Correlation between CT findings and outcomes in 46 Patients with Coronavirus Disease-19

CURRENT STATUS: UNDER REVIEW

nature research

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DOI:

10.21203/rs.3.rs-23430/v1

SUBJECT AREAS

Nuclear Medicine & Medical Imaging

KEYWORDS

Coronavirus infections, Tomography, X-ray computed, Pneumonia, Lung disease

Abstract

Purpose: The aim of this study was to retrospectively analyze chest Computed Tomography (CT) findings in COVID-19 pneumonia and identify features associated with poor prognosis.

Methods: This retrospective review included 46 patients with RT-PCR confirmed COVID-19 infection. Basic clinical characteristics and detailed CT features were evaluated and compared between patients who recovered (n = 40) from coronavirus and those who expired (n = 6). Chest CT examinations for ground-glass opacity, crazy-paving pattern, consolidation, and fibrosis were scored by two reviewers. The total CT score comprised the sum of lung involvement (5 lobes, scores 1-5 for each lobe, range; 0, none; 25, maximum) was determined.

Results: We analyzed clinical data from 46 patients (26 males and 20 females; age 9-82 years) with confirmed COVID-19 pneumonia were evaluated. The chest CTs showed 27 (58.7%) patients had ground-glass opacity, 19 (41.3%) had ground glass and consolidation, and 35 (76.1%) patients had crazy-paving pattern. None of the patients who expired had fibrosis, in contrast to six (15%) patients who recovered from coronavirus. Most patients had subpleural lesions (89.0%), bilateral (87.0%) and lower (93.0%) lung lobe involvement. Diffuse lesions were present in four (67%) patients who succumbed to coronavirus, but only one (2.5%) patient who recovered ($p = 0.000$). CT identified a greater area of lung lobe involvement in patients who died ($p = 0.000$). In the group of patients who expired, the total CT score was higher than that of the recovery group (17.2 ± 7.8 vs. 7.1 ± 4.3, $p = 0.005$). Patients in the death group had lower lymphocyte count and higher C-reactive protein than those in the recovery group ($p = 0.011$ and $p = 0.041$, respectively).

Conclusion: The CT of patients with COVID-19 mainly showed ground-glass opacity and ground-glass opacity plus consolidation, with a peripheral lower lobe preference. Early fibrosis may correlate with well prognosis. Lymphopenia, elevated C-reactive protein, and high CT score in conjunction with diffuse distribution of lung lesions are indicative of disease severity and short- term mortality.

Introduction

The emergence of a novel coronavirus from Wuhan, China, has become a public health threat [1]. Since the detection of the coronavirus in late December 2019, sporadic imported cases among

travelers returning from China have been reported by several countries. A novel enveloped RNA beta-coronavirus was discovered by unbiased sequencing in samples from patients infected by the novel coronavirus; it has currently been named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[2]. On February 12, 2020, the World Health Organization (WHO) officially designated the disease as Coronavirus Disease 2019 (COVID-19)[3]. Clinically, the dominant symptoms include fever and respiratory discomfort. Gastrointestinal symptoms are uncommon, suggesting a difference in viral tropism compared with seasonal influenza, SARS-CoV and MERS-CoV. The fatality rate is estimated to be approximately 1.4%-3.2% [4].

In the past several weeks, chest Computed Tomography (CT) findings at baseline and short- term CT follow-up have been steadily published in studies [5-9]. Typical CT imaging of COVID-19 pneumonia include bilateral, peripheral, and basal predominant ground-glass opacity, consolidation, or both. Serial chest CT during recovery from COVID-19 pneumonia showed four stages of lung abnormalities manifested as (1) ground-glass opacity with the development of (2) crazy-paving and (3) increased consolidation (i.e., more extensive lung involvement), and (4) slow resolution. However, the severity of lung damage evaluated by CT and its differences between patients who recovered and those who expired have not been well studied. There is insufficient time from the symptom onset to the final outcome, especially death; therefore, it is essential to find early predictors of clinical outcomes.

Here, we describe in detailed the distribution or the extent of lung abnormalities in COVID- 19 patients upon admission and analyze its association with final outcomes. The purpose of this study was to identify the features and draw specific patterns of lung abnormalities on admission to facilitate better clinical decisions, timely therapeutic strategy, and reduce mortality.

Material And Methods

This retrospective study was approved by medical ethical committee, and written informed consent was waived.

Diagnostic and recovery Criteria of COVID-19 Pneumonia

According to the preliminary diagnosis and treatment protocols from the National Health Commission

of the People’s Republic of China, the final diagnosis for COVID-19 pneumonia was determined by real-time fluorescence polymerase chain reaction from throat swabs of suspected patient. The patients with confirmed COVID-19 pneumonia were hospitalized and isolated for treatment. The recovery criteria were as follows: (1) no fever for greater than 3 days, (2) respiratory symptoms significantly improved, (3) improvement in the radiological abnormalities on chest CT, and (4) at least two negative COVID-19 nucleic acid detection within an interval of one day.

Patients

In this study, records for patients diagnosed with COVID-19 pneumonia were reviewed retrospectively for the period from 1 January 2020 to 20 February 2020 in this single-center study. The patient recovered or died within two month of hospitalization, and the interval between the first or last CT scan and RT-PCR must be less than 3 days. Patients with COVID-19 confirmed by RT-PCR testing were enrolled, and both chest CT scan and RT-PCR testing were conducted within an interval of three days or less.

Chest CT protocols

All of the images were obtained on Optima 660, GE, America with patients in the supine position. The main scanning parameters were as follows: tube voltage = 120 kVp, automatic tube current modulation (30–70 mAs), pitch = 0.99–1.22 mm, matrix = 512 × 512, slice thickness = 10 mm, field of view = 350 mm × 350 mm. All of the images were then reconstructed with a slice thickness of 0.625–1.250 mm with the same increment [10].

CT image analysis

All of the chest CT images were reviewed by two radiologists (Q.L. and G.M.L with 5 and 15 years of experience in interpreting chest CT imaging, respectively), including main CT feature and lesion distribution, to determine total CT scores by consensus. Referring to international standard nomenclature defined by the Fleischner Society glossary and peer-reviewed literature on viral pneumonia, the main CT features were described using terms including ground-glass opacity (GGO), crazy-paving pattern, consolidation, and fibrosis. Reticulation with associated architectural distortion and mild traction bronchiectasis are considered to be related to fibrosis.

The lung involvement of all these abnormalities was quantitatively estimated according to the area involved. Each lung lobe was visually scored from 0 to 5; 0, no involvement; 1, <5% involvement; 2, 25% involvement; 3, 26%–49% involvement; 4, 50%–75% involvement; 5, >75% involvement. The total CT score was the sum of the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement). The distribution of pulmonary abnormalities was classified as predominantly subpleural (mainly the peripheral one-third of the lung involved), diffuse (continuous involvement without respect to lung segments), or random [5].

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics Software (version 23.0; IBM, Chicago, IL USA). Quantitative data were presented as mean ± standard deviation (minimum-maximum) and the counting data as the percentage of the total unless otherwise specified. The comparisons of non-paired data were evaluated using the Mann-Whitney U test or Chi-squared test [5]. A p-value of <0.05 was defined as statistical significance.

Results

1. Patient characteristics:

A total of 46 patients (26 males and 20 females) were included in the study. The average age was 50 ± 17 years (range: 9–87). Patients who succumbed to COVID-19 pneumonia were older than those who recovered (72 ± 14 vs 47 ± 16, $p = 0.001$). Patients with diabetes or hypertension are more likely to die than those without the previous history of chronic illness (5/15, 33.0% and 1/31, 3.0%, respectively $p = 0.018$; **Table 1**).

The most prevalent presenting symptoms include fever (22, 48.0%) and cough (6, 13.0%) or both (18, 39.0%). The laboratory test for patients was often normal, with the most frequent abnormalities being a mild leucopenia, reduced lymphocyte count, and elevated C-reactive protein. Patients who died had lower lymphocyte levels and higher C-reactive protein than those who recovered (**Table 1**). These patients underwent initial CT scans from the symptom onset with a mean interval of 5 ± 3 days (range: 1–15 days). A total of 86 pulmonary CT scans was performed and each CT scan had an interval of three days or less from RT-PCR diagnosis. After initial symptom onset, 40 patients

recovered with a mean hospitalized period of 23 ± 9 days (range: 9–42) and six patients died after a mean hospitalized period of 16 ± 8 days (range: 8–25).

2. Chest CT Evaluation

Ground-glass opacity (GGO), crazy-paving pattern (GGO with superimposed inter- and intralobular septal thickening), and consolidation were the main CT findings in early-stage COVID-19 pneumonia (**Figure 1** and **Figure 2**). Of all patients examined, 27 (58.7%) had ground-glass opacity, 19 (41.3%) had ground-glass and consolidation in combination, and 35 (76.1%) patients had crazy-paving pattern. Fibrosis was observed in six (6/40, 15.0%) patients who recovered, and none of the six patients died with COVID-19. Cavity, mediastinal lymphadenopathy, and pleural effusion were not observed. The number of lung lobes involved in those who died of COVID-19 showed no significant differences than those who recovered (3.7 ± 1.4 vs 4.5 ± 1.2, p = 0.096). The area of lung lobes involved in the recovery group was greater than that in expired (p = 0.000; **Table 3**). In those patients who died, the total CT score was greater than those who recovered (17.2 ± 7.8 vs 7.1 ± 4.3, p = 0.005; **Table 2**). Finally, subpleural lesions (41/46, 89.0%) were more common than central or diffuse lung lesions (5/46, 11.0%). Of the patients who died, four (4/6, 67.0%) had diffuse lesions while only one (1/40, 2.5%) patient who recovered had diffuse lesions. Patients with diffuse lung lesions were more likely to die than those with subpleural lesions (4/5, 80.0% vs 2/41, 4.8%, p = 0.000; **Table 2**). The majority of patients had bilateral (40/46, 87.0%) and lower (43/46, 93.0%) lung lobes involvement.

Discussion

The main CT findings of COVID-19 consist of ground-glass opacity, consolidation, and crazy-paving pattern, which were similar to those described by several groups of investigators [11, 12]. Our study highlights the clinical implication of CT findings as a prognostic indicator in patients with COVID-19. Comparing those who recovered with those who did not, neither ground- glass opacity, consolidation, or crazy-paving pattern is associated with final outcomes. However, fibrosis was observed in six (13%) who recovered and none who died. We speculate that fibrotic changes may have resulted from organizing pneumonia pattern of lung injury with COVID-19. Min Jae et al. [13] found the remaining

opacity of MERS of intubation group and fibrosis was as sequela on follow-up chest radiographies. Similar to other acute lung injuries, fibrosis is thought to be the result of resolution[14, 15]. Fibrosis in the early stages, assuming all of the patients to be in an early stage of infection who underwent initial CT scans from the symptom onset with a mean interval of 5 ± 3 days, may be associated with good prognosis in early chest CT examinations. Pleural effusion was not present in the patients with COVID-19 in our patients. Karuna et al. [16] reported that the early appearance of pleural effusion was a predictor of short-term mortality in patients with MERS; however, this relationship was absent in our patients with COVID-19.

High CT lung score was a sign of poor prognosis and was associated with short-term mortality. Patients who died had higher CT lung scores compared with those who recovered in our study, indicating the rapid development of the disease process and the largest area of the lung occupied by pneumonia. In support of our study, Zhao et al. [17] reported that CT involvement score can help in evaluation of the severity and extent of COVID-19. The area of the affected lung lobes in expired patients was greater than those who recovered. Also, predominant peripheral distribution (89%) of abnormalities was observed in our study; however, four (66.7%) patients who died and one (2.5%) who recovered showed diffuse distribution of lung lesions. Patients with diffuse lung lesions are more likely to die than those with subpleural lesions (4/5 vs. 2/41, $p = 0.000$). These factors are consistent with diffuse alveolar damage patterns that may cause worse outcomes for patients. Xu et al. [18] also have reported a COVID-19 patient death with diffuse lung involvement on X-ray images and pathological findings of pulmonary edema and clear film formation through biopsy sample taken from lung, indicating acute respiratory distress syndrome (ARDS). Our results suggest that high CT scores coupled with diffuse distribution of lung lesions on admission were responsible for ensuing ARDS and a poor prognosis in most patients.

Significantly reduced lymphocytes and elevated C-reactive protein are two clinical indicators of fatal prognosis in patients with COVID-19. Patients who died from COVID-19 had higher C- reactive protein and lower lymphocytic count than the recovery group. Lymphocyte were reduced in death group reflecting a deficiency of adaptive immune response. Lymphopenia and high plasma levels of C-

reactive protein may be related to cytokine storm in patients with COVID-19, as postulated by a previous report [1]. In our study, the older age and chronic medical illness, including diabetes and cardiovascular disease, were statistically associated with mortality; however, we did not see a statistically significant difference between two groups in sex. These factors were congruent with the MuLBSTA score [19] for predicting mortality in viral pneumonia and may have played a role in the death of patients with COVID-19. Our results suggest that both lymphopenia and elevated C-reactive protein are common clinical features in the patients with COVID-19 and might be key factors associated with disease severity and mortality.

Our study has several limitations. It is retrospective and includes only 46 patients with confirmed COVID-19. Due to the X-ray radiation damage and the high infectivity of COVID-19, multiple CT re-examinations for the dynamic observation was limited. In the future, we aim to collect more follow-up CT data to compare the evolution and outcome of the disease.

Conclusion

In conclusion, older age with chronic medical illness, lymphopenia, elevated C-reactive protein, and high CT score in conjunction with diffuse distribution of lung lesions in COVID-19 are indicative of a poor prognosis and short-term mortality.

Declarations

Authors' contributions: Guihua Jiang, Cheng Li, and Guangming Li designed the study; Qiang Lei was a major contributor in writing the manuscript; Hui Chen and Wen Xu collected the imaging and clinical data; Xiaofen Ma, Junzhang Tian, and Yunfan Wu revised it critically for important intellectual content. All of the authors have read and approved the manuscript.

Compliance with ethical standards:

Funding: This study was funded by the National Natural Science Foundation of China (grant number U1903120, 81771807 and 81901729).

Conflict of Interest: Author Qiang Lei declare that he has no conflicts of interest. Author Guangming Li declare that he has no conflicts of interest. Author Junzhang Tian declare that he has no conflicts of interest Author Xiaofen Ma declare that she has no conflicts of interest Author Yunfan Wu declare that

she has no conflicts of interest. Author Hui Chen declare that he has no conflicts of interest. Author Wen Xu declare that she has no conflicts of interest. Author Cheng Li declare that he has no conflicts of interest. Author Guihua Jiang declare that he has no conflicts of interest.

Ethics approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: This retrospective study was approved by medical ethical committee of Guangdong Second Provincial General Hospital and the written informed consent was waived.

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Tables

Table 1: Comparison of Final Outcome According to Clinical Characteristics.

Clinical features	Outcome		P
	Recovery (n = 40)	Non-survivors (n = 6)	
Sex			0.328
Male	21 (45.7)	5 (10.9)	
Female	19 (41.2)	1 (2.2)	
Age (year)			0.002
≤60	34 (73.9)	1 (2.2)	
>60	6 (13.0)	5 (10.9)	
Chronic medical illness			0.018
Yes	10 (21.7)	5 (10.9)	
No	30 (65.2)	1 (2.2)	
Laboratory			
Leukocyte (x109 cells/L)	5.3±1.9	5.7±2.1	0.683
Lymphocyte (x109 cells/L)	2.6±1.5	1.4±0.5	0.011
C-reactive protein (mg/L)	31.8±33.1	107.3±82.3	0.041

Note: Continuous parameters presented as mean±SD, categorical data as n (%).

Table 2: Comparison of Final Outcome According to CT Findings.

CT Findings	Outcome		P
	Recovery (n = 40)	Non-survivors (n = 6)	
Ground-glass opacity			0.680
yes	24 (52.2)	3 (6.5)	
no	16 (34.8)	3 (6.5)	
Ground-glass opacity plus consolidation			0.680
yes	16 (34.8)	3 (6.5)	
no	24 (52.2)	3 (6.5)	
Crazy paving			1.000
yes	30 (65.2)	5 (10.9)	
no	10 (21.7)	1 (2.2)	
Distribution			0.000
Subpleural	39 (84.6)	2 (4.4)	
Diffuse	1 (2.2)	4 (8.8)	
Number of lung lobes involved	3.7±1.4	4.5±1.2	0.096
CT score	7.1±4.3	17.2±7.8	0.005

Note: Continuous parameters presented as mean±SD, categorical data as n (%), CT = Computed Tomography.

Table 3: Comparison of Final Outcome According to Lung Lobes Involved, by area on CT.

Area of lung lobes involved	Total (n = 169)	Recovery (n = 142)	Non-survivors (n = 27)	P
CT lesion extent				0.000
≤24%	112 (66.3)	107 (63.3)	5 (3.0)	
25–49%	27 (16.0)	23 (13.6)	4 (2.4)	
50–75%	16 (9.4)	8 (4.7)	8 (4.7)	
>75%	14 (8.3)	4 (2.4)	10 (5.9)	

Note: Data are number (%) of lung lobes, CT = Computed Tomography.

Figures

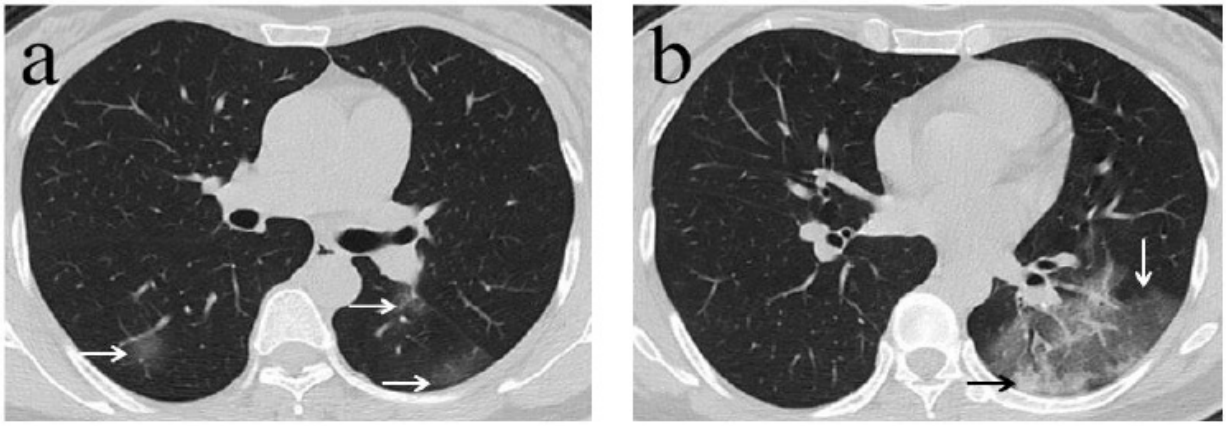

Figure 1

A 45-year-old woman with history of recent travel to Wuhan presented with fever for one day. (a, b) Non-contrast enhanced chest Computed Tomography (CT) showed multiple peripheral patchy ground glass opacities in both lower lobes (white arrows). CT scan also demonstrated consolidation in the left lower lobe (black arrow). CT involvement score was 5.

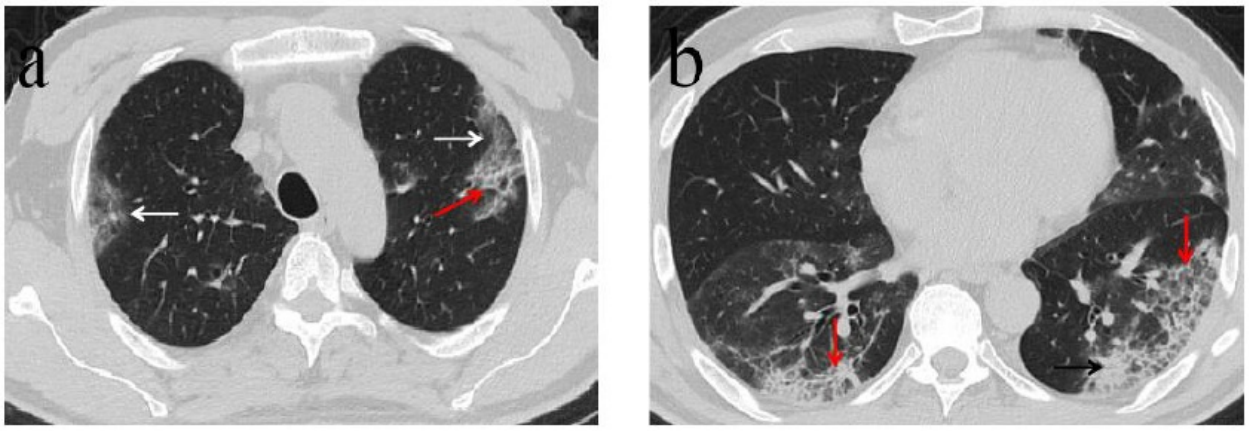

Figure 2

A 57-year-old man with a history of recent travel to Wuhan presented with fever for 10 days. (a, b) Non-contrast enhanced chest Computed Tomography (CT) showed multiple peripheral patchy ground glass opacities (white arrows) and crazy-paving pattern (red arrow) in both lower lobes. CT scan also demonstrated consolidation in the left lower lobe (black arrow). CT involvement score was 11.