Original Article

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TANAFFOS

Association Between CT Finding Changes and Clinical Course in COVID-19 Patients: A Single Center Retrospective Study

Ali Akbar Mahdavi [1], Masoomeh Raoufi [1], Mina Hashemi [1], Rezvan Aghaiepour [1], Hossein Mardanparvar [2], Sina Asaadi [3], Mehrdad Bakhshayesh Karam [4]

[1] Department of Radiology, Imam Hossein Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [2] Department of Nursing, Faculty of Nursing & Midwifery, Hormozgan University of Medical Sciences, Bandar Abbas, Iran, [3] School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran, [4] Department of Radiology, Masih Daneshvari Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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Correspondence to: Bakhshayesh Karam M
Address: Department of Radiology, Masih Daneshvari Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Email address:Mehrdadbakhshayesh@yahoo.com

Background: This study aimed to summarize the baseline and radiological characteristics of patients with COVID-19 and investigate the correlation between clinical outcomes and radiological findings in the first week after admission.

Materials and Methods: A single-center retrospective study was carried out on confirmed cases of COVID-19 based on RT-PCR and chest CT scan findings according to Iran's National Guidelines for defining COVID-19 in patients admitted to Imam Hossein Hospital, Tehran, Iran. Baseline and chest CT scan characteristics of patients were investigated, and their correlation with the change in clinical outcome was reported.

Results: 72 patients (50%) with a mean age of 54.65±16.2 years were in two periods of time including the first day of diagnosis and 6.0±3.4 days later. Based on CT scan Severity Score (CTSS) changes (decrease/no change or increase) during the study, patients were divided into two groups of CTSS progression (n=47) and CTSS no-progression (n=25). Diabetes mellitus (20%) and hypertension (19.1%) were the most frequent comorbidities among the patients in the non-progression and progression groups, respectively. There was no significant difference in demographic features including age and gender, and comorbidities (P>0.05). On the first day of diagnosis, there was no significant difference in blood tests and radiological findings and the number of patients who managed out-patients or in-patients in both groups. However, on the second evaluation day, patients in the progression group had significantly higher CTSS in comparison with the non-progression group (13.11±4.7 vs. 9.48±4.2, P=0.003), and the clinical situation in 15 patients in progression changed from out-patient to in-patient (p=0.033). Only chest CT imaging score was a potential parameter associated with the change in clinical progression (P=0.030, RR=10.18, 95, CI=1.25-89.72).

Conclusion: Increasing CTSS is a strong predictor of worsening clinical outcomes during hospitalization in COVID-19 patients.

Keywords: Clinical outcomes; Radiological findings; COVID-19

INTRODUCTION

In December 2019, an RNA virus belonging to the family of coronaviruses, which primarily leads to respiratory system infection, spread worldwide initiated from Wuhan, Chin (1-4). This pneumonia which started in late 2019 and challenged the world (5, 6), was named coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO) (7). Although much clinical and epidemiological literature has been published; however, the spread is still ongoing, and the early warning parameters for disease progression remain incomplete (8-11).

The lung is one of the most important human organs, and pulmonary involvement is a major concern for COVID-19 patients (12, 13). Computed tomography (CT) is an easy, practical, and accessible tool (14) that has been introduced as a helpful way for COVID-19 diagnosis. Its sensitivity is higher than real-time polymerase chain reaction (RT-PCR) in some cases and is being used in centers that are dealing with a lack of RT-PCR equipment (15, 16). Besides the diagnosis of COVID-19, recently, chest CT changes during the disease and its association with patient outcomes is one of the most interesting topics (17).

Although various CT findings such as ground-glass opacity (GGO), crazy-paving pattern, and consolidation have been reported in patients with COVID-19; however, they are not specific in these patients and might not have been seen in all cases.

This study aimed to summarize the baseline and radiological characteristics of patients with COVID-19 during their management and investigate the correlation between clinical setting change and radiological findings in the first week after admission to find reliable chest CT scan biomarkers that could predict clinical course in patients with COVID-19.

MATERIALS AND METHODS

In this retrospective single-center study, baseline characteristics including demographic data, routine blood tests, and chest CT imaging, were collected on the first day and second time at 6.0±3.4 days after diagnosis of COVID-19 in 72 patients. Diagnosis of COVID-19 was made based on positive RT-PCR and chest CT scan following Iran's National Guidelines on diagnosis and management of COVID-19. Based on these guidelines, patients with acute respiratory infection who do not positively respond to the usual pneumonia treatment, have a recent travel history to China, have respiratory symptoms with any severity, and those who have physical contact with an individual diagnosed with or suspected to have COVID-19, were considered suspected cases for COVID-19.

All participants provided written informed consent during their admission. The study protocol and informed consent documents were reviewed and approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences.

Demographic data including age, gender, underlying disease (diabetes mellitus, hypertension, hyperlipidemia, hypothyroidism, and asthma), length of first related symptom to the final diagnosis of COVID-19, laboratory findings, and clinical setting (out-patient, in-patient, and ICU admission) in the first day and second round of measurements were collected for all cases.

Low-dose lung CT scans were performed using a 16-detector CT scanner (SIEMENS; Emotion; SOMATOM) in a supine position, and patients were instructed on breath-holding to minimize motion artifacts. Chest CT scans were reviewed by a radiologist with 12 years of experience in the radiology department for involvement and severity of each lobe, the pattern of involvement such as ground glass, consolidation, crazy paving, reverse halo, and consolidation. CT severity Score (CTSS), which was introduced by Pan et al., was used to determine the severity of lung parenchymal involvement (17). Based on this semi-quantitative scoring, each of the 5 lung lobes was visually scored from 0 to 5 as: 0) no involvement; 1) < 5% involvement; 2) 5-25% involvement; 3) 26-49% involvement; 4) 50-75% involvement; and 5) >75% involvements. The total CTSS was the sum of the individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement). Chest CT scan findings and progression were reported by an expert radiologist who was completely blind to clinical and laboratory findings.

Data Analysis

The results were presented as mean ± standard deviation (SD) or frequency (%). Differences in variables between the individual groups were analyzed using the Mann-Whitney, Chi-square, and Fisher's Exact test based on variable types. A two-tailed $p < 0.05$ was considered significant for all tests. Statistical analysis was done by SPSS software version 25.0 (Armonk, NY: IBM Corp, USA).

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Shahid Beheshti University of Medical Sciences approved this study. Ethical considerations were approved by this committee with an ethics code of IR.SBMU.MSP.REC.1399.038. Accordingly, written informed consent was taken from all participants before any intervention. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

RESULTS

In total, 72 patients admitted to Imam Hossein Hospital with a definite diagnosis of COVID-19 based on RT-PCR (n=48.6%) and chest CT (51.4%) were reviewed in this study. Of these patients, 47 patients (65.3%) experienced a decrease in CTSS at the second time of evaluation (6.0±3.4 days after diagnosis), and 15 patients (20.8%) got worse (out-patient management to in-patients or need for ICU admission).

In this study, patients were divided into two groups: patients whose CTSS decreased/had no change (Non-progression) and whose CTSS increased (Progression) during the disease course. Diabetes mellitus (20%) and hypertension (19.1%) were the most frequent comorbidities among the patients in the non-progression and progression groups, respectively. There was no significant difference in demographic features of patients, including mean age and gender, comorbidities, as well as duration between first symptoms and final diagnosis in both groups (Table 1).

Table 1. Baseline characteristics of COVID-19 patients

	Non-progression (N =25)	Progression (N =47)	P-value
Age (Year)	57.04 ± 16.8	53.38 ± 16.0	0.462
Gender (Male)	10(40%)	26 (55.3%)	0.322
Comorbidities			
DM	5(20%)	6(12.8%)	0.491
HTN	8 (32%)	9(19.1%)	0.253
Asthma	1(4%)	1(2.1%)	1.00
Hypothyroidism	2(8%)	4 (8.5%)	1.00
HLP	2(8%)	4 (8.5%)	1.00
Date of first symptom to final diagnosis(days)	7.59 ± 5	6.46 ± 3.7	0.571

On the first day of diagnosis, the most frequent chest CT scan abnormalities were GGO and consolidation in both groups. There was no significant difference in blood tests and radiological findings and the number of patients who managed out-patients or in-patients between both groups (Table 2). However, on the second day of radiologic evaluation (6±3.4 days after diagnosis), patients in the progression group who had significantly higher CTSS in comparison to the non-progression group, showed a significant change of clinical characteristics which resulted in the need for admission of 15 patients in progression groups who were managed in out-patients setting (Table 3).

Table 2. Blood tests, radiological findings, and clinical situation of patients on the first day of diagnosis

	Non-progression (N =25)	Progression (N =47)	P-value
Blood Routine Tests			
WBC	6.65 ± 2.1	7.77 ± 8.1	0.295
Lymph	17.88±8.2	23.31 ± 13.9	0.152
CRP	71.30±64.23	52.09 ± 63.3	0.193
ESR	43.31±23.2	34.38 ± 25.5	0.362
Procalcitonin	3.03±2.8	2.55 ± 2.0	0.961
PCO2	40.53±7.4	43.76 ± 8.0	0.152
Radiological Findings			
GGO	10(40%)	26 (55.3%)	0.328
Reveres Halo	1(4%)	2(4.3%)	1.00
Consolidation	9(36%)	12(25.5%)	0.414
Crazy-paving	0	0	1.00
CTSS	10.20 ± 4.5	8.43 ± 4.8	0143
Clinical Setting			
Outpatients	6 (24%)	17 (36.2%)	0.405
Ward	19 (76%)	29 (61.7%)	
ICU	0	1 (2.1%)	

Data are presented as mean ± standard deviation. WBC: white blood cell; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; GGO: ground-glass opacity

For finding factors that are correlated with worsening of the clinical setting, evaluated variables including age, gender, disease history, chest CTSS, WBC, lymphocytes, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin were included in the univariate analysis. Only chest CT imaging score was a potential parameter associated with change in clinical progression (p=0.03, RR=10.18, 95, CI=1.25-89.72).

Table 3. Blood tests, radiological findings, and clinical situation of patients on the second day of evaluation

	Non-progression (N = 25)	Progression (N =47)	P-value
Blood Routine Tests			
WBC	7.15 ± 2.6	7.63 ± 4.4	0.874
Lymph	22.59 ± 10.6	23.65 ± 12.1	0.691
CRP	18.66 ± 26.0	37.58 ± 37.6	0.143
ESR	48.75 ± 20.8	49.4 ± 22.0	0.806
Procalcitonin	2.00 ± 0.0	2.05 ± 0.45	1.00
PCO2	29.22 ± 25.4	28.80 ± 21.1	0.785
Radiological Findings			
GGO	10 (40%)	10 (21.3)	0.107
Reveres Halo	1(4%)	0	0.346
Consolidation	11(44%)	30(63.8%)	0.130
Crazy-paving	0	0	1.00
Mixed	3	8	0.739
CTSS	9.48 ± 4.2	13.11 ± 4.7	0.003*
Clinical Setting			
Outpatients	6 (24%)	2 (4.3%)	0.033*
Ward	19 (76%)	44 (93.6%)	
ICU	0	1 (2.1%)	

Data are presented as mean ± standard deviation. WBC: white blood cell; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; GGO: ground-glass opacity

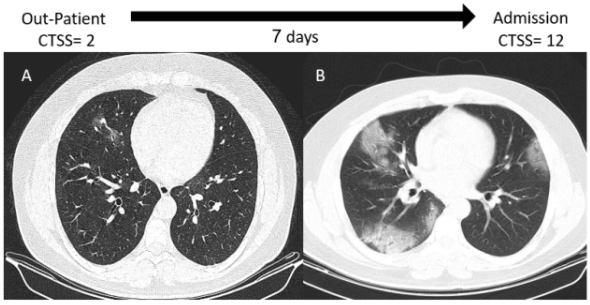

Figure 1. Examples of imaging progression in chest CT of a 38-year-old male (A & B)

DISCUSSION

The purpose of this study was to determine whether higher chest CT involvement in patients with COVID-19 is associated with a worsening clinical course. We studied patients' radiologic and clinical courses in 6.0±3.4-day intervals from the diagnosis. Our results showed that increasing the severity of lung involvement in chest CT is associated with the worsening of the clinical situation and increases the need for admission.

Nowadays, various CT findings are reported in patients with COVID-19. Ground-glass opacity, Crazy-Paving, and consolidation are major patterns that are introduced by different investigators. Similarly, our study showed the presence of GGO (50.0%), consolidation (29.2%), and reversed halo (4.2%) on the first visit. However, these findings are not pathognomonic of lung involvement in COVID-19 patients, and some patients can present with a normal chest CT despite testing positive for COVID-19.

Besides CT scan findings, various studies are focusing on CT change in patients with COVID-19 and its correlation with outcomes in different courses of disease. Pan et al. showed that in patients recovering from COVID-19, lung abnormalities on chest CT scans showed the greatest severity approximately 10 days after the initial onset of symptoms (17). In a study by Raoufi et al., patients with lower CTSS, lower pulmonary artery CT diameter, and round-shape opacity had a lower rate of mortality (18). In a study by Gharebakhshi et al., results showed that lung radiologic findings of COVID-19 patients can be used as a predictor of their outcomes (19). Moradkhani et al. stated that pulmonary CT finding is a mortality predictor for COVID-19 patients (14). The previous studies also approved this finding and reported that radiological findings can be used as a COVID-19 patient outcome predictor (20-24).

Results of our study showed that change in CTSS, which is introduced by Pan et al. (17), is compatible with a change in the clinical setting of patients with COVID-19, and increased CTSS is correlated with worsening clinical course. Yang et al. showed that in 273 patients with COVID-19, age, Monocyte-lymphocyte ratio, homocysteine, and the period from onset to admission could predict imaging progression on chest CT from COVID-19 patients (9). In another study by Liu et al., age, history of smoking, maximum body temperature at admission, respiratory failure, albumin, and C-reactive protein were introduced as factors that could lead to the progression of COVID-19 pneumonia (25). The imaging pattern of multifocal peripheral ground glass or mixed opacity with predominance in the lower lung is shown to be highly suspicious of COVID-19 in the first week of disease onset (26).

Although our results showed the usefulness of CTSS in predicting the clinical course of patients with COVID-19,

this study suffers from some limitations. First, due to a lack of laboratory diagnostic kits, the diagnosis was made by CT findings in some cases, according to Iran's National Guideline for COVID-19 guidelines. Second, the follow-up period was short; more solid outcomes should be considered in the future. Third, the sample size wasn't enough; because, with an increase in the sample size, the difference in some variables may become significant.

This study was conducted on a limited population; for this reason, these results could not be generalized to all people. Therefore, it is suggested to conduct studies with a higher sample size and in different places to compare with the results of the present study.

CONCLUSION

Based on the results of the present study, despite the presence of different radiologic findings in CT scans, only increasing CTSS was a strong predictor of worsening clinical outcomes (out-patient to admission or need for ICU admission) during admission.

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Conflicts of interest

The authors declare that there is no conflict of interest.

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