Role of CT Scan in Diagnosis of COVID-19 Infection: A Review

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This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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1. INTRODUCTION

The highly contaminant infectious diseases Severe Acute Respiratory Syndrome, or COVID-19, caused by Coronavirus Disease 2019 (SARS-CoV-2), caused more than 2.9 million deaths worldwide, the most serious of the global health crisis since the 1918 influenza pandemic, have had a catastrophic effect on world population [1]. COVID-19 has devastated several regions globally and has overwhelmed several health care systems since it was designated a global pandemic. The epidemic also caused loss of employment as a result of extended shutdowns that affected the worldwide economy [2]. While significant clinical research progress has led to a better understanding of the virus (SARS-CoV-2) nature, and better management of the disease (COVID-19), restricting the dispersal of this virus has become a major concern since SARS-CoV-2 continues to wreak havoc around the world with several countries suffering from the second or third wave of outbreaks of viral disease mainly caused by the development of SARS-CoV-2 [3].

Rapid detection of COVID-19 is crucial for maintaining patient's health and more importantly for quick isolation of the patient to stop the spread of the infection. In order to evaluate COVID-19 infection, healthcare professionals should extract thorough clinical information on the start and the duration of symptoms, history of travel, exposure to persons with COVID-19 infection, pre-existing diseases and medication history [4]. COVID-19 should be quickly examined in patients with characteristic clinical evidence susceptible to COVID-19 such as fever, cough, sore throat, loss of taste or smell, malaise, and myalgia. In addition to symptomatologic individuals, SARS-CoV-2 infections should be examined in patients with atypical symptoms of COVID-19 or those with a high-risk known SARS exposure [5].

Radiologists should be aware of the features and patterns of imaging manifestations of the novel COVID-19 infection. A variety of imaging features have been described in similar coronavirus-associated syndromes. Due to an alarming spread of COVID-19 outbreak throughout the world, a comprehensive understanding of the importance of evaluating chest CT imaging findings is essential for effective patient management and treatment [6].

Because pneumonia is typically the case with this viral illness, X-rays play an important role in monitoring, and diagnosis. Imaging examinations may cover chest x-rays, ultrasound or computed tomography (CT) of the chest. In clinically suspected situations, CT is considered the primary imaging modality and is important for monitoring changes of imaging throughout treatment [7]. Consequently, CT has been regarded by clinicians in suspected cases of COVID-19 as an efficient diagnostic instrument. The results of the CT scan may also give information on the severity of the condition. Chest CT can detect early stages of illness and...
allow for patient isolation [8]. Furthermore, given the similarity of most viral pneumonia imaging patterns, the CT characteristics identified in many recent studies may be useful in distinguishing virus from other pathogens causing pneumonia and triaging patients [9].

The typical CT findings were peripheral ground glass patterns and a lack of dense consolidation or pleural effusion. It is strongly advised to focus on COVID-19 variety in order to better understand COVID-19 and achieve correct diagnoses, as well as better therapy and management [10,11]. In this review, the diagnosis of COVID-19 is discussed and CT characteristics are defined based on the newest research for the diagnosis and management of COVID-19.

2. LITERATURE REVIEW

Kim et al. found that the diagnostic usefulness of chest CT is dependent on the prevalence of COVID-19 infection in the investigated group. Chest CT screening of individuals with suspected illness has a poor positive predictive value in places where the incidence is low. In the case of an epidemic rush of patients at the emergency department, on the other hand, doctors will confront a severe issue of quick triage based on disease presentation and severity. Patients whose diagnoses are uncertain belong to the group with intermediate likelihood and may benefit from a chest CT scan to check for signs of COVID vs other conditions [12].

Lieveld et al. describe the validation of a CT reporting tool in the diagnosis and severity evaluation of COVID-19 in 741 individuals using CT imaging and reverse transcriptase polymerase chain reaction (RT-PCR) correlation. This equates to a positive predictive value of 76.4 percent and a negative predictive value of 94.6 percent, suggesting that CT imaging may be more useful in ruling out than ruling in illness. These findings strongly support the use of CT scanning in the diagnostic route of patients with suspected COVID-19, especially when RT-PCR is not available quickly or the result is unexpected [13].

In earlier investigation, Tao et al. found that CT chest had a greater sensitivity than RT-PCR in a wider sample of 1014 patients. 59 percent of the 1014 patients had positive RT-PCR findings, and 88 percent had positive chest CT scans. Based on positive RT-PCR data, the sensitivity of chest CT in detecting COVID-19 was 97 percent. 75 percent of patients with negative RT-PCR results had positive chest CT findings; of 308, 48 percent were judged extremely likely instances, while 33 percent were considered probable cases. Prior (or parallel) to the initial positive RT-PCR findings, 60% to 93% of patients had an initial positive CT compatible with COVID-19. Before the RT-PCR findings were negative, 42 percent of patients improved on follow-up chest CT scans [14].

Kovács et al investigated the sensitivity, specificity, and practicality of chest CT in identifying COVID-19 when compared to real-time polymerase chain reaction (RT-PCR). The results showed that the sensitivity was high (67–100%) while the specificity was low (25–80%). However, the sensitivity of RT-PCR has been shown to be low (53–88 percent), therefore it cannot be used as a reliable ground truth. Given the RT-low PCR's sensitivity, the "reverse calculation technique" revealed that CT might have a better specificity (83–100%) [15].

In a research conducted in Shanghai, China, on 38 suspected COVID-19 patients (presumably all asymptomatic), chest CT demonstrated a sensitivity of 100%, specificity of 25%, and accuracy of 47% [16]. A research from Rome, Italy, found that chest CT had a high sensitivity (97%) but a low specificity (56%) when compared to RT-PCR in symptomatic patients [17].

Wang et al., found the sensitivity for chest CT to be 84% (95% confidence interval: 73%–92%) when conducted in 0–5 days of symptom onset. The sensitivity increased to 99% (95% confidence interval: 93%- 100%) if the chest CT was obtained on day 6–11 [18].

Brun et al. conducted a study to assess inter-reader agreements and diagnostic accuracy of chest CT to identify COVID-19 pneumonia in patients with intermediate clinical probability during an acute disease outbreak, reporting that a chest CT scan can be used for triage of patients with intermediate clinical probability with very good inter-observer agreements and diagnostic accuracy. RT-PCR testing on 307 patients revealed that 174 were positive and 133 were negative. The areas under the curve (AUC) were 0.94 and 0.94, respectively [19].

Awulachew et al. conducted systematic review and meta-analysis to analyze the existing
literature on CT imaging features of patients with COVID-19 pneumonia reported that; out of 5041 COVID-19-infected patients, about 98% had abnormalities in chest CT, while about 2% have normal chest CT findings. Among COVID-19 patients with abnormal chest CT findings, 80% had bilateral lung involvement. Ground-glass opacity (GGO) and mixed GGO with consolidation were observed in (65%) and (18%) patients, respectively. Consolidations were detected in (22%) patients with COVID-19 pneumonia. CT images also showed interlobular septal thickening in about 691 (27%) patients [6].

The chest CT results of 81 individuals with COVID-19 were investigated in a research from Wuhan, China. CT scans revealed bilateral lung involvement in 79% of the patients, peripheral distribution in 54%, and diffuse distribution in 44%. GGO with poorly defined borders, smooth or irregular interlobular septal thickening, air bronchogram, and thickening of surrounding pleura were the most prevalent chest CT findings [20].

In a comprehensive meta-analysis of 9907 verified cases, Zarifian et al. showed that the most common CT findings were GGOs (77.18 percent), reticulations, and air bronchograms (41.61 percent). Pleural thickening (33.35%) and bronchial wall thickening (15.48%) were the most common unusual airway findings. Lesions were most commonly found bilaterally (75.72%) and peripherally (65.64%), while 8.20% of patients had no abnormal findings and 6.01 percent had pre-existing lung diseases [21].

Inui et al. investigated the chest CT results on cases from the "Diamond Cruise Ship" and discovered that imaging abnormalities were more prevalent in symptomatic (79%) than asymptomatic (54%) laboratory-confirmed COVID-19 patients. However, ground-glass opacities were more prevalent in asymptomatic individuals (83 percent) than in symptomatic patients (41 percent) [22]. Meng et al. from Wuhan investigated the development of chest CT in asymptomatic laboratory-confirmed COVID-19 patients for 54 days and discovered comparable findings of GGO and interlobular septal thickening. They discovered that 27% of individuals finally got sick, had aberrant inflammatory markers, and had lymphopenia [23].

GGO appearance was described as the most prevalent chest CT finding in COVID-19 patients in a research by Song et al. [24]. GGO was the most prevalent CT finding in 57 percent of COVID-19 patients in a case study of 21 patients by Chung et al., and bilateral disease was observed in 76 percent of COVID-19 patients [25]. However, in verified cases, CT results may be normal as well [26].

Adams et al. conducted a systematic review and meta-analysis of the COVID-19 chest CT imaging signature across 28 investigations including a total of 3,466 patients. Normal chest CT imaging results had a pooled frequency of 10.6 percent. The pooled frequency of posterior predilection was 90.0 percent, ground-glass opacity was 81.0 percent, bilateral abnormalities were 75.8 percent, 73.1 percent for left lower lobe involvement, 72.9 percent for vascular thickening, and 72.2 percent for right lower lobe involvement. Pleural effusion had a pooled prevalence of 5.2 percent, lymphadenopathy had a prevalence of 5.1 percent, airway secretions/tree-in-bud sign had a prevalence of 4.1 percent, central lesion distribution had a prevalence of 3.6 percent, pericardial effusion had a prevalence of 2.7 percent, and cavitation/cystic changes had a prevalence of 0.7 percent [27].

CT Features in COVID-19: The imaging results vary with the patient’s age, comorbidities, immunity condition, stage of infection at the time of scanning, and drug interventions. The imaging features of COVID-19 are lesions, which are important in the aspect that they show dominant distribution, quantity, shape, density and concomitant signs vary [5]. In one retrospective study, the initial plain non-contrast CT scans were assessed for presence of GGOs, presence of consolidation, number of lobes affected by ground-glass or consolidative opacities, occurrence of a pleural effusion, presence of nodules, degree of lobe involvement, presence of thoracic, and presence of underlying lung disease such as emphysema or fibrosis [28].

Pneumonia has been identified as the primary cause of lung damage in COVID-19 patients. As a result, the COVID-19 pulmonary lesions are likely to be comparable to those seen in other forms of pneumonia. Interstitial inflammation, substantial consolidation with multifocal bilateral GGOs, bilateral involvement, evident peripheral or subpleural distribution, posterior portion or lower lobe preference, and numerous lesions are typical imaging characteristics of COVID-19 pneumonia [29].
Ground glass opacity (GGO): is the non-specific hazy opacification of the lung with no obliteration of bronchial or vascular markings. Fluid partial filling of the lung alveoli, interstitial thickening, or partial collapse of the lung alveoli are all possible pathologies. The most prevalent finding on chest CT in patients with COVID-19 pneumonia is GGO, which is generally characterized as patchy, peripheral, bilateral, and subpleural. In general, single or multiple GGOs are found in COVID-19 individuals, either unilaterally or bilaterally, and are dispersed peripherally in the lung's subpleural region [30-32]. Because the specific pathophysiological process is unknown, it is not clear why GGOs are the first CT symptoms. As the hyaline membrane between the alveolar walls, alveolar exudation, and edema are not visible, the first pathological observation is widespread alveolar injury. Pure GGOs are particularly prevalent in COVID-19 individuals and in those in the early stages of illness [33]. However, in an increasing number of cases, GGOs are associated with additional symptoms such as reticular patterning and/or thickening of interlobular septa, the development of crazy-paving patterns, and consolidations. The presence of typical round GGOs diminishes as the illness progresses, while the emergence of patchy GGOs and consolidations rises [34]. The major CT chest results in all papers published in radiology journals or other imaging journals are ground glass opacification. Guan et al. observed GGO in all 53 COVID-19 patients (100%) in a study with 53 patients [35]. Ng et al. found an 86 percent incidence of GGO, with the remaining patients having GGO with consolidation [36].

Consolidations: is described as a region of enhanced attenuation that obscures the bronchial and vascular marks and is caused by fluid, exudates, transudate, blood, or neoplastic cells filling the alveolar spaces. COVID-19 Consolidation Pneumonia is patchy or segmental, irregular or nodular, and primarily subpleural and peripheral, with a reported prevalence of 2–64 percent depending on illness duration [37]. Consolidation appears in the advancing stages or in-patient cohorts with severe COVID-19 infections. The underlying mechanism of consolidation is consistent with the clinical alterations in the lungs of COVID-19 patients, which show all components of diffuse alveolar injury, including damage to alveolar epithelial cells, development of a hyaline membrane, and type II pneumocyte hyperplasia. Consolidation via fibroblastic proliferation with extracellular matrix and fibrin production is particularly common in COVID-19 patients [38,39].

Consolidation is distinguished by numerous, patchy, or segmental regions dispersed in the subpleural areas or along the bronchovascular bundles on CT. Consolidation can also be used to predict disease progression [40]. Consolidations often emerge 10–12 days after the beginning of symptoms, following the formation of GGO. GGOs often grow into consolidations and cohabit alongside consolidations during the progressive stage [41]. In a research conducted by Song et al., the incidence of consolidation was substantially greater in older patients (> 50 years) than in younger patients, as well as in patients who had symptoms for more than four days [42].

Air Bronchogram: is described as air-filled bronchi in a densely populated region, with a reported incidence ranging from 28 to 80 percent of patients. On a backdrop of high-density parenchyma without air, the emergence of an air bronchogram, represented by a pattern of "air-filled bronchi" with low attenuation, was seen [43]. However, the phrase "air bronchogram" appears to be misleading due to the low density of mucus in the bronchi, which is more comparable to a gelatinous mucus plug than air [44]. In reality, the gelatinous mucus in the bronchi might cause minor bronchial dilatation. The gelatinous mucus plug in COVID-19 patients seems to be of extremely low density, akin to that of air, against a background of sick, high-density lung tissue. It is generally an indication of severe illness, appearing after the second week of symptoms, and can be seen in both GGO and consolidation [45].

Crazy paving sign: It is made up of thicker interlobular septa that are overlaid on GGO. This symptom indicates alveolar edema and an interstitial inflammatory response. The prevalence of crazy paving in children is estimated to be 20%, which is slightly lower than the incidence in adult patients (27.7%) [46]. For youngsters, further research with a bigger sample size are required to offer a more presentative frequency. Interestingly, despite the fact that the crazy paving sign is a symptom of progressive disease and its presence may signal that the disease is nearing the peak stage, it is
the first CT sign to resolve in the absorptive stage, although the consolidation and GGO can last for up to 26 days [45,47].

**Reticulations:** which manifest as lineal interlobular or intralobular density are very late findings in COVID-19 patients, with a reported frequency of 48.5–59 percent [31]. Reticulations are generally connected with clinical development of the illness. Reticulations are most likely produced by lymphocyte infiltration of the interstitial tissues, which results in interlobular and septal thickening. In several investigations, the reticular pattern was a frequent pattern, ranking third behind GGO and consolidation [42].

**Halo sign:** is described as the opacity of ground glass surrounding a nodule or bulk. Previously, this symptom was thought to be an indication of fungal infection, viral pneumonia, or hyper vascular metastases. Although it has been documented in numerous investigations [48], the halo sign is less prevalent and not specific for COVID-19 pneumonia. The cause of the formation of this symptom is unknown, although it might be connected to angio-invasive fungal infections or hyper vascular metastases that cause bleeding surrounding lesions, viral infections, or organizing pneumonia [49]. In a research by Bai et al., 26% of COVID-19 and 21% of instances of other viral pneumonia had halo signs and 21% found it to be a not useful indication when COVID-19 needed to be differentiated from other viral pneumonia [50].

The reversed halo indication is a GGO region surrounded by an almost full consolidating ring. The processes postulated in COVID-19 are either disease progression with consolidation development in GGO areas or consolidated areas with central area resolution leaving a dense-tonic area. The reversed halo symptom is generally noticed in a reasonably lengthy period and the existence of that sign indicates that pneumonia organization may be one of the causes for pneumonia in COVID-19 [51,52].

**Fibrosis:** Some investigations showed the characterization of fibrosis seen in the shape of stripes, reticulations and even honeycomb patterns in chest CT images of individuals with COVID-19 infections [53]. Fibrosis may either suggest the absorption of pulmonary lesions or imply fibrous hyperplasia. There is evidence, however, that fibrosis is more likely to occur in people with high inflammatory measurements, including C-reactive protein (CRP) and IL-6 and prolonged hospitalisation stays in patients with severe infections [54]. During COVID-19 infection, a pulmonary band, notably the development of an irregular interface with a Parenchymal band and an irregular interfacet, a coarse reticular pattern, might be viewed as a predictor of pulmonary fibrosis [55].

**Other Signs:** In COVID-19 individuals, lymphadenopathy is not prevalent. When the mediastinal lymph node has a diameter of over 1 cm, the lymphadenopathy is determined. In several investigations in COVID-19 patients, this result was reported with a 2.7% –8% share [56]. A nodule with a regular or irregular outline is less than 3 cm in diameter. The presence of nodules is often typical for viral pneumonitis. In individuals with COVID-19 pneumonia, the incidence of pulmonary nodules described is 3–13% and can be linked with the surrounding halo. A thin linear shadow of 1–3 mm in thickness, parallel with and located within 1 cm from the pleural surface, is the subpleural curvilinear line. About 20% of COVID-19 patients have these symptoms, and edema or fibrosis might be present [57,58].

Vascular enlargement means the extension, which is invariably accompanied by and/or consolidation of GGOs, of the blood arteries around or inside the pulmonary lesions. While this indication has seldom been observed in prior trials, the incidence of this sign in CT scans has been high [59].

Bronchial thickening is less frequent and always occurs in bronchiectasis, bronchiolectasis, and respiratory bronchiolitis-interstitial lung disease. This result is often found in individuals with severe diseases or later phases rather than in early phases of the disease [60].

A complicated network of linear opacities is present in the reticular pattern of CT images generated by interlobular and intralobular septal thickening by the lymphocyte infiltration. In a past research, reticular infiltration of the lungs with severely bilaterally densely consolidated postmortem CT indicated that there was widespread alveolar injury in eight individuals [61].

Pleural changes are caused by pleural densification and pleural effusion, and the first is
more prevalent. Pleural thickening and pleural effusion in individuals with COVID-19 are very unusual. The incidence of pleural spreading described is around 27–32% [62].

The lymphatic mediastinal nodes will be expanded when the diameter of the short axis is at least 1 cm. Mediastinal lymphadenopathy is not a common characteristic in individuals with COVID-19, with a frequency of 1–6%. The appearance of swollen lymph nodes is often regarded to be an indication of serious or critical illness. The presence of lymph nodes can also suggest bacterial infection overlapping [63].

3. CONCLUSION

CT relies heavily on the detection and treatment of COVID-19 pneumonia. COVID-19 pneumonia frequently exhibits a bilateral patchy appearance of ground-glass infiltration, consolidation, air bronchogram, crazy pavement appearance, fibrosis, and other symptoms as the illness progresses. While the bilateral and peripheral distribution and consolidation of GGOs is thought to be the most common and typical imaging features of individuals with COVID-19 infections, CT characteristics can change across persons and over time. Furthermore, chest CT plays an essential role in follow-up since CT characteristics vary with illness progression and expected therapy, which physicians should be aware of right once.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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252
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