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Review Article

Imaging in diagnosis and management of COVID 19: A short review

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ABSTRACT

Since the outbreak of COVID 19 in early December 2019, the WHO has reported over 33 million cases and more than one million deaths worldwide. The Pandemic has thrown all forms of life out of gear and has transformed into a global emergency, causing widespread havoc. There is currently no treatment for the disease and early diagnosis is also becoming more challenging. This review focuses on the structure of the virus, its etiology, epidemiology with emphasis on diagnosis and imaging.

Key Messages: The COVID 19 pandemic has thrown life out of control with the new norm. Here we review the Diagnosis of COVID with an emphasis on imaging.

1. Introduction

Coronaviruses (Covs) are considered to be large, enveloped viruses having the genetic material as single stranded RNA (+).[1] These viruses were earlier known to cause Rhinitis and diarrhea in humans.[2] Many classes of coronaviruses are known to exist, including those which cause mild upper respiratory tract infections. Coronavirus Disease 2019 (COVID-19) is a respiratory illness that was identified in Wuhan and has spread among humans since December 2019.[3] Before COVID-19, the world witnessed an outbreak of severe acute respiratory syndrome (SARS) caused by SARS-CoV during 2002 in Guangdong, China. This affected around 8098 individuals and caused 774 deaths in at least 6 countries.[4] Following this outbreak, during 2012, the Middle East respiratory syndrome (MERS) caused by MERS-CoV in the Middle east surfaced.[5] To date, MERS-CoV has infected about 2468 individuals and caused 851 deaths worldwide.[6]

The new Corona virus is known to have originated in bats and further transmitted to humans via intermediate animals which are still unknown.[7,8] The disease caused by the new species, termed as COVID 19, has been declared a Pandemic by the World Health Organization (WHO).[9] The symptoms of COVID 19 infections are manifested primarily in the lung region, while other organ systems could also get affected.[10] The infection manifests itself as a mild fever, dry cough and breathlessness, but other symptoms like headache, lightheadedness and fatigue may also occur.[11] Mortality rates appear to be more in older, immuno compromised patients and those with comorbidities.[12]

1.1. The virus

The CoVs are RNA viruses with a crown like appearance (coronam) attributed to the glycoprotein spikes on its envelope.[7] They belong to the order Nidovirales of the coronaviridae family, and the Betacoronavirus genus.[13] The viral particles measure around 80 to 160 nm. The coronaviridae family has been classified into 4 genera—alpha (α) coronavirus, beta (β) coronavirus,

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gamma (γ) coronavirus, and delta (δ) coronavirus.[14] The coronaviruses and β coronaviruses infect only warm-blooded animals. The γ coronaviruses and δ coronaviruses infect birds, but some of them can also infect mammals. The nucleocapsid is found within the envelope having a helical symmetry, which makes the virion distinct from the other viruses. The structural proteins found are the S protein (Spike), M Proteins (membrane), E protein (Envelope) and N protein (nucleocapsid).[15,16] All these proteins are embedded in the $3'$ end of the viral genome. The spike protein gains access to the Endoplasmic reticulum via N terminal signals and is glycosylated.[17–20]

1.2. Epidemiology

It is reported that all age groups are susceptible to the virus. The infection is transmitted via droplet nuclei during sneezing or coughing.[7] The disease may be symptomatic or asymptomatic. The nasal cavity is known to have higher viral burden that the throat which might be the fine line between symptomatic and asymptomatic patients.[16] A few individuals may act as "super spreaders". The mean incubation period for the virus was reported to be 5.2 days.[19] Unusual cases may have incubation period of even 19 days.[20]

1.3. Diagnosis of COVID 19

1.3.1. Lab-based Tests: RT-PCR molecular testing

The primary method of detection of COVID-19 is the RT PCR[21] (detection of viral nucleic acid), involving 2 steps: extraction of viral RNA and PCR amplification and probe based detection. But this process is known to be cumbersome and delays in receiving results.[22]

2. Reverse-Transcription-Loop-Mediated Isothermal Amplification (RT-LAMP)

This test involves amplification of nucleic acid at a particular temperature and is viral gene specific. This is known to be a lot more sensitive than RT-PCR tests.[23]

2.1. Antigen-based tests

This test involves the use of a double antibody sandwich enzyme-linked immunoassay which identifies the nucleoprotein of the SARS-CoV-2. This is accomplished via the use of microplates pre coated with the specific antibodies against the virus, and also uses horseradish peroxidase (HRP)-labeled secondary antibody against the same protein. The method is relatively simple and rapid.[24]

3. Potential Role of Imaging in Diagnosis and Management of COVID 19

As per WHO and other authorities from the medical fraternity, it is understood that the definitive test for SARS-CoV-2, the virus causing COVID-19, is the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test and is believed to be highly specific, but with sensitivity reported as low as 60-70% and as high as 95-97% depending on the country. Thus, according to the experts, false negatives are a real clinical problem and several negatives might be required in a single case to be confident about excluding the disease.[22] The role of Imaging in the setting of COVID-19 is emerging and evolving every day. The Centers for Disease Control (CDC) does not currently recommend CXR or CT to diagnose COVID-19. Viral testing remains the only specific method of diagnosis. Confirmation with the viral test is required, even if radiologic findings are suggestive of COVID-19 on CXR or CT. Health care workers have found imaging to be a very valuable method for early diagnosis of the condition.[25] The radiologist's role becomes very important during these times.[26] Medical imaging techniques like Chest Tomography (CT) has played a vital role in the early detection and management of the virus. The lung presents itself with lesions with ground glass opacities, bilateral shadowing, fibrosis etc.[27] This plays a key role in monitoring the conditions of patients.[28]

The workflow indicated in Figure 1 recommends doing an X-ray as a triaging imaging pathway before employing a CT scan.

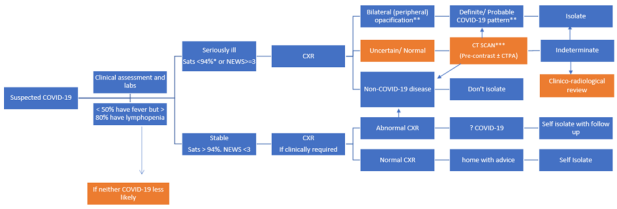

Fig. 1: Radiology decision tool for suspected COVID-19: Courtesy: https://www.bsti.org.uk/training-and-education/covid-19-bsti-imaging-database/)

4. Case History

The American College of Radiology (ACR) recommends that facilities may consider deploying portable radiography units in ambulatory care facilities for use when CXRs are considered medically necessary. The surfaces of these machines can be easily cleaned, avoiding the need to bring patients into radiography rooms. The most common abnormal finding in the chest x-ray scan of a suspected COVID-19 patient is ground glass opacities (Figure 2) meaning that some portion of the lungs look like a hazy shade of grey instead of being black with fine white lung

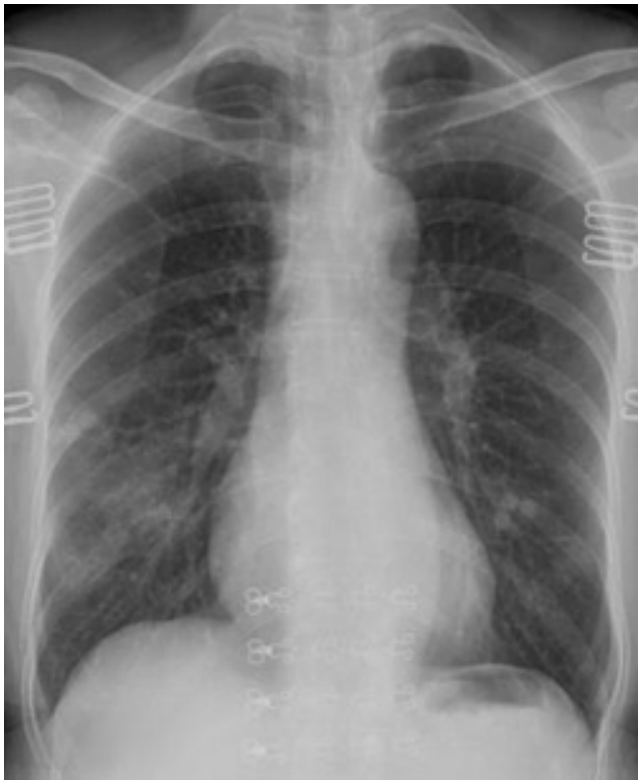

Fig. 2: Chest x-ray scan of a suspected COVID-19 patientCourtesy: https://radiologyassistant.nl/chest/covid-19/covid19-imaging-findings

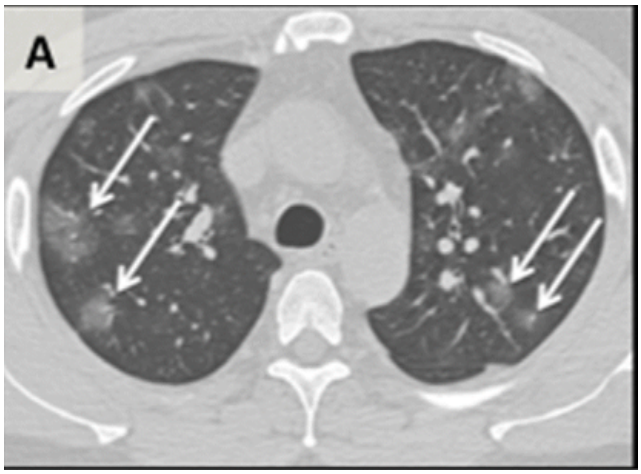

Fig. 3: An axial CT image obtained without intravenous contrast in a 36-year-old male shows bilateral ground-glass opacities in the upper lobes with a rounded morphology (arrows).[29]

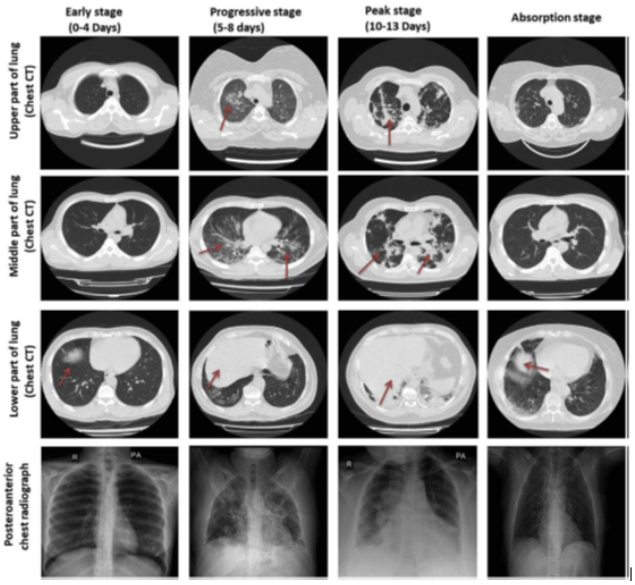

Fig. 4: Chest X-rays and computerized tomography (CT) images of COVID-19 patients. Four stages in COVID-19 patients; 1: early stage (0–4 days), 2: progressive stage (5–8 days), 3: peak stage (10–13 days), and 4: absorptionstage[30]

markings for blood vessels.[31,32]

As per an article published in healthcare-in-europe.com.[33] chest X-ray is the first method to diagnose Covid-19 coronavirus infection in Spain. Getting results of the PCR test may take several hours. The chest X-ray is a discriminating element. As per Dr. Milagros Martí de Gracia - Vice President of the Spanish Society of Radiology (SERAM), President of the Spanish Society of Emergency Radiology (SERAU) and head of the department of emergency radiology at La Paz Hospital in Madrid "Usually the absence or presence of pathological findings on chest X-ray is determining to send the patient home or keep him/her under observation But if the clinical suspicion is high and the PCR or/and chest X-ray is normal, a chest CT is indicated". CT scans have been shown to be one of the valuable tools to rapidly and accurately diagnose COVID-19 infection and help triage patients for treatment. CT scans allow us to see the early changes in the lungs caused by COVID-19. Initial publications in the literature show that CT may provide relevant information to clinicians during diagnosis, as well as in disease monitoring/characterization/staging.[28] Among the most common features observed in CT imaging are ground glass opacifications (GGO), consolidation and a bilateral, peripheral distribution of nodules (Figure 3).

Chest CT examination is known to be advantageous as it requires a shorter examination time and results may be rapid. The high resolution images pose another very good advantage. Further these results have a higher degree of reproducibility.[31] Early characterization of lung lesions,

and also assessing the severity makes this technique a lot better. Follow up imaging showed rapidly changing images and in patients who recovered from COVID-19 pneumonia. The chest CT abnormalities appeared to gradually decrease two weeks after the initial onset of symptoms. Hence this has been proposed to be a rapid and accurate method of diagnosis.[31] An image of the phases of recovery is shown below in Figure 4.

On 7th April, RSNA Published multinational consensus statement from the Fleischner SocietyStatement on Chest Imaging and COVID-19. As per the report:

1. Imaging is indicated for patients with moderate to severe features of COVID-19 regardless of COVID-19 test results.
2. Imaging is indicated for patients with COVID-19 and evidence of worsening respiratory status.
3. CT is indicated in patients with functional impairment and/or hypoxemia after recovery from COVID-10.
4. COVID-19 testing is indicated in patients incidentally found to have findings suggestive of COVID-19 on a CT scan.

5. Discussion

Chest CT has a high sensitivity for diagnosis of COVID-19. Chest CT may be considered as a primary tool for the current COVID-19 detection in epidemic cases.[34] Chest CT had a low rate of missed diagnosis of COVID-19 (3.9%, 2/51) and may be useful as a standard method for the rapid diagnosis of COVID-19 to optimize the management of patients.[35]

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8. Conflict of Interest

No conflict of Interest is reported

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