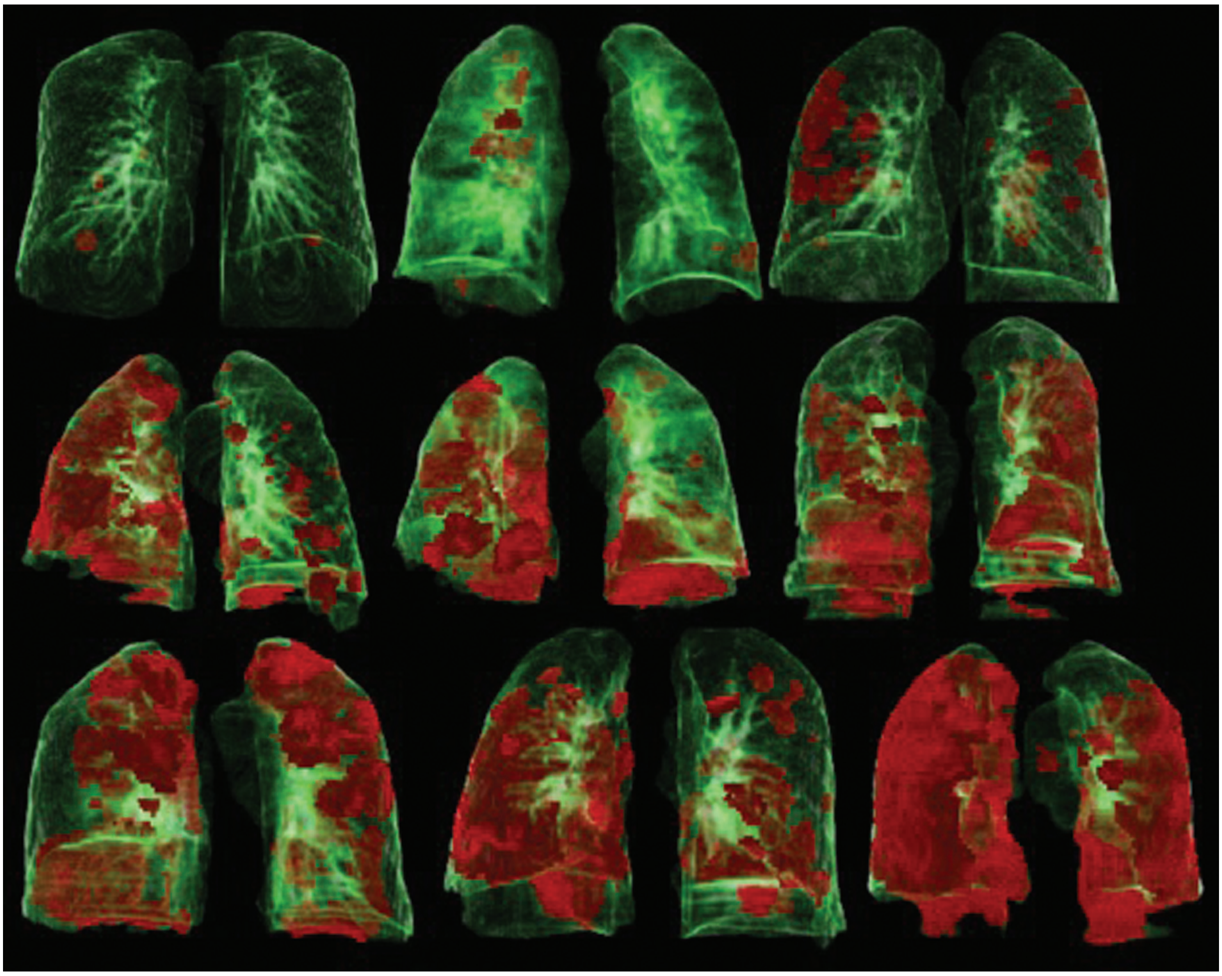

Fig. 41 CT pneumonia analysis: carried out for nine patients showing varying degrees of lung involvement from mild to severe. CT, computed tomography.

indicating a recent infection start to rise from day 5 and IgG indicating an older infection start to rise after 14 days. The IgG levels tend to rise over the next few months. The duration of antibodies that persist is unknown as SARS-CoV-2 is a fairly new infection.[72]

Persistence for at least 60 days is documented with personal communications indicating the persistence of antibodies at even 4 months.

Antibodies from the previous coronavirus SARS-CoV-1 persisted for between 2 and 6 years. The level of antibodies can be measured in serum with quantitative assays.

There are two main categories of IgG antibodies, binding and neutralizing. Binding antibodies bind to the nucleocapsid of the SARS-CoV-2 virus. These bind to the pathogen; however, not necessarily render the pathogen noninfectious. The main utility is to demonstrate the extent of prevalence of the disease in the community. Neutralizing antibodies are antibodies to the spike protein which binds to the receptor-binding domain of the spike, rendering the pathogen noninfectious, as it is unable to bind with the ACE receptor, thus the virus cannot enter the cell. These are known as neutralizing antibodies. Similar principle is encountered in vaccine development. The sensitivity of both assays is very high at 100% with a specificity of 99.8%.

Health care workers are particularly vulnerable to contract SARS-CoV-2, especially at the workplace. They also do not have the luxury of work from home thus need to commute to their health care facility often by public transport, being exposed to community mobility. Further, they may reside in hot spots/containment zones. A serosurvey among health care workers is useful, A high percentage of staff with neutralizing antibodies lends safety to coworkers and patients.[9]

High-Resolution Computed Tomography as a Surrogate for Vaccine Efficacy

The present pandemic continues unabated with increasing ferocity with each wave. The only way out of this pandemic appears to be creating herd immunity to the virus, either innate from infection or vaccination. There are three important terms to determine the efficacy of vaccines, namely, vaccine efficacy, vaccine effectiveness, and breakthrough infections. Vaccine efficacy refers to the ability of the vaccine to reduce the incidence of infection. In a controlled clinical environment, the number of vaccinated individuals getting infected versus the number getting infected after receiving a placebo.

Vaccine effectiveness refers to the rate of infection occurring in the real world. More importantly are the term breakthrough infections when infection breaks through the vaccine shield. Breakthrough infections have been seen with all vaccines as the efficacy and effectiveness of all vaccines are not 100%. In view of breakthrough infections, the real effectiveness of vaccines will be to reduce the severity of infection in terms of the development of pneumonia, hospitalization, and mortality. Merely adding up the number of positive RT-PCR following vaccination will be not of much value; however, what would be important is a measure of the severity of breakthrough infections as compared with nonvaccinated individuals or between different vaccines/vaccination schedules/vaccine combinations.

The CT severity index is a surrogate for determining the severity of illness, it would be a useful and realistic tool to evaluate the real effectiveness of vaccines in reducing the severity of the disease. Initial studies applying this thought process have been performed, the initial results have demonstrated a reduced CT severity index in vaccinated individuals as compared with nonvaccinated individuals.[8]

These results would be important to understand the value and contribution of vaccination, especially in individuals who are not keen on vaccination, thus propelling the planet toward herd immunity.

Infection Control in Imaging Department

We are seeing the most unbelievable and unprecedented time of our lives accompanied with significant uncertainty as to what the future has in store for us. As lockdowns are eased, it is time to get back to work! The pandemic is no way over, hence the risk of transmission and contraction of infection continues to remain significant. SARS-CoV-2 is the virus which causes COVID-19. This is a highly infectious disease which spreads human to human via droplets, aerosols, and fomites. Materials which may carry infection on their surfaces are known as fomites, this is a new word for many. The virus may survive on different surfaces for different periods of time such as cardboard 24 hours, stainless steel 48 hours, and plastic 72 hours.[6]

Wherever there are regions of high human contact, such as workplaces, social gatherings, entertainment zones, shopping areas, airports, and during transportation, transmission may occur from human to human. The only way to attempt to control the spread is to break the human-to-human contact chain. This is the reason why lockdowns have been instituted, so that there is minimal human-to-human contact. However, for survival and combatting the infection, the high human contact zones during lockdown are health care facilities, supermarkets, and pharmacies. Health care establishments are particularly hotspots for infection of uninfected patients, as well as health care professionals. The imaging department is a critical component of any health care facility, thus a high human contact zone. There is need for an SOP for imaging departments to limit transmission of disease from infected patients to health care workers, health care workers to other health care workers, and infected health care workers to uninfected patients. We must not allow the imaging department to become a hotspot, and consequently if it becomes a containment zone, will be a disaster for any health care facility.

There are four main aspects in attempting to control transmission of disease in a health care facility. These are social distancing, PPV, hygiene, and surface decontamination.

Social Distancing

To achieve social distancing in an imaging department, it is very important to reduce the number of human beings in the department by controlling the traffic and crowding in the department. These measures can be both on the patient's side and departmental staff's side. Number of patients can be reduced by scheduling appointments, so that there is no waiting and crowding in the department. Elective procedures, such as mammography, DEXA, lung cancer screening, ILD, follow-up studies, and others, should be postponed as much as possible. A decision to scan patient should be based on how imaging will impact patient care. A discussion with the clinician often helps to decide whether imaging should be performed or not. In the past, we actively marketed imaging and welcomed a crowded imaging department. In this pandemic, we need to do the opposite which is actually market imaging, so that the imaging department is not a crowded zone. Only one relative per patient should be allowed. Since the number of patients and relatives will be reduced, number of waiting room chairs should be reduced by 50%. This also assures social distancing in the waiting areas. On the departmental staff side, to achieve social distancing, only health care workers necessary for primary care are retained on the premises. The rest are encouraged to work from home. Front- and back-office staff can work from home, reports can be transcribed, appointments given, and patients' queries and patient preparation can all be done by calls diverted to the secretarial staff at home. Only skeleton staff to cater to reduced load of patients is maintained. PACS is easily available, very affordable with high data transfer rates available, and imaging specialists can report from home. A dream come true for many! In addition, imaging specialists can use voice recognition dictation software like Augnito and Dragon to dictate their reports. These are nearly 100% accurate with no learning curve, no training required, and not accent dependent. Consequently, there is no need for transcriptionists. Thanks to Augnito, we have dispensed with transcriptionists, a cost saving. Staff on the premises needs to be divided into teams, consisting of all essential staff, paramedical staff, technicians, residents, and consultants. These teams should work in different shifts on different days. They should not meet and interact. The idea being in case one team is exposed to a COVID-19-positive patient and needs to be quarantined the other team can take over. If this is not done, the department can be crippled with a large number of staff being sent into quarantine. It is also important to separate staff into two groups as follows: (1) those who are in direct contact and (2) those who are in indirect contact with COVID-19-positive patients. This will help reduce cross-infection. They should not be allowed to mix, also one should try and create zones such as clean zone, buffer zone, and a contaminated zone. Those coming from contaminated zones should be disinfected in the buffer zone before entering the clean zone. A hotspot which is totally against social distancing is the lunchroom where staff tend to gossip, share lunch boxes, as a result of which lunch room should be monitored well, the timings of lunch staggered, reduce the number of users at a time. Above all, very important to educate the staff.

Screening patients to weed out potential infectors is useful, but far from successful as nearly 70% are asymptomatic. Prior to entry into the department, as well as prior to giving an appointment the patient should be questioned for signs and symptoms of fever, sore throat, dry cough, diarrhea, headache, loss of taste, and smell. Temperature checks may be done on entry to department but as 70% may be asymptomatic carriers, this has limited value.

Personal Protective Equipment

These are the most visible aspect of protection against COVID-19. Of great value when safe distance cannot be maintained between health care worker and COVID-19-positive/suspect. These consists of mask, gown, gloves, face, eye protection, head cover, and shoe covers, depending on the type of exposure whether aerosol generating or not that level of exposure.

Masks: these are the most used PPE. A discussion on types of masks is very important, as there have been several confusing, contradictory, inconsistent, and mixed messages with frequent flip-flops from the authorities, both international, as well as national. This has essentially been based on a short supply of masks and a desire to ration their use. Masks are important as asymptomatic COVID-19 patients constitute 70% of cases, as well as symptomatic patients start shedding the virus for a few days before they are symptomatic.

There are three types of masks, cloth masks, surgical masks, and respirators. Cloth masks are the simplest and cheapest, as they can be homemade or mass produced. They are useful for non–health care workers and uninfected patients. These are useful in public places where it is difficult to maintain 6-feet distance such as grocery stores and pharmacies. However, cloth masks have no significant filtration capabilities as they are 50 times less effective than an N95 mask.

Surgical masks are triple layered where the innermost layer is of absorbent material, absorbs moisture from the wearer's breath to prevent getting wet easily, the middle layer is the important layer which consists of melt-blown material and acts as a filter, and the outer layer repels liquids. The surgical masks have pleats to increase the surface area, so nose, mouth, and chin are covered. The utility of surgical masks is to protect a patient during a procedure. If surgeon coughs or sneezes, patient should not get infected. Surgical masks also protect the surgeon from splashes of fluid such as blood and large particle droplets. Surgical masks are not designed to protect the surgeon from infection. It has a loose fit and allows air to enter from the sides, therefore does not provide any protection from airborne infections.

Respirator masks are utilized to prevent inhalation of air borne infectious material, vapors, dusts, and smoke. They have a high filtration frequency to airborne particles. These are classified based on the filtration capabilities, as well as type of substance filtered. They are also classified according to American and European standards. The American standard is based on the substance filtered, they are classified into N, P, and R types. N stands for when nonoily particles are filtered, P stands when oily particles are filtered such as with exhaust fumes, and R is when some oily particles are filtered. These are further classified based on their filtration efficiency and percentage of particles above 0.3 microns filtered; hence, 95, 99, and 100%. N95 can filter 95% of particles greater than 0.3 micron. Similarly, the European standards define these as filtering face piece respirators (FFP). These are classified as FFP1, FFP2, and FFP3 based on their level of filtration, as well as leakage along the sides. FFP1 is useful for dust, FFP2 for influenza group of viruses, FFP3 for asbestos. N95 has become a synonymous name for both American and European standard masks. These masks have two characteristics, an air filtration system to prevent passage of microorganisms and noxious substances. To achieve this millions of polypropylene, microfibers are layered on top of each other. These are then electrostatically charged to maintain their ability to filter microorganisms or microparticles. The second characteristic is the tight fit. It creates a facial seal, so as not to allow any air to seep in from the sides.

Two new words that we are now getting familiar with is donning and doffing. Donning is the wearing of PPV, whereas doffing is the removal of the PPV. Donning and doffing a mask is of great importance as incorrect donning may not protect the health care worker, as well as give a false sense of security. Incorrect doffing may result in contact with the outer potentially contaminated surface resulting in transmission of infection.

The procedure for donning of a face mask will start with hand hygiene, place the mask on the face, covering the nose and mouth, secure the elastic bands, upper one on the crown of the head, and the lower one below the ear at the base. Next is to fit and mold the flexible nose clip. Finally ensure it fits snuggly around the nose, face, and chin with an adequate seal (►**Fig. 42**). A tip to ensure the nose clip has formed an effective seal is if reading glasses fog up the seal is not effective, then the nose clip needs to be tightened to prevent an air leak.

Also, once the N95 is worn, it is important to see that there is user seal check to see that the respirator is donned correctly, and this must be done every time the respirator is donned. This will ensure that there is a tight seal. To test the seal, a positive seal check is done when on exhalation the face piece should bulge, and a negative seal check is done on inspiration the face piece should collapse. It is very important that if an individual has a beard, one should shave the beard as the tight fit is not possible with a beard.

The doffing again starts with hand hygiene. It is very important not to contact the front surface of the masks,

Fig. 42 Technique for donning a mask.

because this may be potentially contaminated. To avoid this, grasp the bottom elastic, bring it forward over your head, then with the upper strap over the head and remove the mask holding both ties, so the masks is not touched at all. Dispose the mask off as infectious waste

There are numerous controversies and queries regarding N95 masks. These are regarding valved or unvalved masks, the reuse of masks, when to discard, as well as fake N95 masks.

Valved masks have a one-way valve which is an exhalation valve. This is very useful for the user as it provides comfort, prevents condensation inside the mask, misting of glasses, and helps the individual breathe easier. On the other hand, the unvalved traps heat and vapor from the mouth. The valved should not be used by a COVID-19-positive, as it will contaminate the surrounding. The user is safe, but the surroundings are not safe if the others are not wearing N95 masks.

Another important point is when to discard the N95 mask. If you see any tears or holes, if it does not form an effective seal to the face, if it becomes wet or visibly dirty, contaminated with blood, body fluids, or respiratory nasal secretion, as well as after every aerosol-generating encounter, it should be discarded. N95s can be reused. Air drying for 72 hours kills the virus, moist heat, chemical sterilization with H_2O_2, whatever is done should not affect the fit or compromise filtration capabilities. A simple way to reuse N95 is to keep three N95s, after each day put the N95 in the paper bag and then reuse after 3 days. Valve mask should be washed with water and soap. One should also be careful about fake N95s, this is a common issue that occurs when there is shortage. A recent study reveals 60% of N95 did not achieve required filtration, some only achieved 35% filtration rather than 95%.[73]

The N95 should be certified by the National Institute for Occupational Safety and Health (NIOSH).

An often-asked question is which mask should be worn. Well, everybody should wear a mask and that is the law now. For non–health care workers, ideally, a surgical mask should be the choice, though this may not be possible ,as it is a disposable mask, multiple may be required in a day, as they get moist easily and therefore may become unaffordable for the wearer. A three-layer cotton mask is a useful alternative though not as effective. Its advantages are reusable and washable.

For health care workers, the ideal is an N95. If not available, surgical mask is an alternative. If a surgical mask is used it must be worn properly, with good hand hygiene and disposed of properly.

Face shield and goggles: these are to be used to prevent contamination of mucus membranes of eyes, nose, and mouth due to droplets generated by coughing and sneezing. They can help to prevent inadvertently touching the eye, nose, and mouth with a contaminated hand and very useful during aerosol generating procedures. Goggles should have a tight fit providing a good seal with the skin of face and surrounding regions. They should accommodate prescription glasses. Face shield should cover side of the face laterally, forehead superiorly, as well as chin inferiorly. An antifog feature helps to improve clarity.

Gloves: these are useful in creating a barrier between the wearers hand and contaminated surfaces. It prevents a contaminated hand from directly touching the eyes, nose, and mouth, thus breaking the contact chain. However cross contamination across surfaces may occur. In fact, frequent hand washing is found to be superior. Nitrile gloves are recommended over latex, as they are more chemical resistant to disinfectants especially chlorine. Allergic dermatitis may also occur to latex. Nonpowdered are preferred over powdered.

Coveralls/gowns: these create a barrier, preventing exposure to contaminated droplets/secretions/body fluids. These are very useful when a health care worker needs to be within 1 meter of a COVID-19-positive/suspect. Coveralls provide a 360-degree protection, as they cover the entire body. Gowns are equally acceptable. There is a lack of a comparable evidence regarding the efficacy of overall and gowns. The gown should cover torso from the neck to the knee and arms till the wrist, as well as wrap around the back. These are fastened at the neck and the back. An apron can be worn over the gown. There are stringent standards for PPE quality in acting as an impervious barrier to biological and chemical hazards. These are monitored by many standards such as Sitara, Satara, DRDO, ISO-16603/class 3 exposure pressure, or equivalent.

Shoe covers: these are made of impermeable fabric to cover shoes, providing personal protection preventing contamination of footwear.

Head covers: coverall do not require head covers as part of the coverall. When a gown is used or an aerosol generating procedure is done, a head cover is required. This should cover the head and back off the neck, all hair and hair extensions need to be included within the head cover.

Donning and doffing of coverall/gown: like masks, the donning/doffing process is very important. Every donning and doffing process starts with hand hygiene. The order of donning and doffing vary between different institutions; however, the principles stay the same. The outer surface of the PPE is always considered contaminated; therefore, the gown is removed after unfastening the ties and gown pulled away from the body at the level of the neck, shoulders, touching only the inside of gown. Once doffed the gown is turned inside out and folded and rolled up into a bundle and discarded in a waste container. Similarly, gloves are removed inside out, always sanitizing first and after. Ideally, doffing is done in front of a mirror or a colleague to ensure no mistakes are made; inadvertently, the outer contaminated surface should not be touched.

Surface Decontamination

Surfaces should be divided into two types as follows: (1) minimal hand contact surfaces such as floors and ceiling, these can be cleaned once a day; And (2) frequent hand contact surfaces where there is frequent hand contact such as high touch surfaces, doorknobs, light switches, walls, keyboards, mouse, and others. These should be cleaned more frequently, every 4 hours. There are different materials which can be used for sanitization of contact surfaces, 62 to 70% ethanol, 0.1 to 0.5% sodium hypochlorite, 2% glutaraldehyde, and 0.5% H_2O_2. All these reduce the infectivity of the virus by a factor of 3 after minute of contact. It is important not to sweep rooms, as this will cause aerosolization, wet mop should only be used. For equipment, monitors, and keyboards, wet wipes should be used.

There may be aerosolization into examination rooms by a COVID-19-positive patient, air exchanges are required to remove potentially infectious particles by circulating fresh air. The time required to change the air in the room with fresh air is important. This depends on the number of air exchanges. The greater the air exchanges, the faster the room air is recirculated. Generally, most imaging departments have six air exchanges per hour. Positron emission tomography-CT (PET-CT) has 23/24 air exchanges per hour to remove isotopes. Therefore, it is better to image COVID-19 patients in PET-CT, as the higher air exchanges ensure a shorter closure time of the CT examination room.

Equipment cleaning: surface decontamination of imaging equipment is very important, especially after imaging COVID-19 suspect/COVID-19-positive patients.

Portable X-ray is the most used imaging equipment in evaluation of COVID-19 patients at the bedside. A dedicated portable X-ray machine should be placed in the COVID-19 ward. This should not be moved out to avoid cross-contamination. The machine should be covered by surgical drapes. Postimaging, the drapes are discarded as infectious waste. The imaging detector is what encounters the patient, therefore needs the most attention. The detector is put inside two disposable bags, easy and practical are commonly available black garbage bags. The radiographer dons PPE and takes the X-ray. Post–X-ray, the detector with double bag is removed. The outer bag is sanitized by the radiographer, he then hands it to another radiographer waiting outside the COVID-19 ward who takes the detector with inner bag, the outer bag is discarded as infectious waste by the radiographer in the COVID-19 ward. The radiographer outside sanitizes the inner bag and then removes the detector processing, discarding the inner bag. The external surface of detector should also be sanitized.

Sonography is often required for evaluation of deep venous thrombosis, as well as for abdominal complaints. Initial recommendation for using sonography for lungs at point of care has not taken off. The process is quite time consuming, requiring donning and doffing of radiologist, as well as sonography machine. There is a significant learning curve for radiologists to achieve competence. The information available does not seem to view what is available from a portable chest X-ray. Again, a dedicated machine should be placed in the COVID-19 ward. Preferably a hand-held machine, if not cart type. The cart should be stripped of all paraphernalia, such as printers and gel bottles, and gel sachets would be useful. The machine should be covered by drapes which postprocedure are discarded. Postprocedure, the probes, cord, and machine surfaces are wiped down with alcohol wipes. The probes may be covered in plastic.

CT scan has made a huge impact for triage and determines the severity of infection. Ideally, if two or more CT machines are available, then one should be dedicated for COVID-19 patients. PET-CT is utilized in the morning hours and is free in the afternoon onwards, it also has much higher air exchanges, so it is useful to utilize the PET-CT for COVID-19 CT. The CT table is covered with a disposable polythene sheet or soft cloth soaked in chlorine concentration of 2,000 mg/L, prior to scanning patient. Postprocedure, the table and gantry are cleaned with alcohol 60 to 75%. The room is kept closed for air exchanges postprocedure. The time required is based on the number of air exchange

Psychological Aspects

Imaging department staff suffer from psychological pressure, especially the fear of contracting the disease at the workplace, further carrying the disease home. Reassurance, education about safe practices, and boosting morale are very important. Shorter working hours help a lot, as they are away from home for shorter periods, encouraging frequent phone calls to their homes is very useful to reassure staff and people at home, something many work practices did not encourage in the past, that is, personal calls. Family support helps boost the morale of staff a lot. If they are apprehensive about carrying the disease home, they may be accommodated on the hospital premises or nearby hotels.

Economic Aspects

Due to social distancing and fear of stepping out, patients are not visiting health care facilities, this has resulted in a 70% drop in imaging volumes. This is a problem for health care facilities, as imaging department works as a catalyst to generate work for health facilities. There is always a pressure to image which always works against social distancing. It is important to then cut costs, till the top line picks up again.

One of the low hanging fruits is if you still print films. With the fear of fomites this is the best time to get out of this wasteful expenditure. Move to compact disk (CD), electronic transfer of images, and cloud storage. These are all very reasonable and should help reduce the bottom line by 10 to 30%. Other measures, reduce number of staff by automating appointments, patient queries, dictating, and transcribing reports. Stop referral fees can be useful. Imaging departments are going to feel the pinch for getting new equipment. Managements are not going to be keen to give high-end equipment, toys for the boys, everything will need to be financially justified. An area of controversy is regarding the recent trend to have specialist and sub specialist imaging specialists. These are a significant expense on the professional side. Managements may be keen to curtail professional expenses and possibly look toward multimodality, multiorgan imaging specialists. On the flip side, managements may be happy to outsource specialty reporting to imaging specialists who serve multiple centers/institutions to cut professional costs.

Where Have All the Diseases Gone?

With the COVID-19 pandemic showing no signs of letting up, we need to grapple with a new normal. Less work for sure, this may not be so bad, more time for hobbies, more time with family, more time to do what you always wanted to do. Hopefully, this less work will allow us to move back from volume-based practices which we were all forced to get into, back into value-based practices, and thus bring health care back from being an industry with all its ills, to being a profession once again.

Finally, COVID-19 appears to be supporting Darwin's theory of natural selection. Individuals with lifestyle diseases are worse off with COVID-19 maybe a message for us to get fitter and for sure more hygienic!

Conclusion

In conclusion, this pandemic taught us the immense value of imaging. CT has played a stellar role in this pandemic, much against the recommendations and guidelines issued by numerous national societies.[2] The following inferences can be drawn:

- Public health tool to detect COVID-19 pneumonia when RT-PCR is falsely negative, this could have a significant impact in controlling a pandemic when early detection of as many cases is possible to contain spread of disease and consequently bring a pandemic under control quicker. HRCT has the added advantage of a very quick turnaround time as compared with RT-PCR. CT can play a previously undiscovered role as a public health tool to detect super spreaders early. The important point to remember CT may be negative in a positive RT-PCR individual and vice versa, so they are complementary investigations and not competitive. Unfortunately, imaging societies across the globe missed this point and advised against the utilization of HRCT for this important purpose and recommended only RT-PCR be used. This lack of utilization of HRCT may possibly be termed as one of the missing keys in controlling the pandemic.
- Triage of patients: probably, the most important contribution of CT has been the CT severity index or percentage of lung involvement. Not only does the CT severity index demonstrate the extent of lung involvement which helps prognosticate, but this has played a pivotal role in triaging, due to the sheer number of infections in each wave the main fear is the over burdening of medical facilities, thus it becomes very difficult to determine which patients deserve what treatment facilities in a very short period. The severity of lung involvement correlates extremely well with oxygen requirement, type of oxygen requirement invasive/noninvasive or ICU admissions.**4** This triaging by HRCT can and helped tremendously in reducing the burden on medical facilities during the pandemic waves. AI is playing a strong role to accurately quantify the extent of disease removing subjectivity. Another important conclusion is that AI at present will not be able to replace the experienced radiologists but will function as a useful ally.
- Complications of COVID-19: imaging has played its traditional role of detecting disease severity and complications, especially progression to ARDS, white out lungs, pulmonary thromboembolism, complications of mechanical ventilation, and barotrauma, where bedside portable chest X-ray has played an excellent role, as well as the extrapulmonary complications, such as cardiac, neurological, and fungal infections, where MRI has played a primary role.
- Vaccine efficacy: HRCT is playing out a new undescribed and evolving role in the pandemic by its ability to demonstrate disease severity, thus assisting in determining vaccine efficacy.

Conflict of Interest
None declared.

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