The Extent of Lung Involvement Based on CT-Scores, Compared to Clinical Symptoms and Laboratory Findings in COVID-19 Patients

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Abstract- Novel coronavirus disease 2019 (COVID-19) has become a public health concern with over 6.5 million cases and 390,000 deaths around the world. This research aimed to find an association between computed tomography (CT) scores and clinical and laboratory findings to estimate the extent of lung infection in patients with COVID-19. The study sample enrolled 129 patients diagnosed with COVID-19 from January to February 2020. The chest CT images and clinical data were reviewed, images were segmented and scored by the degree of involvement from 0 to 4, and the relationship between them and clinical and laboratory findings were analyzed statistically. This study included 74 men and 59 women with a mean age of 55.08 years. Different abnormalities were observed; the mean CT score was 8.52 (7.83 to 9.21) and the most frequent lesions were GGO and consolidation. Our results revealed significant differences between groups categorized by dyspnea, sore throat, and low oxygen saturation concerning CT scores. There was also a significant correlation between CT scores and WBC counts and CRP levels (P<0.05). The evidence from this study implies that clinical and laboratory data, such as CRP, dyspnea, lymphopenia, and symptom onset closely correspond to chest CT scores and may be employed as initial tools to estimate the extent of lung involvement in COVID-19 patients.

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Keywords: Clinical symptoms; Computed tomography; Coronavirus disease 2019 (COVID-19); Lung infection

Introduction

Many cases of pneumonia due to the SARS-CoV-2 virus emerged in Wuhan, China in December 2019 (1) resulting in a devastating pandemic with a dramatic impact on public health and the economy. As of 5 June 2020, more than 6,500,000 positive COVID-19 cases have been reported worldwide and roughly 394,000 individuals are confirmed to have died. The number of positive cases surpasses 167,000 in Iran. The World Health Organization declared this outbreak a global pandemic emergency and reported fever, cough, dyspnea, and fatigue as the most common symptoms of COVID-19. Real-time fluorescence polymerase chain reaction (RT-PCR) plays a crucial role as a standard test in the diagnosis of COVID-19 (2); however, positive computed

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tomography (CT) results have been found in cases with false-negative RT-PCR (3,4). Recent studies have suggested that CT scan is more than 90% sensitive in the diagnosis of COVID-19 (5); furthermore, it may be useful for follow-up and evaluation of illness progression to modify treatment strategies (3,6).

Unilateral or bilateral ground-glass opacities (GGO), consolidation, and other findings such as pleural effusion, crazy paving, and Broncho-vascular thickening on chest CT-scan have been considered as a hallmark of COVID-19 (5,7,8). By visual assessment, the high value of chest CT imaging in diagnosis is certain these days (9); quantitative assessment of CT images seems favorable for predicting patient prognosis and clinical findings (6,10). In light of the recent pandemic, the increasing number of CT scans performed and the radiation exposure to patients undergoing CT scans has caused serious concern to health professionals (11-14).

Moreover, CT scanners are not widely available in all clinics or small hospitals. With this in mind predicting lung involvement based on clinical symptoms and initial laboratory results may be of great value. The aim of this research was 25 to therefore find an association between CT scores and clinical and laboratory findings to estimate the extent of lung infection in COVID-19 patients.

Materials and Methods

Patients

This study enrolled 129 consecutive patients during the COVID-19 pandemic initially considered infected with either positive CT-scan results or positive RT-PCR test on throat swabs or lower respiratory tract specimens in Markazi province, Iran from March 16th to March 31st, 2020.

Clinical data

Clinical symptoms and laboratory findings including age, body temperature, gender, level of consciousness, headache, the onset of symptoms (gradual or sudden), nasal congestion, history of diabetes (DM), systematic hypertension (HTN), malignancy, immunodeficiency disorders, renal failure or transplantation, and smoking were documented in questionnaires by four infectious disease specialists. Furthermore, the following findings were also recorded; blood pressure, CRP levels, hemoglobin, AST, ALT, LDH, creatinine, and differential blood cell counts. Blood gas analyses were performed by measuring O2 saturation via a pulse oximeter. Lymphocyte counts less than 1150 and platelet counts less than 140000 counts were considered lymphopenia and thrombocytopenia, respectively.

Chest CT imaging and findings

CT images were acquired by GE 16-slice scanner optima CT 580 manufactured in the United States and a 16-slice Toshiba scanner Alexion model using the following parameters: 100 kVp, smart mA tube current modulation activated, helical mode, 1.375:1 pitch, 512*512 matrix size, large field of view, and axial, sagittal, and coronal images were reconstructed in two modes of high resolution: 1.5 mm slice 49 thickness, high spatial resolution kernel and standard: 3.75 mm slice thickness lung kernel. End inspiration breath-held images were obtained in the supine position with arms up. Chest CT images were viewed and interpreted by a radiologist with 16 years of experience. The form was filled by a radiologist blinded to the patient's name and information; they indicated the type of abnormality(s), the location and involvement of the lungs, and other findings from the images. For localization, each lung was divided into three regions upper, middle, and lower while the zonal involvement was scored between 0 to 4 (0%=0, 0-25%=1, 26-50%=2, 51-75%=3, 76-100%=4). The summation of scores for all segments in both lungs was considered as criteria for lung involvement. The correlation between these scores and clinical data was evaluated.

Statistical analysis

According to the results of the Kolmogorov-Smirnov test and the equality of variances test (Levene's test), the distribution of data was not normal. Therefore, the non-parametric U-man Whitney test was applied to compare the mean CT score between various categories. Data analysis was performed by using IBM SPSS statistical software version 16 (Build 1.0.0.1347; IBM, New York, USA.) with a 95% confidence interval.

Results

In this study, 129 positive CT results of patients (74 men and 55 women) with a mean age of 55.08 (95% CI: 52.33-57.83) were included. Overall, 43.4% of patients had a fever (duration range: 0-20 days), 38.8% had a headache, 67.4% had a dry cough, 57.4% had dyspnea, 8.5% had nasal congestion, 10.1% had a runny nose, 64.3% had fatigue, 37.2% had nausea, 48.8% had lack of appetite, 14.7% had a sore throat, 47.3% had a skeletal pain, 24% had diarrhea, 3.1% had a decreased consciousness, and 20.2% had hyposmia. The onset of symptoms was gradual in 84.5% and sudden in others. The mean CT-74 score was 8.52 (95% CI: 7.83-9.21 and

min/max: 1/19). Figure 1 demonstrates an example of a CT image with a score of 7. Individual lobar scores are as follows; RUL: 2, RML: 1, RLL: 2, LUL: 1, LLL: 1. Table 1 compares the mean CT score to various clinical findings. According to our results, the mean CT score of patients with dyspnea and also patients with O2 Saturation<93% was significantly higher than patients without these findings. However, the mean CT score in patients with nasal congestion and sore throat was significantly lower than those without these findings. Interestingly, the mean CT score was higher in patients with a sudden onset of symptoms compared to those with a gradual onset. There were also differences between CT scores and other clinical findings, however, they were not statistically significant.

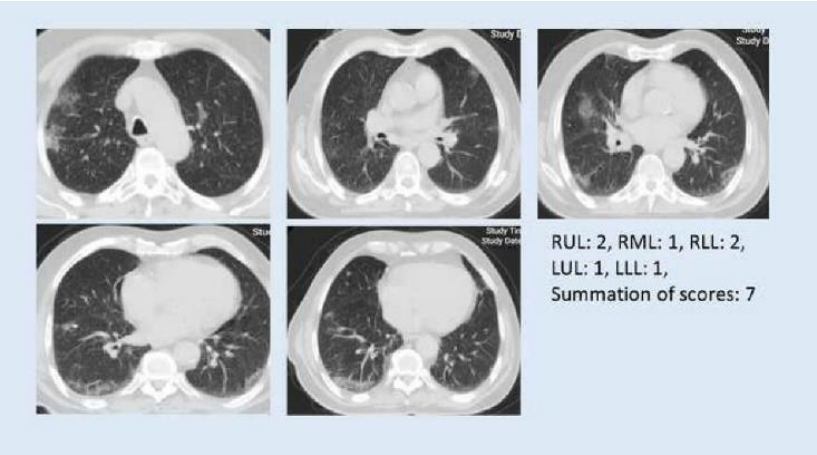

Figure 1. Axial CT images of a patient at several planes. The summation of scores was equal

Table 1. Comparison mean of CT score based on clinical findings

Clinical signs		Mean	SD	*P*
Fever	No	8.32	4.22	0.570
	Yes	8.73	3.72	
Headache	No	8.55	4.08	0.914
	Yes	8.48	3.84	
Dry cough	No	8.04	3.46	0.312
	Yes	8.75	4.2	
Dyspnea	No	7.65	3.48	0.027
	Yes	9.17	4.21	
Nasal congestion	No	8.70	3.99	0.033
	Yes	6.17	3.28	
Runny nose	No	8.48	4.04	0.959
	Yes	8.53	3.57	
Fatigue	No	8.13	4.48	0.497
	Yes	8.67	3.71	
Nausea	No	8.82	4.30	0.200
	Yes	7.93	3.38	
Anorexia	No	7.87	4.10	0.080
	Yes	9.11	3.79	
Sore throat	No	8.84	3.95	0.016
	Yes	6.47	3.64	
Skeletal pain	No	8.46	4.15	0.957
	Yes	8.50	3.82	
Diarrhea	No	8.44	4.13	0.830
	Yes	8.61	3.54	
Decreased consciousness	No	8.43	3.97	0.131
	Yes	11.50	3	
hyposmia	No	8.64	4.04	0.362
	Yes	7.88	3.69	
SO2	>93%	5.36	3.1	0.000
	<93%	9.42	4	
Onset of signs	Gradual	8.13	3.72	0.024
	Suddenly	11.06	4.69	

SD: standard deviation, The *P* was calculated by U-man Whitney test in 0.05 levels of statistical significance, SO2: oxygen saturation level

Mean CT scores were compared to lymphopenia, thrombocytopenia, and PT as summarized in Table 2. The results highlighted a statistically significant correlation between mean CT scores and the presence of lymphopenia and positive CRP levels according to the *P*. In other words, the mean CT score in patients with lymphopenia was significantly higher than in patients without lymphopenia. The mean CT score was also higher in patients with positive CRP levels than those patients with negative CRP levels. Mean differences in CT scores were not significant for thrombocytopenia and PT.

Table 2. Comparison mean of CT score based on laboratory findings

Laboratory findings		Mean	SD	*P*
Lymphopenia	No	7.11	3.27	0.006
	Yes	9.13	4.12	
Thrombocytopenia	No	8.77	4.15	0.211
	Yes	7.80	3.40	
PT	Normal	8.53	3.48	0.867
	Abnormal	6.68	4.71	
CRP	Negative	7.11	3.72	0.010
	Positive	9.07	3.95	

SD: standard deviation, the *P* was calculated by U-man Whitney test in 0.05 levels of statistically significant, PT: Prothrombin, CRP: c-reactive protein

Table 3 summarizes the association between CT scores and other laboratory findings. Accordingly, there was a significant correlation between CT scores and WBC counts, LDH, ALT, and AST. In other words, an increase in these laboratory parameter increases the CT-score and vice versa. The strongest correlation was related to LDH. On the contrary, no significant difference was identified between CPK and CT-scores.

Table 3. Correlation between CT score and laboratory findings

Laboratory findings	Mean	SD	R	*P*
WBC (per µl)	4755.23	21.72.6	0.258	0.004
CPK (mg/dL)	131.01	120.19	0.137	0.182
LDH (U/L)	459.88	183.13	0.440	0.000
ALT (U/L)	34.38	38.08	0.222	0.035
AST (U/L)	33.57	24.31	0.252	0.016

SD: standard deviation, r: Pearson correlation coefficient, the *P* was calculated by Pearson correlation coefficient in 0.05 levels of statistically significant, WBC: white blood cell, CPK: Creatine phosphokinase, LDH: lactate dehydrogenase, ALT: alanine aminotransferase, Aspartate aminotransferase

Discussion

CT acts as an important tool in the early diagnosis and follow-up of patients infected with the SARS-CoV-2 virus (3,15,16). In this study, we evaluated Chest CT findings and symptoms of patients diagnosed with COVID-19 infection. In the majority of patients, the abnormalities were seen in more than one lobe of the lung, which is a different pattern compared to formerly described bacterial infections (16,17). Therefore, we defined and calculated a CT score to quantify and include the extent of lung infection for all lobes. The most common lesions were ground glass opacities, consolidation, and a mixture of both patterns; moreover, pleural effusion was less frequently found. These findings are consistent with recent studies (8,9,18). Our results revealed a significant difference between CT scores and patients with dyspnea and an oxygen saturation≤93% which is also in line with recent reports (16,19). In other words, hypoxic patients had higher CT scores. On the contrary, upper respiratory symptoms of nasal congestion and sore throat had significantly lower CT scores compared to mild or no upper respiratory symptoms.

The onset of signs and symptoms is also of great value in estimating the extent of lung involvement, where sudden onset is related to a higher degree of lung involvement (*P*=0.024). Concerning laboratory findings, patients with positive CRP levels and lymphopenia had

significantly higher CT scores. There was also a significant positive correlation identified between CT scores and WBC counts and AST levels (P<0.05); importantly, this correlation is not strong enough to be considered as a predictive criterion taking into account the low amount of r constant.

As stated in the introduction, we aimed to obtain a relationship between clinical symptoms and laboratory data with quantified CT scan results. The feasibility of non-imaging data in estimating the extent of 124 lung involvement was evaluated. It was found that clinical and laboratory data may serve as an available initial tool to estimate lung involvement on CT scans. Consequently, CT findings may be easily predicted with acceptable precision in small clinics where the CT scanner is not available or too busy, or for patients with higher sensitivity to ionizing radiation such as pregnant women and younger patients.

The evidence from this study implies that clinical and laboratory data, such as CRP, dyspnea, lymphopenia, and symptom onset closely correspond to chest CT scores and may be employed as initial tools to estimate the extent of lung involvement in COVID-19 patients.

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