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SE DE SE		E OF HRCT CHEST IN COVID-19 : A ERATURE BASED REVIEW	KEY WORDS: COVID-19, SARS-COV-2, GGO, HRCT
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Coronavirus Disease (COVID-19) has become a worldwide pandemic lately. Most people experience mild to moderate respiratory illness and recover without requiring special treatment. Older people with comorbidities are more likely to develop serious illness. Imaging plays a cardinal role in early detection and prompt action pertaining to the severity of disease status. In this literature based review objective is to designate typical and atypical imaging findings, staging			

and follow-up of COVID-19 patients.

INTRODUCTION World Health Organization has declared Coronavirus disease 2019 (COVID-2019) caused by SARS-CoV-2 to be a pandemic and public health emergency of international concern on march 11 2020[1]. As of June 25, 2020, the epidemic had spread to more than 200 countries and more than 3 million individuals have contracted the virus worldwide with 451950 reported deaths, including more than 600000 confirmed cases and 15000 deaths in India. However, these numbers are probably underestimated as not all patients are tested, especially those who are asymptomatic, or with only mild symptoms and no associated comorbidities.

The gold standard for confirming COVID-19 relies on microbiological examination and was identified employing deep sequencing analysis [2]. The virus, named severe acute respiratory syndrome coronavirus2 (SARS-CoV-2) [3], is phylogenetically closest to bat SARS-like coronavirus but in a separate clade with increased infectivity. SARS-CoV-2 proved to have the ability for efficient human-to-human transmission [4]. The explosion of confirmed cases of COVID-19 has been overwhelming, even though the mortality of COVID-19 is lower than that of SARS-CoV and MERS-CoV.

The route of transmission (i.e., isolation of suspected cases, disinfection) is the most effective way to fight the COVID-19 outbreak. The epidemiologic, laboratory and clinical features of COVID-19 pneumonia have been described [5]. However, infections by other viruses, such as influenza A and influenza B, can cause the same clinical symptoms as COVID-19, which makes the clinical diagnosis of COVID-19 pneumonia difficult, especially during flu season. For the large number of cases of suspected COVID-19, laboratory detection is time-consuming and may not be available for all people with suspected infection owing to the shortage of test kits for SARS-CoV-2. These challenges increase the risk of spread by free movement of people with highly suspected disease. In addition, the laboratory test can have false negative results^[6].

Role Of HRCT chest in diagnosis

The standard of reference for confirming COVID-19 relies on microbiological tests such as real-time polymerase chain reaction (RT-PCR) or sequencing [7]. However, these tests might not be available in an emergency setting and their results are not immediately available. Computed tomography (CT) can be used as an important complement to RT-PCR for diagnosing COVID-19 pneumonia in the current epidemic context. Indeed, when the viral load is insufficient, RT-PCR can be falsely negative while chest CT shows suggestive abnormalities [7-8]. A large series based on 1014 patients reported a 97% sensitivity of chest CT for the diagnosis of COVID-19, while the mean time interval between initial

negative and positive RT-PCR was approximately 5 days [7]. Thus, CT can play a pivotal role in the early detection and management of COVID-19 pneumonia [9], at least for patients who have been symptomatic for more than three days. Indeed, 56% of patients imaged during the first 2 days following symptom onset may have normal CT findings^[8].

COMMON FEATURES IN HRCT

To date, many descriptive studies and case reports have focused on the CT manifestations of COVID-19 [10-19] According to the literature, the characteristic patterns and distribution of CT manifestations: ground glass opacification (GGO), bilateral involvement, peripheral distribution, and multilobar (more than one lobe) involvement . Although, the typical findings of chest CT images of individuals with COVID-19 are multifocal bilateral patchy ground-glass opacities (GGOs) or consolidation with interlobular septal and vascular thickening, mostly in the peripheral fields of the lungs . The most common morphology of these opacities are patchy and round ones, followed by triangular and linear ones [20,21] . The triangular or angular GGOs under the pleura with thickened internal interlobular septa is considered a new sign that one research paper has termed the "spider web" [21]. Special classic signs, including "crazy paving" or "reverse halo", can also be seen, while cavitation, nodules, pleural effusions, and lymphadenopathy are rare.

Other CT findings included interlobular septal thickening, bronchiectasis, pleural thickening, and subpleural involveme ment, with various rates across the studies [19-21]. Pleural effusion, pericardial effusion, lymphadenopathy, cavitation, CT halo sign, and pneumothorax were less common or rare ^[22-24].

Spatial distribution :

The pooled incidence of various patterns of distribution across all the abnormal CT's varies among different patients. As per the available literature, the Bilateral distribution of the opacities (mostly GGOs or mixed lesions) in a peripheral/subpleural distribution mainly located posteriorly in the lungs (was the hallmark feature of the distribution of lesions due to COVID-19) in our review. A few studies described the lobar distribution of the lesions. The lesions were most commonly seen in lower lobes with a higher incidence of each of the lower lobes in the pooled analysis.

Imaging pattern in different Age group:

Varying pattern in different ages, facilitate more accurate diagnosis and the development of treatment strategies. According to the data available so far, there were fewer lesions in younger age groups and adolescents than in middle

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aged and older patients. The lesions showed varying agerelated differences in distributions of the lung lobe and lung field. With increase in age, the lesions appeared to be mostly GGO with interlobular septal thickening or a crazy paving pattern, and the possibility of the appearance of 5–10 cm large patchy opacity and \geq 10 cm larger patchy opacity was likely to increase.

Middle-aged and older patients had more severe lung involvement and lobe involvement and, at the same time, the lesions were accompanied more often by air bronchograms. Possible reasons for these findings are as follows: 1) adolescent cases are mostly third-generation infection cases, which may involve mainly family cluster cases . Furthermore, COVID-19 has weak virulence, resulting in lighter imaging signs in these patients [25], 2) minors have immature lung structure development, resulting in atypical HRCT signs, and, 3) a COVID 19 attack on the immune system is more likely to cause diffuse alveolar damage and a large number of inflammatory exudations in middle-aged and older patients with more baseline diseases, the key finding is that the middle-aged and elderly patients have the most severe representation of parenchymal findings, and follow with the morphological appearance that seems to be particularly limited in youngest group, which provides certain support for clinical individualized treatment of patients of different ages.

Chest HRCT scans are helpful for screening, treatment management, and follow-up evaluation of suspected patients with COVID-19 infections, and they are complementary to clinical symptoms (fever), epidemiological history (direct or indirect exposure with COVID-19 positive people), and laboratory indicators. Therefore, it is essential to make full use of chest HRCT scans to achieve a comprehensive diagnosis and guide treatment for patients with COVID-19 infection. It is worth noting that the epidemiological pre-test risk drives the diagnosis towards COVID-19, which otherwise does not have a specific pattern compared to any other infectious interstitial infiltrate with further diffuse alveolar damage (DAD) or organizing pneumonia (OP).

IMAGING FEATURE WITH VARYING STAGING/SEVERITY OF COVID-19

COVID-19 pneumonia CT features change over time, with different presentations according to the phase and severity of lung infection. Pan et al. investigated lung changes by time in patients who recovered from COVID-19 [26]. They classified the evolution of lung abnormalities into four stages (early 0-4 days, progressive 5–8 days, peak 9–13 days, and absorption \geq 14 days) according to time periods. They visually quantified the extent of CT abnormalities. Each of the 5 lung lobes was visually scored from 0 to 5 as follows: 0 for no involvement , 1 for < 5% involvement, 2 for 25% involvement, 3 for 26%-49% involvement , 4 for 50%–75% involvement , and 5 for > 75%involvement [26]. The total CT score ranged from 0 to a maximal value of 25. They found that the total CT score increased until about 10 days after symptom onset and then gradually decreased. Regarding the category of CT abnormalities, stage 2 was characterised by an increase of GGO extent, with a crazy-paving pattern more frequently observed [27]. On the opposite, in stage 3, consolidation was the main feature with a decreased GGO ratio.

CT findings in the intermediate stage of the disease were characterized by an increase in the number and size of GGOs, a progressive transformation of GGO into multifocal consolidation . with septal thickening and development of a crazy-paving pattern [27]. The transformation of GGO into linear consolidation is typical for evolution towards organizing pneumonia, which is a nearly universal response to lung injury whether it is focal or diffuse, due to infection, radiation therapy or following drug-induced pneumonitis^[26]. Wang et al. also evaluated longitudinal changes and confirmed that pure ground glass was the most common observation after symptoms onset, whereas a mixed pattern combining ground glass with irregular linear opacity peaked on illness days 6-11 [29]. In patients with clinical worsening not explained by an extension of lung opacities on CT, pulmonary embolism should be suspected and a contrastenhanced CT examination should be performed if possible, taking into consideration the clinical severity and the renal function. Of note, patients with severe COVID-19 pneumonia have a marked elevation of d-dimers, so that these d-dimer levels does not help identify those who have superimposed pulmonary embolism^[30].

Pan et al. [31] showed the temporal course of CT changes in 21 confirmed cases of COVID-19. In early stages, the majority of their patients showed more GGO and a lower number of involved lobes compared with the later follow-up scans. However, intensification of a crazy paving pattern, increase in the number of involved lobes, and appearance of consolidative opacities occurred in most patients over time. On average, CT findings were most prominent on day 10 of the disease. After day 14, improvement in imaging findings was reported in 75% of the patients, including decreased number of involved lobes and resolution of crazy paving pattern and consolidative opacities [31].

DISCUSSION:

CT imaging can demonstrate typical patterns of imaging manifestations that could be used to diagnose COVID-19. In this review, we describe the key imaging findings for diagnosis, stratification, and early follow-up of patients with COVID-19 based on various HRCT imaging characterstics, after compiling the data from published literature. The source of this literature was pubmed and Google scholor.

GGOs, whether in isolation or coexisting with other lesions like consolidations, interlobular septal thickening, or crazypaving, were uniformly the commonest lesions among all the studies, according to our review. In one of the large case series by Wang et al, all the 138 patients included in the study had GGOs [29]. Bilateral, peripheral/subpleural, posterior distribution of the opacities with a lower lobe predominance was the most common distribution pattern, which is in agreement with previous studies. However, it is to be noted that the pooled incidence in our review revealed that the prevalence of GGOs was quite higher and that of mixed lesions with mixed lesions being reported more commonly than before, in contrast to the previous review^[32].

The CT findings in COVID-19 are attributed to infection of type II alveolar epithelial cells via ACE2 receptors by the SARS-CoV virus. The virus replicates and triggers cellular apoptosis in alveolar cells. Pathological changes in COVID-19 resemble those of severe acute respiratory syndrome (SARS) and middle Eastern respiratory syndrome (MERS) [33]. The viral particles released from the cell infect other cells, inducing the release of proinflammatory cytokines and causing wide spread alveolar epithelial damage. This leads to exudation into the alveolar space with diffuse alveolar damage and fibrin-rich hyaline membranes. This produces the ground glass opacities and consolidations encountered on CT. Aberrant healing mechanisms are triggered which cause scarring of the epithelium causing fibrosis at resolution ^[34]

The imaging findings in COVID-19 closely resemble those of MERS and SARS leading to a notion that it is a part of the acute lung injury caused by viral pneumonia. The mortality rate of COVID-19 is lower than that of these previous viral pneumonias. RT-PCR from the samples collected from the sputum or throat swab currently serves as the gold standard for the diagnosis of COVID-19. However, the reports take hours to arrive and it also has a high false negative rate. The

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sensitivity of RT-PCR may be as low as 60-70%, mainly attributed to insufficient samples. Therefore, patients with pneumonia due to COVID-19 may have lung abnormalities on chest CT but an initially negative RT-PCR^[31].

Chest CT has proven to be a useful supplement to RT-PCR and has been shown to have high sensitivity to diagnose this condition early [36]. However, some authors have shown that as many as 50% of the patients with positive RT-PCR can have a normal CT at 0-2 days after symptom onset [31]. Keeping all these considerations, Fleischer Society has released its recommendations for the use of imaging during this pandemic [35]. Imaging is not routinely indicated in asymptomatic patients for screening or in low-risk patients with mild clinical symptoms. Imaging is now indicated in a patient with COVID-19 only if he/she has moderate to severe pneumonia or worsening respiratory status or is at risk of progression or those with functional impairment or hypoxemia after recovery. In these subsets, CT in combination with laboratory testing should be used judiciously to diagnose and monitor the response to treatment.

CONCLUSION:

In conclusion, CT imaging can help in early diagnosis, staging, treatment planning and initial follow-up of patients with COVID-19. The most common CT manifestations are bilateral, periph-eral/subpleural, posterior GGOs with/without consolidations with a lower lobe predominance. It is pertinent for the radiologists and the clinicians to be familiar with various manifestations of COVID-19 on CT, so that they can impact the clinical decision making and management for these patients, which is the need of the hour, more than ever.

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