Original Article

Accuracy of Noncontrast Chest Computed Tomography in COVID-19 Infection: An Observational and Retrospective Study

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Abstract

Objective: During the novel coronavirus pandemic, great challenges are becoming prominent, such as early and rapid diagnoses using simple and readily available tests. Chest computed tomography (CT) scan plays a major role in the diagnosis and monitoring of the complications with high specificity. The purpose of this study is to assess the accuracy of nonenhanced chest CT scan in the diagnosis of coronavirus disease 2019 (COVID-19) disease in suspected patients. **Materials and Methods:** Eighty four suspected patients were included in this retrospective study from March 1, 2020, to April 1, 2020, who underwent both nonenhanced chest CT scan and real-time polymerase chain reaction (PCR) test for COVID-19 disease. **Results:** The total number of initial reverse transcriptase (RT)-PCR-positive results was 52 (61.9%) patients and that of negative results was 32 (38%) patients. Out of the total number of positive RT-PCR tests, only fifty (96%) patients showed positive CT findings. Of the total number of negative RT-PCR tests (32 [38%] patients), only 8 (25%) patients showed negative CT results. With RT-PCR results as the reference standard, the sensitivity, specificity, and the accuracy of chest CT in indicating the COVID-19 infection were 96.15%, 25%, and 69.04%, respectively. Ground-glass opacity (GGO) was seen in all positive CT patients (74 [100%]), mixed GGO was seen in 27 (36.4%) patients, and consolidation was seen in 36 (48.6%) patients which was subsegmental in 28 (37.8%) patients. Vascular dilatation sign was seen in 61 (82.4%) patients, crazy paving sign was seen in 31 (41.9%) patients, reverse halo signs were seen in 23 (31%) patients, and air bronchogram was seen in 39 (52.7%) patients. **Conclusions:** Highly characteristic and specific bilateral multifocal GGOs were reported as the classical/typical chest CT features of COVID-19 infection with high confidence rate, although it may vary in different patients' parameters and stages so that chest CT imaging has very high sensitivity (96.15%) for the diagnosis of COVID-19 in epidemic areas with high pretest probability for disease, and it is recommended to be included as a decision-making diagnostic test in suspected patients with RT-PCR-negative results.

Keywords: Coronavirus disease 2019, ground-glass opacity, reverse transcriptase polymerase chain reaction

Introduction

In the early January 2020, there was an outbreak called coronavirus disease (COVID-19), which became an emergency global problem as declared by the WHO in the late January in having significant mortality in more than thirty countries in February 2020.[1,2]

At present, the virus pandemic has affected more than 180 countries, and there are 1.3 million confirmed cases and about 72,638 deaths. In Iraq, on August 2020, a total covid-19 confirmed cases was 234,934 with a total reported deaths of 7,042 cases.[3]

The widespread nature of COVID-19 all over the world in a very short period in the absence of specific therapeutic drugs of vaccines, requires the use of rapid and accurate diagnostic tests that are readily available for early disease prevention and management. Computed tomography (CT) is strongly recommended in suspected COVID-19 cases for initial diagnoses, evaluation, and follow-up.[4-7] The Diagnosis and Treatment Program (6th version) published by the National

Access this article online	
Quick Response Code:	**Website:** www.medjbabylon.org
	DOI: 10.4103/MJBL.MJBL_47_20

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Submitted: 24-Jul-2020 **Accepted:** 02-Aug-2020
Published Online: 16-Sep-2020

How to cite this article: Hammoodi ZH, Al-Khafaji HF, Al-Murib ZH, Al-Esawy HK, Baiee AS, Al-Shimmary AA. Accuracy of noncontrast chest computed tomography in COVID-19 infection: An observational and retrospective study. Med J Babylon 2020;17:282-7.

Health Commission of the People's Republic of China[8] had defined the diagnosis of viral pneumonia based on radiologic features by radiologists as one of the diagnostic criteria for COVID-19.

As the number of reported cases of COVID-19 infection continues to increase, radiologists encounter more patients with this infection. A high index of suspicion and detailed exposure and travel history are critical to considering this diagnosis. For an appropriate clinical setting, bilateral ground-glass opacities (GGOs) or consolidation at chest imaging should prompt the radiologist to suggest COVID-19 infection as a possible diagnosis. Furthermore, a normal chest CT scan does not exclude the diagnosis of COVID-19 infection.[9]

Seven coronaviruses are known to cause disease in humans. Two strains, severe acute respiratory syndrome-coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus, have zoonotic origins and have been linked to the outbreaks of severe respiratory illnesses in humans. Although COVID-19 infection is believed to have a zoonotic origin, person-to-person transmission has been documented.[10,11]

Radiology (radiography, ultrasound, CT, radiologists, and technicians) plays an essential role in COVID-19 crises with a great step up in hospitals to fight in frontlines against the coronavirus pandemic, especially where reverse transcriptase-polymerase chain reaction (RT-PCR) is limited or false negative and in patient triage.

Currently, RT-PCR or gene sequencing of respiratory or blood specimens are generally the reference standard of COVID-19-confirmed patients, however, the initial positive rates of RT-PCR are only in 30%–60% because of the controversy in sampling sites, transportation media, and kit performance.[12]

Noncontrast chest CT is an easy, fast, and noninvasive test, which is readily available in most of the Iraqi cities, together with typical chest CT findings in most COVID-19 patients, for example, ground-glass densities, nonorganizing pneumonias, crazy paving, and architectural distortion, giving CT chest examination an essential role in diagnoses.[13] Temporal changes of chest CT findings are important in patient follow-up and sometimes are essential in the diagnoses of COVID-19 infection in RT-PCR-negative patients.

With the limited sensitivity of initial RT-PCR (60%), CT chest may reveal abnormalities in asymptomatic and RT-PCR-negative patients.[14] Multiple classic/typical and atypical chest CT findings are seen in RT-PCR-confirmed COVID-19 infection,[15] these are: GGO, reticular pattern, crazy paving pattern, air bronchogram, airway changes, pleural changes, subpleural curvilinear line, fibrosis, vascular enlargement, air bubble sign, nodules, and halo sign.

GGO is defined as hazy area with slightly increased density in lungs without obscuration of bronchial and vascular margins, due to partial displacement of air due to partial filling of airspaces or interstitial thickening.[16]

In patients with COVID-19, GGOs are in the form of uni- or bilateral peripheral subpleural distribution.[8,17] Chung *et al*. were the first to describe GGO as the earliest and most common CT finding in 57% of COVID-19-infected patients,[13] which were confirmed in subsequent studies in up to 98% of patients. These represent pulmonary edema and hyaline membrane formation, which may be accompanied by reticular and/or interlobular septal thickening and consolidation. GGO together with small areas of consolidation forms organizing pneumonia.

The reticular pattern is defined as thickened pulmonary interstitial structures such as interlobular septa and intralobular lines, which manifests as a collection of innumerable, small, linear opacities due to interstitial lymphocyte infiltration, and this is the second common chest CT finding in COVID-19 infection.[18,19] As the disease course gets longer, the prevalence of reticular pattern could increase in COVID-19 patients.

The crazy paving pattern is seen as thickened interlobular septa and intralobular lines with superimposition on a GGO background, resembling irregular paving stones. Pathologically it result from the alveolar edema and interstitial inflammation of acute lung injury, reported 5%–36% COVID-19 patients.[20] In the presence of diffuse GGO and consolidation, crazy paving pattern can be the signal of COVID-19 entering progressive or peak stage.[21]

Air bronchogram is a pattern of air-filled/low-attenuation bronchi on a background of an opaque high-attenuation airless lung. Autopsy findings show this sign to be a gelatinous mucus in the lung bronchus, often accompanied by slightly bronchiolar dilatation (bronchiolectasis).

Airway changes include bronchiectasis and bronchial wall thickening. Bronchial wall thickening has been reported in around 10%–20% of COVID-19 patients, possibly due to inflammatory damage of the bronchial wall, bronchial obstruction, proliferation of fibrous tissue, fibrosis, and tractive bronchiectasis in severe/critical patients.

Pleural changes include pleural thickening (32%) and pleural effusion (5%).[21] The presence of pleural effusion suggests a poor prognosis in COVID-19.

Subpleural curvilinear line is a thin curvilinear opacity with 1–3-mm thickness, lying <1 cm from and parallel to the pleural surface, which is reported in around 20% of patients, which might relate to pulmonary edema or fibrosis.[22]

Fibrosis or fibrous stripes might be seen in about 17% of COVID-19 patients, which may form during the healing of pulmonary chronic inflammation or proliferative diseases; with gradual replacement of cellular components by scar tissues, it may indicate good prognosis with stabilizing disease,[8] whereas others regards fibrosis might indicate a poor outcome and may subsequently progress to peak stage or result in pulmonary interstitial fibrosis.[22]

Vascular enlargement described as the dilatation of pulmonary vessels around and within the lesions on CT images is possibly more common in COVID-19 patients with 1 week after the onset of symptoms, which may be due to damage and swelling of the capillary wall caused by pro-inflammatory factors.[23]

Air bubble sign (cavity) refers to a small air-containing space in the lung which might be the pathological dilation of a physiological space or a cross-section of the bronchiolectasis or associated with the process of consolidation resorption.

Another chest CT finding that might be seen in RT-PCR-confirmed COVID-19 infection is nodules. A nodule refers to a rounded or irregular opacity with well- or poorly defined edges, measuring <3 cm in diameter, and is frequently associated with viral pneumonia, reported in 3%–13% of COVID-19 patients. It may be multifocal, solid, irregular nodules or with visible halo sign.

Halo sign is defined as nodules or masses surrounded by ground glass, and it is very rarely seen in COVID-19 infection. Chest CT scan showing high accuracy rate in correlation between temporal CT findings and COVID-19 progression and in assessing severity index,[24,25] reverse halo sign may also be seen.

The aim of this study was to assess the accuracy of nonenhanced chest CT scan in the diagnoses of COVID-19 disease in suspected patients.

Materials and Methods

Study design and patients

On February 24, 2020, the first case of COVID-19-positive infection case was confirmed in Iraq in a foreign student in Al-Najaf city, with the total number of confirmed cases reaching 1378 cases and 78 deaths till March 13, 2020. In this observational, retrospective study, 84 clinically suspected patients with COVID-19infection were included, from March 1, 2020, to April 1, 2020, who are assessed and evaluated by a COVID-19team (physicians, radiologists, and microbiologists). Any patient with a combination of three criteria (fever, cough, normal or low white blood cell or lymphocyte count, a history of recent travel to an epidemic region, or a history of contact with a COVID-19-positive patient) were included. The mean age of the participants was 50.8 years, with a range of 18–77 years [Table 1]. At the same time, both nonenhanced chest CT scan and nasopharyngeal swab RT-PCR tests were done; the enrolled patients were divided into four groups as follows: the first group included fifty patients with positive CT scan and RT-PCR and the second group included 24 patients with positive CT scan and negative initial RT-PCR. These patients undergo repeated CT and RT-PCR tests after 3 days, which may be repeated up to three times, 3 days apart with re-evaluation and re-classification by the COVID-19team to assess the dynamic and temporal CT changes, which are important in confirming the diagnoses in RT-PCR-negative patients.

Table 1: Patient characteristics

	Number of patients (84), *n* (%)
Age (years)	
<20	2 (2.3)
20-60	51 (60.7)
>60	31 (36.9)
Male	56 (66.6)

The third group included two patients with negative CT and positive RT-PCR test; these patients are isolated and managed according to clinical triage. The fourth group included eight patients with negative CT and negative RT-PCR, who were reevaluated considering other diagnoses.

Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. The study was carried out with patients' verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee (Babil health directorate).

Computed tomography acquisition protocol

Non enhanced chest CT was done in all patients in supine position in end-inspiratory phase. Chest CT was done on 64-slice and 16-slice CT Philips Healthcare, Brilliance 64 or Brilliance 16 scanners, Holland), at 5/5-mm slice thickness with reconstruction at 0.6 mm and 1.5 mm lung window, 100–120 kV, 100–250 mAs, pitch 0.8, and rotation time 0.4–0.5 s. After each patient's examination, strict disinfection precautions were followed according to the department guidelines.

The cases were evaluated by experienced radiologists. The mean volume CT dose index ($CTDI_{vol}$) was 4.9 ± 0.8 mGy (standard deviation) (range, 2.8–6.2 mGy).

Results

Analyses of computed tomography findings

The following CT features were assessed: appearance (GGO, consolidation, or mixed GGO); number of lung lobes involved; shape of lesions (nodular, segmental, and patchy); characteristic signs such as crazy paving, reverse halo sign, vascular dilatation, and air bronchogram; and extrapulmonary signs (pleural effusion/thickening and mediastinal lymphadenopathy [LAP]) [Table 2].

GGO was seen in all positive CT patients (74 [100%]), mixed GGO and consolidation was seen in 27 (36.4%) patients [Figures 1 and 2], and consolidation was seen in 36 (48.6%) patients which was subsegmental in 28 (37.8%) patients.

Vascular dilatation sign was seen in 61 patients (82.4%) [Figure 2]. Crazy paving sign was seen in 31 (41.9%) patients, and air bronchogram was seen in 39 (52.7%) patients. Posterior subpleural thickening was seen in 12 patients (16%)

Table 2: Computed tomography features and early computed tomography findings of suspected coronavirus disease 2019 patients (*n*=74)

CT features	Number of patients (%)
Ground glass	
Multifocal rounded	70 (94.6)
Mixed GGO	33 (44)
Peripheral	66 (89)
Mid-lower zones	71 (96)
Posterior zones	68 (92)
Consolidation (segmental/subsegmental)	33 (44)
GGO with consolidation	28 (38)
Vascular enlargement	47 (64)
Tree in bud	1.4 (2)
Crazy paving	50 (68)
Reverse halo sign	13 (18)
Nodular lesions	12 (16)
Air bronchogram	60 (82)
Cavity	0
Lymphadenopathy	0
Pleural effusion	0
Right lower lobe	37 (71.1)
Left lower lobe	21 (40.3)
More than one lobe involved	49 (94.2)
Pleural thickening	12 (16)

GGO: Ground-glass opacity, CT: Computed tomography

[Figure 3]. Pleural thickening was also seen in 12 patients (16%) [Figures 4 and 5]. Reverse halo signs were seen in 23 (31%) patients [Figure 6]. Pleural effusion, mediastinal LAP, and cavitation were not reported in this study.

A number of studies suggested reporting pro forma or consensus statements published by many radiological societies such as Radiological Society of North America, American College of Radiologists, and British Society of Thoracic Imaging, which can help radiologists to standardize imaging language, which is used in this study.

Regarding the initial RT-PCR tests, the total number of positive results was achieved in 52 (61.9%) patients and the total number of negative results was seen in 32 (38%) patients. Of the total number of positive RT-PCR tests, only fifty (96%) patients showed positive CT findings. Of the total number of negative RT-PCR tests, i.e., 32 (38%) patients, only 8 (25%) patients showed negative CT results. With RT-PCR results as the reference standard, the sensitivity, specificity, and accuracy of chest CT in indicating COVID-19 infection were 96.15%, 25%, and 69.04%, respectively.

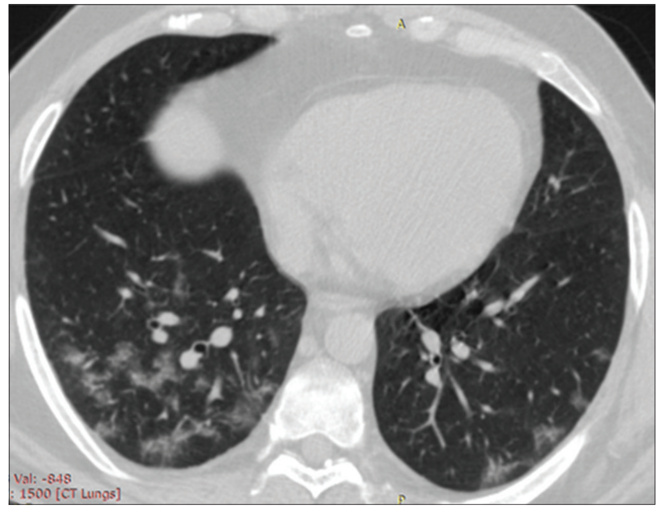

Figure 1: Bilateral multifocal ground-glass opacity

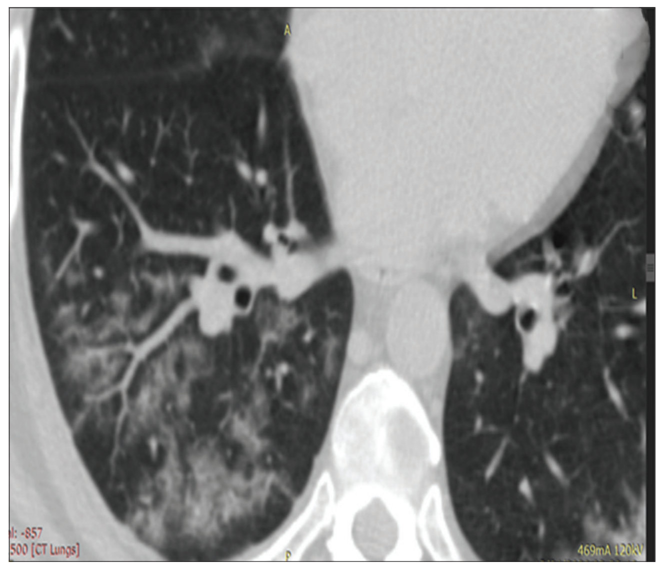

Figure 2: Mixed patch of ground-glass opacity with vascular dilatation sign

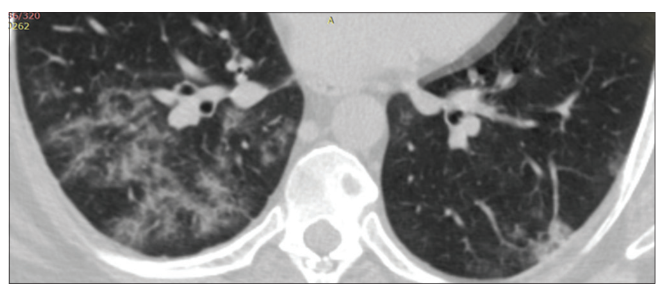

Figure 3: Posterior subpleural thickening

Discussion

The COVID-19 pandemic is a rapidly spreading disease with disastrous consequences all over the world, so early diagnoses and management are essential. Although RT-PCR test is the definitive reference tool for diagnosing COVID-19infection, CT is playing an essential role in management because it is fast, is noninvasive, is practical, and is readily available.

RT-PCR has high specificity rate but has low sensitivity (60%–97%),[26,27] which means that false-negative cases may reach hundreds of thousand persons, which is a real clinical problem. RT-PCR results may require 24 h for providing the final results, which causes diagnostic delay in some centers.

Figure 4: Small subpleural linear fibrotic changes

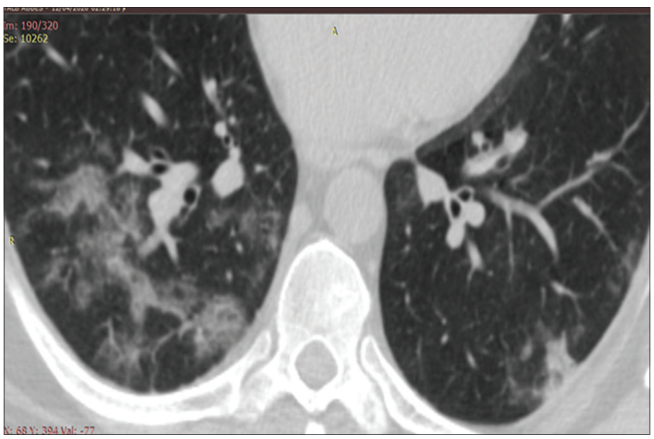

Figure 5: Small left subpleural nodule

Figure 6: Reverse halo sign

SARS-CoV-2 virus has predilection to pulmonary interstitium causing edema and thickening of the whole layers of interlobular interstitium and peri-bronchovascular spaces manifesting as GGO, which is the earliest and the most common and most characteristic sign of the COVID-19 infection. In this study, CT findings of GGO were seen in fifty (96%) patients with early disease positivity of COVID-19, which were multifocal in 47 (90%) patients, mixed GGO-consolidation in 22 (42%) patients, showing peripheral lung distribution in 45 (86.5%) patients, more prominent in mid and lower zones in 48 patients (92%), and in right lower lobe in 37 patients (71.1%), with more than one lobe involved in 49 (94.2%) patients; these findings are consistent with those of other studies conducted worldwide.[13,28]

Consolidations (nonlobar, segmental, and subsegmental) was seen in 33 (44%) patients with or without GGO. Other less frequent but classical signs seen in COVID-19 patients are crazy paving in 32 patients (61.5%), reverse halo sign in 10 patients (19%), which are seen most commonly in late-presenting patients. With these characteristic CT chest findings, in the COVID-19 epidemic, radiologists can confidently report the diagnoses of COVID-19 infection depending on CT features. A significant number of patients (24 patient [28.5%]) showing positive chest CT findings with high probability of COVID-19 infection but with negative initial RT-PCR, i.e., false positive, possibly due to overlapping of CT findings with other viral pneumonias in general, but in current COVID-19 epidemic and low sensitivity of RT-PCR, this high index of suspicion is important in rapid isolation and in patient triage meanwhile waiting for confirmation of diagnoses by repeated RT-PCR and repeated CT chest (to confirm temporal CT changes) with continuous re-evaluation by covid19 team (radiological, serological, clinical, epidmiological) of such patients.

False-negative CT results (positive RT-PCR and negative CT) were seen in only two (2.3%) cases, which may be explained by the low disease severity, compatible with the findings of a previous study by Chan *et al*.[29] Pleural effusion, cavities, and lymphadenopathy were not found.

Many limitations of this study were seen, such as small sample size, no follow-up CT scan changes were included in this study, presence of false-positive and false-negative CT results, and lack of clinical comparison, which may give us more support in clinical and radiological diagnoses. Owing to the low sensitivity of RT-PCR test (possibly due to technical errors, manufacturer variation, low patient viral load, and improper sampling), together with occasional long waiting times to get the laboratory results, some Chinese researchers support the use of chest CT for screening COVID-19 patients with clinical and epidemiologic features compatible with COVID-19 infection, particularly when RT-PCR testing is negative.[30]

Conclusions

Rapid and early diagnoses of COVID-19 patients are the cornerstone in isolating and controlling this pandemic. Highly characteristic and specific bilateral multifocal GGOs were reported as the classical/typical chest CT features of the COVID-19 infection with high confidence rate, although it may vary in different patients' parameters and stages. This study shows that CT imaging has very high sensitivity (96.15%) in the diagnosis of COVID-19 in epidemic areas with high pretest probability, and it is recommended to be included as a decision-making diagnostic test in suspected patients with RT-PCR-negative results, although further research should be continuously updated.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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