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Chest CT manifestations in 187 laboratory-confirmed patients with COVID-19: a retrospective study

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Abstract

Background: The coronavirus disease-2019 (COVID-19) outbreak, first reported in Wuhan, China, has quickly spread around the world within a month, causing a global health emergency. This study aimed to image patients with laboratory-confirmed COVID-19 to provide a more comprehensive overview of the disease, in order to help the clinical diagnosis and management.

Methods: In this retrospective study, the sample comprised of 376 patients with suspected COVID-19 from April 18 to June 10, 2020. Only 187 patients were included with laboratory-confirmed coronavirus infection. The chest CT images and clinical data were reviewed and the relationship between them was analyzed.

Results: In total, 187 cases with laboratory-confirmed COVID-19 were included. Fever, dry cough, and muscle ache were the most frequent clinical symptoms. Lymphopenia and an increased CRP level were the most common laboratory findings. The prominent CT manifestations were ground-glass opacity (95/187 cases, 50.8%), consolidation (90/187 cases, 48.1%), and GGO plus a reticular pattern (82/187 cases, 43.9%). Most of the lesions were multiple with the predominant peripheral distribution.

Conclusion: Chest CT examination has a crucial auxiliary role in the diagnosis and evaluation of the current COVID-19 pandemic.

Keywords: SARS-CoV-2, Coronavirus disease-2019, COVID-19, Infection, Chest CT.

ABBREVIATIONS

CT; Computed tomography
COVID-19; Coronavirus disease 2019
SARS-CoV-2; Severe acute respiratory syndrome coronavirus 2
WHO; World Health Organization
RT-PCR; Reverse-transcription polymerase chain reaction
ARDS; Acute respiratory distress syndrome
COPD; Chronic obstructive pulmonary disease
CBC; Complete blood count.
CRP; C-Reactive Protein
ESR; Erythrocyte Sedimentation Rate
AST; Aspartate transaminase
ALT; Alanine transaminase
kVp; Kilovoltage
mA; Milliampere
HU; Hounsfield unite
GGO; Ground glass opacity
CT-SS; CT severity score
SPSS; Statistical Package for Social Science
RR; Respiratory rate
SARS; severe acute respiratory syndrome
MERS; Middle East respiratory syndrome

BACKGROUND

Since December 2019, an outbreak of a new acute viral respiratory disease caused by a novel coronavirus (SARS-CoV-2) has been reported in Wuhan city in central China. [1] On February 12, 2020, the World Health Organization (WHO) reported that the official name of this disease was coronavirus disease-2019 (COVID-19). Afterward, WHO declared an epidemic caused by the new coronavirus leading to a degree of public panic. [2,3]

The SARS-CoV-2 is a new coronavirus species, which has never been previously described in the human being. Firstly, it was found that some persons had contact with an animal market, suggesting an animal-to-human spread. Shortly afterward, a human-to-human spread had occurred with a new sort of acute respiratory infectious disease and was thought to be primarily transmitted via respiratory droplets with a median incubation period of four days [4,5].

Common clinical symptoms of patients infected with coronavirus involve fever, dry cough, muscle ache, and fatigue. Besides, some patients could have expectoration, sore throat, or diarrhea. Moreover, in some critical cases, acute respiratory disease, renal failure, and even death have occurred. [6]

With the rapid spread of the SARS-CoV-2 infection worldwide, we need a more rounded view of the role of chest CT imaging in its detection. It was found that chest CT examination has a crucial role in early screening and diagnosing patients with suspected COVID-19. The previous studies established that the majority of COVID-19 patients displayed common chest CT features, including ground-glass opacities and consolidation with bilateral peripheral or multi-lobes involvement [7,8]. Patients with clinical manifestations of COVID-19 and negative RT-PCR but positive CT imaging should be isolated to prevent wide-spread infection. [9]

Increasing evidence suggested that these chest CT features can not only be used to screen suspected patients but also provide a diagnostic method for COVID-19 caused acute respiratory distress syndrome (ARDS). Several studies also reported that chest CT appearances in COVID-19 patients following treatment play an essential role in treatment evaluation and follow-up. [10] The most apparent chest CT abnormalities were still noticeable for ten days but disappeared at 14 days after the initial onset of symptoms. [11]

In this study, we report the chest CT manifestations of COVID-19 with different severity to provide a more comprehensive overview of the disease, to help the clinical diagnosis and management, and aid the radiologists to familiarize the possible COVID-19 imaging features.

Patients and methods

Search Strategy

We reviewed 187 cases with laboratory-confirmed COVID-19 referred to the CT unit in the National Liver Institute, Menoufia University from April 18 to June 10, 2020. The study was approved by the Research Ethics Committee of the National Liver Institute and patient consent was waived. Different clinical and laboratory data were acquired from a detailed medical record gathered respectively in a standardized form.

Clinical assessment

The following clinical data were assessed: sex, age, cough, expectoration, muscle ache, fatigue, abdominal pain or diarrhea, headache, sore throat, dys-

pnea as well as the presence of co-morbidities including systemic hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), coronary heart disease, chronic kidney disease or immunodeficiency. Tobacco smoking should also be recorded.

All patients underwent routine laboratory tests like CBC, Serum ferritin, D-dimer, inflammatory marker (CRP), and liver function tests (AST & ALT). RT-PCR for novel coronavirus from nasopharyngeal swab as well as high-resolution chest CT scan was also done. A patient with suspected COVID-19 met the following criteria: fever, cough and/or shortness of breath, lymphopenia, elevated CRP level, elevated serum ferritin or D-dimer with no improvement noted after receipt of anti-influenza and supportive treatment for 3 days and/or a history of close contact with confirmed COVID-19 patient.

Laboratory-confirmed COVID-19 patients with positive RT-PCR were only enclosed in our study. The exclusion criteria were concurrent pulmonary bacterial or fungal infection as well as patients with negative RT-PCR for novel coronavirus infection.

Chest CT Technique

Scanning was performed by a 128-slice CT scanner (Aquilion 128; Toshiba Medical Systems, Tochigi, Japan) using the following parameters: 120 kVp, 150 mA, 1.484 pitch, reconstruction matrix of 512-512, slice thickness of 1.0 mm, and field of view of 350 x 350 with high spatial resolution algorithm. All cases were scanned in a supine position during breath-holding at full inspiration from the lung apices down to the costophrenic angles. All CT images were evaluated using a lung window, with a window level of −500 HU and a window width of 1500 HU and a mediastinal window with window level 40 and width 350.

Image Analysis

All CT data were transferred from the archive to a workstation (Vitrea 2.2 or Osrix), via internal network conections. All images were independently reviewed by three consultant radiologists, with 5, 12, and 13 years of experience. The location, size, shape, and number of the abnormal features on chest CT were carefully observed and recorded. In the case of discordant reading, a consensus was reached by a discussion between them. The CT images were fully assessed and the predominant findings were categorized into lung, bronchial, and pleural changes.

Lung changes were differentiated into the following subcategories: ground-glass opacity (GGO; increased parenchymal attenuation without veiling the underlying lung vessels), consolidation (homogeneous increased parenchymal density with the blurring of the underlying vessels), GGO plus a reticular pattern (GGO with inter-/intralobular septal thickening, giving crazy-paving pattern), vacuolar sign (a small transparent shadow of < 5 mm in size noted within the lesion), vascular dilatation sign (dilated small vessels within the lesion), fibrotic bands (an irregular strip lesion), halo sign (focal consolidation with surrounding GGO halo) and reverse halo sign. Subpleural line (a linear shadow 2–5 cm in length seen in parallel to the chest wall) and subpleural transparent line (a thin transparent line appearing between the lesion and the visceral pleura).

Bronchial changes were grouped into two subcategories: air bronchogram (an air-filled bronchus within the pulmonary lesion) and bronchial distortion. *Pleural changes* were also grouped into two subcategories: pleural thickening and pleural effusion. Lymph node enlargement was also assessed.

The distribution of lung abnormalities was predominantly peripheral (involving mainly the peripheral "one-third" lung), followed by central and diffuse (peripheral & central) lung involvement.

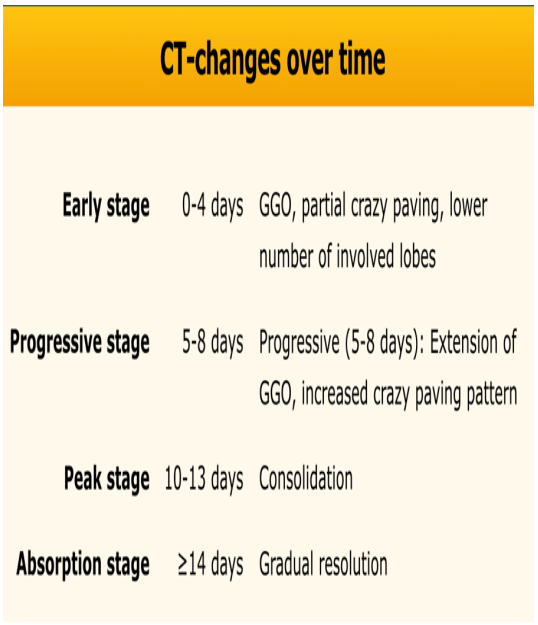
Chest CT severity score assessment

This score uses lung opacification as a surrogate for the extension of the disease in the lungs. According to the anatomical structure, both lungs were divided into 20 regions, in which the apicoposterior segment of the left upper lobe was subdivided into apical and posterior segmental regions, while the anteromedial segment of the left lower lobe was subdivided into anterior and basal segmental regions. The lung opacities in all of the 20 lung regions were evaluated on chest CT using scores of 0, 1, and 2 if parenchymal opacification involved 0%, less than 50%, or equal or more than 50% of each region respectively. The CT-SS was defined as the sum of the individual scored in the 20 lung segmental regions, ranging from 0 to 40 points.

Statistical Analysis

The data collected were tabulated and analyzed by the Statistical Package for Social Science (SPSS) version 26.0. Parametric data were presented with a mean ± standard deviation and non-parametric data with median and range. The prevalence of CT imaging findings was estimated as the percentage of patients showing each abnormality. Screening of

cases using the chi-square or the Fisher exact test will be done. So, we easily process and deploy analytics faster with flexible deployment options to find insights about the course of the disease.



RESULTS

Characteristics and clinical manifestations

Of the total 376 patients with suspected COVID-19, laboratory-confirmed 187 patients with COVID-19 were enrolled in our final cohort, including 121 males and 66 females (mean age, 34.3 years; range, 21-79 years).

Our patients with confirmed coronavirus disease 2019 had various symptoms at the disease onset, with fever noted in all patients (100%), dry cough in 181 of 187 patients (96.8%), with only 29 of 187 patients (15.5%) showed cough with sputum. Sore throat noted in 175 patients (93.6%), muscle ache in 177 patients (94.7%), fatigue in 173 patients (92.5%), headache in 153 patients (81.8%), shortness of breath in 145 patients (77.5%), and gastrointestinal symptoms, including abdominal pain and diarrhea, in 102 patients (54.5%).

Routine blood tests were done for all patients with 185 of 187 patients (98.9%) had lymphopenia. The CRP level was elevated in all 187 patients (100%). Of our studied patients, 54

(28.9%) had elevated D-dimer and 112 (59.9%) had elevated serum ferritin with elevated liver enzymes (AST &ALT) in about 99 of 187 patients (52.9%).

In our study, co-morbid conditions or diseases were recorded; for example, systemic hypertension was noted in about 83 of 187 patients (44.4%), diabetes mellitus in 40 patients (21.4%), coronary heart disease in 11 patients (5.9%%) with chronic obstructive pulmonary disease (COPD) in only six patients (3.2%). No chronic kidney disease or immunodeficiency was observed. We found 70 of 187 patients (37.4%) to be smokers. Table 1 summarizes the demographic and clinical features of our confirmed COVID-19 patients.

Chest CT Findings

With regard to lesion distribution **(Table 2),**

Features	No. (%) of patients (n = 187)
Sex:	
• Male	121 (64.7)
• Female	66 (35.3)
Symptoms:	
• Fever	187 (100)
• Dry cough	181 (96.8)
• Expectoration	29 (15.5)
• Sore throat	175 (93.6)
• Muscle ache	177 (94.7)
• Fatigue	173 (92.5)
• Shortness of breath	145 (77.5)
• Abdominal pain & diarrhea	102 (54.5)
Laboratory findings:	
• Lymphopenia	185 (98.9)
• Elevated CRP level	187 (100)
• Elevated D-dimer	54 (28.9)
• Elevated serum ferritin	112 (59.9)
• Elevated AST & ALT levels	99 (52.9)
Co-morbidities:	
• Hypertension	83 (44.4)
• Diabetes mellitus	40 (21.4)
• Coronary heart disease	11 (5.9)
• COPD	6 (3.2)
Smoking:	
• Smokers	70 (37.4)
• Non-smokers	117 (62.6)

Table 1: Demographic and clinical features of our patients with confirmed COVID-19:

Note: Percentages/Total with confirmed COVID-19 in parentheses.

Distribution	No. (%) of patients (n = 187)
Lung involvement	
• Unilateral	57 (30.5)
• Bilateral	130 (69.5)
Lesion multiplicity	
• Single lesion	39 (20.9)
• Multiple lesions	148 (79.1)
Lesion location	
• Peripheral	109 (58.3)
• Central	10 (5.3)
• Peripheral & central	68 (36.4)

Table 2: Distribution for CT abnormalities in our Patients with confirmed COVID-19:

Note: Percentages/Total with confirmed COVID-19 in parentheses.

CT abnormalities were predominantly involving both lungs in 130 of 187 patients (69.5%) with only 57 patients (30.5%) presented unilateral (Right or Left) lung involvement. We divided the lesion location into peripheral, central, and diffuse (peripheral & central) with the predominant peripheral location in about 109 of 187 patients (58.3%) followed by diffuse involvement in about 68 patients (36.4%) and finally, central location in only ten patients (5.3%). Of our 187 patients, 148 (79.1%) presented by multiple parenchymal lesions with a single lesion in only 39 (20.9%). The average time from initial disease onset to chest CT examination was 7 ± 4 days.

In terms of lung abnormalities, ground-glass opacity (GGO), consolidation and crazy-paving pattern were the most common CT findings, with reported rates of 51% (95/187), 48% (90/187) and 44% (88/187) respectively. Besi-

des that, other lung changes were also observed as halo sign; 62 (33.2%), reverse halo sign; 55 (29.4%), vacuolar sign; 38 (20.3%), vascular dilatation sign; 23 (12.3%), fibrotic bands; 52 (27.8%), subpleural line; 44 (23.5%), subpleural transparent line; 11 (5.9%) (**Table 3)** **(Figure 1&2)**.

CT Signs	No. (%) of patients (n = 187)
Lung changes	
• GGO	95 (50.8)
• Consolidation	90 (48.1)
• Crazy-paving pattern	82 (43.9)
• Halo sign	62 (33.2)
• Reverse halo sign	55 (29.4)
• Vacuolar sign	38 (20.3)
• Vascular dilatation sign	23 (12.3)
• Fibrotic bands	52 (27.8)
• Subpleural line	44 (23.5)
• Subpleural transparent line	11 (5.9)
Bronchial changes	
• Air bronchogram	85 (45.5)
• Bronchus distortion	37 (19.8)
Pleural changes	
• Thickening of pleura	49 (26.2)
• Pleural effusion	7 (3.7)
Lymph node enlargement	5 (2.7)

Table 3: CT Signs of COVID-19 in our confirmed patients:

Note: Percentages/Total with confirmed COVID-19 in parentheses.

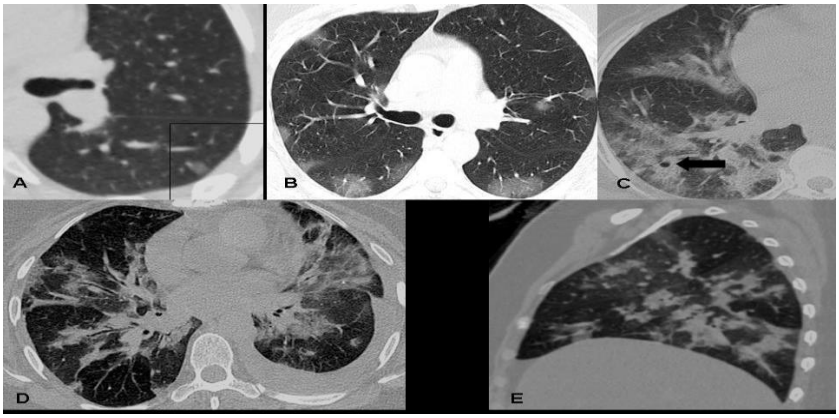


Figure 1: Non-contrast MDCT chest showing variable lesions distribution in the lungs of 5 patients with COVID-19.

A. 20-year-old man. CT image done on day 3 after the onset of symptoms shows solitary focal ground-glass nodular opacity with the posterior basal peripheral location at the left lower lobe "black box".
B. 44-year-old man. CT image done on day 8 of symptoms shows multiple bilateral ground-glass nodular opacityes of both lunges.
C. 39-year-old woman. CT image done on day 6 of symptoms shows multiple bilateral peripheral and central crazy paving patterns; some with vacuole inside "Black arrow" and mixed with areas of consolidation.
D. 48-year-old man. CT image done on day 10 of symptoms shows multiple bilateral central and peripheral lesionns composed of consolidation, crazing paving, and fibrotic bands, with associated left-sided pleural effusion.
E. 37-year-old woman. CT image done on day 9 of symptoms shows multiple lesions of consolidation and crazy paving showing more posterior

lung involvement than the anterior segments.

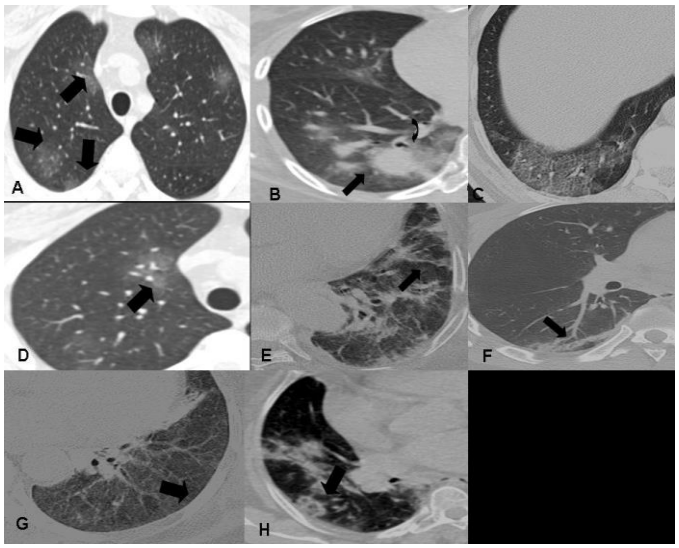


Figure 2: Non-contrast MDCT chest showing patterns of parenchymal lung changes in eight different patients with COVID-19.

A. 55-year-old man. CT done on day 5 after the onset of symptoms shows ground glass nodular pattern "arrows".
B. 40-year-old woman. CT done on day 7 of symptoms shows consolidation "black arrow" surrounded by ground-glass *halo* "curved arrow" at the right lower lobe.
C. 57-year-old man. CT done on day 6 of symptoms shows a crazy-paving pattern at the right lower lobe formed of ground-glass opacity and reticular opacity.
D. 53-year-old man. CT done on day 8 of symptoms shows vascular dilation in the ground glass opacity "arrow".
E. 60-year-old woman. CT done on day 12 of symptoms shows fibrotic bands "arrow" at the left lower lobe.
F. 59-year-old man. CT done on day 13 of symptoms shows a subpleural line at the right lower lobe.
G. 40-year-old woman. CT done on day 11 of symptoms shows a Subpleural transparent line.
H. 54-year-old woman. CT done on day 8 of symptoms shows Ground glass opacity right lower lobe with surrounded consolidation "Reverse halo" "Black arrow"

In terms of bronchial changes **(Figure 3)**, 85 patients (45.5%) had air bronchogram on CT and 37 patients (19.8%) had bronchus distortion. With regard to pleural changes, 49 patients (26.2%) had thickening of pleura and only seven patients (3.7%) had pleural effusion. Also, mediastinal lymph node enlargement was noted in about five patients (2.7%) (**Figure 4)**.

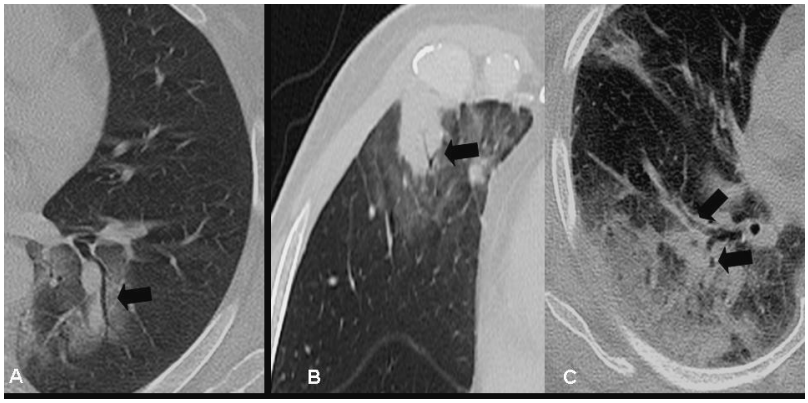


Figure 3: Non-contrast MDCT showing bronchial changes in three different patients with COVID-19.

A. 51-year-old woman. CT done on day seven of symptoms shows air bronchogram within ground-glass opacity at the left lower lobe.
B. 57-year-old man. CT done on day 12 of symptoms shows air bronchogram within consolidation at the right middle lobe, with surrounding ground-glass opacity.
C. 71-year-old man. CT done on day 15 of symptoms shows bronchial wall thickening and distortion within an area of mixed consolidation and ground-glass opacity.

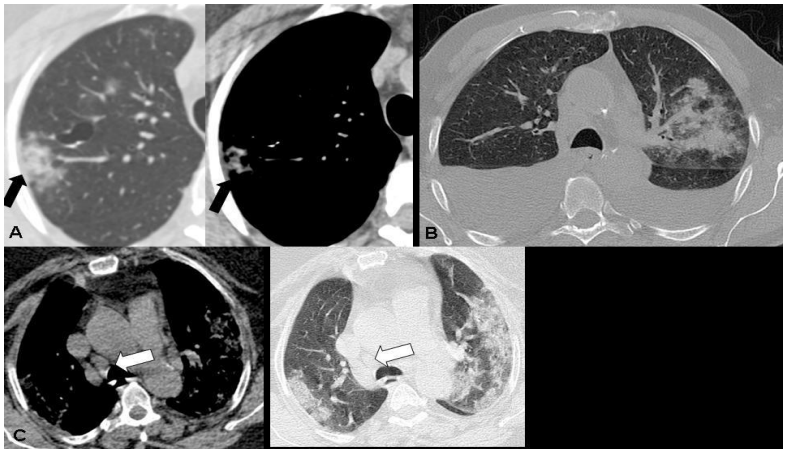


Figure 4: Non-contrast MDCT showing pleural and mediastinal changes in three different patients with COVID-19.

A. 46-year-old woman. CT done on day 8 of symptoms shows pleural thickening overlying area of mixed consolidation and ground-glass opacity at the right upper lobe.
B. 31-year-old man. CT done on day 7 of symptoms shows bilateral pleural effusion coupled with left-sided lung parenchymal changes "consolidation and ground-glass opacity".
C. 72-year-old man. CT done on day 8 of symptoms shows mediastinal pre-tracheal node "arrow". Bilateral lung crazy paving and ground-glass opacity also seen.

The course of the disease within our studied patients could be divided into two phases (early & advanced phases) according to the time of CT examination in relation to the onset of symptoms, an early phase (< 7 days after the onset of symptoms); n=100 patients and an advanced phase (>7 days after the onset of symptoms); n=87 patients. We noted that the frequency of GGO was remarkably higher in an early phase disease. While, the frequencies of crazy-paving pattern, vacuolar sign, fibrotic bands, air bronchogram, bronchus distortion, a subpleural line, a subpleural transparent line, and pleural effusion were significantly higher in patients with an advanced phase disease.

According to the severity of the disease, most of our patients (n=144, 77%) with high CT-SS were categorized as severe cases that met any of the following criteria; respiratory distress, RR ≥ 30 beats/min, and/or resting blood oxygen saturation of finger ≤ 93%. The remaining patients (n=43, 23%) were mild with signs of respiratory infection and had pneumonia changes on CT imaging. No critical patients (requiring mechanical ventilation) were identified in our study.

DISCUSSION

COVID-19 is a new, highly infectious viral respiratory disease caused by a novel coronavirus (SARS-CoV-2) of unclear origin. [12] It is principally transferred by contact between humans and infectious droplets. The novel coronavirus could be identified in nasopharyngeal swabs, sputum, and feces. Early diagnosis and early interference are essential to reduce the incidence and mortality of severe cases. [13]

In the present survey, all cases were adults, and most of the male gender. Fever, dry cough, and muscle ache were continual clinical symptoms. The incidence of expectoration, shortness of breath, and abdominal pain with diarrhea were less common. Regarding the laboratory findings, 98.9% of our patients had lymphopenia and all patients (100%) had an increased CRP level. Consequently, a lower lymphocyte count with a high CRP level was the most delicate criteria. Our findings are in accordance with previous reports of Zhoul et. al [12] who reported similar clinical and laboratory findings.

In reviewing and analyzing the CT findings of 187 patients with confirmed COVID-19, we found that most patients often presented as multiple lesions on the initial CT scan (79.1%) with 20.9% of patients manifested as a single lesion. Considering the range of lung involvement, a predominant peripheral lesion distribution (75.8%) with significant involvement of the lower zones of both lungs was observed. In other words, Gharib and Stern [14] showed that multiple lesions of both lungs encompassed concurrently is not usually spotted in the typical bacterial pneumonia. Wu et al., [13] reported that in comparison with other types of pneumonia, COVID-19 appeared to cause milder clinical presentation and severer pulmonary abnormalities on chest CT imaging.

We found diversified CT signs regarding the lung changes, GGO was the most frequent pulmonary manifesttations, followed by consolidation and GGO plus a reticular pattern "Crazy-paving pattern" with reported rates about 51%, 48%, and 44% respectively. Other detectable CT signs in our study were described previously. The previous findings were in agreement with the results of the recently published studies.[15-17]

On the whole, all patients have not been surveyed by pathology all over the world, so it is impractical to identify the precise pathological COVID-19 manifestations. However, according to the morphological chest CT findings, the pathological presentation could be suggested, although there was no straight evidence. [18]

Compared with the early-phase COVID-19, the advanced-phase disease was associated with a highly increased frequency of crazy-paving pattern, fibrotic bands, bronchus distortion, etc. as described previously, but GGO was significantly less predominant. Our results suggested that chest CT examination could be used to monitor the disease evolution and consequently, predict the disease severity and the prognosis.

Also, we devised a scoring method using the amount of lung opacification involving 20 lung regions as a surrogate for COVID-19 burden. We found that the CT-SS was higher in severe when compared to mild cases. Yang et al., [19] envisioned that the CT-SS relatively straightforward method could provide objective means to expedite the identification of patients with severe disease, especially with limited healthcare resources or PCR testing capabilities.

Wu et al., [13] insisted that the COVID-19 requires to be differentiated from other closely related diseases, such as SARS and MERS. They displayed multiple ground-glass opacities and bilateral pulmonary lesions, with the predominant peripheral distribution. However, SARS and MERS had rapid disease progress and more predominant lung damage than COVID-19 did. [20,21]

Furthermore, COVID-19 should be distinguished from other types of viral pneumonia such as influenza virus, parainfluenza virus, and mycoplasma pneumonia. Radiological finding of bilateral lung involvement is regarded as an additional index and account for the highest score in MuLBSTA system (multilobular affection, lymphopenia, bacterial co-infection, smoking history, hypertension and finally, age) for suggesting the mortality in COVID- 19 patients compared to other viral pulmonary infection [22,23].

The present study has some restrictions. Firstly, this was a retrospective study including a limited patients' number with laboratory-confirmed novel coronavirus-2019 infection. Secondly, none of our patients had a lung biopsy to reflect the pathological data for comparative study. Finally, the course of COVID-19 is short, so, chest CT changes over its whole course have not been totally delineated.

CONCLUSION

CT imaging can play an important role in the early diagnosis and disease stratification of COVID-19. Patchy ground-glass opacities and consolidation were reported as the typical CT manifestations. In this study, we survey the typical and atypical chest CT manifestations and hopefully familiarize radiologists with these different imaging features and make a precise diagnosis. The CT-SS provides a straightforward method for assessing COVID-19 severity. In addition, as the COVID-19 autopsies were in progress, we believe that the radiologic-pathologic conection will be further explored, which is expected to be helpful in confirming imaging features and guiding management.

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