Computed Tomography-based determinants for predicting death and ICU requirement in patients suffering COVID-19

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Research

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Abstract

Background: What has received special attention in recent months is the use of a combination of clinical findings, laboratory markers, and, in addition, the findings of lung Computed Tomography (CT) scan in the design and delivery of risk scoring systems for Coronavirus Disease 2019 (COVID -19) patients. The present study aimed to determine main lung CT-related correlates of disease severity (Intensive Care Units (ICU) requiring) as well as death in COVID -19 patients.

Methods: This cross-sectional study was performed on 515 consecutive patients with definitive diagnosis of COVID-19 admitted to one of the COVID -19 referral hospitals in Tehran. All patients' information was collected through a review of their archives. All patients were evaluated by CT scan of the lungs.

Results: The mean follow-up of patients from the time of admission was 10.85±6.11 days between 1 and 30 days. During this period, a total of 29.1% were admitted to the ICU. Also, the mortality rate of patients was equal to 28.2%. According to multivariable logistic regression model with the presence of death-related correlates, crazy paving pattern, diffuse distribution of lesions, CT Severity Score (CTSS) score >12, the presence of plural effusion or emphysema were the main determinants of COVID -19 related death and should be considered for presenting new scoring system for predicting death following COVID -19 disease. In similar model, CTSS score >12 along with the presence of plural effusion, emphysema, or pulmonary hypertension were the main determinants of requiring ICU admission.

Conclusion: The CT score higher than 12 along with observing the pattern of diffuse distribution of lesions especially accompanied with emphysema, pleural effusion or pulmonary hypertension can predict patient mortality or will determine the need for hospitalization in the ICU.

Introduction

By the end of September 2020, more than 35 million people had been infected with Coronavirus Disease 2019 (COVID-19), leading more than one million deaths worldwide certainly due to the onset of the second and even third waves of disease in some countries [1]. Common clinical manifestations of the disease include acute respiratory syndrome with fever and dry cough, dyspnea, fatigue, and myalgia. About 15 to 20% of patients also experience severe illness, which is associated with mortality of about 2 to 3% [2–4]. In the absence of vaccine or specific treatment available to date, the diagnosis of the disease as quickly and accurately as possible and its severity are essential that can prevent further progression of the disease. However, pharyngeal sampling and using Polymerase Chain Reaction (PCR) technique is still the final reference diagnosis, but it is time consuming and the sensitivity of this test is estimated at about 60 to 70% due to the quality of sampling and the rate of virus replication in the corresponding position [5, 6]. In this regard, Computed Tomography (CT) scan is a rapid and accessible tool for diagnosing and tracking the severity of pneumonia caused by COVID-19 disease [7, 8]. Due to the high influx of patients to emergency and hospital centers, it is necessary to triage as soon as possible the patients who refer and have symptoms suspected of having the disease. According to recent guidelines provided by the

World Health Organization and associations related to the prevention and control of the disease, the use of CT scan of the chest for all patients with manifestations such as dyspnea, polypnea and reduced arterial oxygen saturation is necessary to differentiate between the two groups of patients requires hospitalization or only needs outpatient treatment and follow-up, which should be synchronized with PCR [9]. The use of CT scan due to its high sensitivity, low radiation dose and no need for contrast, has been very useful in screening symptomatic patients, but the presence of low specificity and some atypical changes similar to other pneumonias such as influenza and or adenovirus infections limit its use. Therefore, lung CT cannot be considered as a definitive method of diagnosis for the disease. However, due to the high sensitivity of this tool, it is one of the best methods for estimating the severity of the disease in patients with a definitive diagnosis of COVID-19. In this regard, some algorithms for estimating and predicting disease severity based on CT findings have been proposed. But despite the presentation of all these classification systems, the presentation of a system with the highest sensitivity and specificity in distinguishing mild from severe clinical involvement is still under discussion and study. The present study aimed to determine main lung CT-related correlates of disease severity (Intensive Care Units (ICU) requiring) as well as death in COVID-19 patients.

Methods

This cross-sectional study was performed on 515 consecutive patients with definitive diagnosis of COVID-19 admitted to one of the COVID – 19 referral hospitals in Tehran, Iran between April and September 2020. All patients' information was collected through a review of their archives, and therefore patients with incomplete information about demographic information, CT findings, and disease prognosis were excluded from the study. Definitive diagnosis was made based on a specific COVID-19 diagnostic kit and RT-PCR of the virus genome in the laboratory (isolation of SARSCoV-2 or at least two positive tests of the virus genomic test). All patients were evaluated by CT scan of the lungs. Chest CT scans were performed with CT system Siemens Healthineers, Germany in supine position. The imaging parameters were as follows: tube voltage 100 kVp, current 80 mAs, pitch = 1.5 mm, thickness 1.5 mm. The maximum time between the initial clinical evaluation and CT imaging of patients was one day. The whole image was interpreted by two radiologists who were unaware of each other's interpretation. What was examined in the CT images included the following features: 1) distribution of lesions (peripheral, Axial, bronchovascular perineum, diffuse, anterior, and pericardial), 2) types of lesions (Grand Glass opacities, consolidation, crazy paving pattern, reverse halo sign, centrilobular air space, bronchiectasis traction between lesions, and linear opacities), and 3) underlying pulmonary signs (bronchiectasis, emphysema, pleural effusion, and pulmonary hypertension). The CT severity score (CTSS) was also determined based on the scoring introduced by Kunwei et al. in this scoring system, all five lobes of both lungs are evaluated for the presence of disease-related lesions. Each lobe scores between 0 and 4 based on the percentage of lobar involvement in the form of 0 (0%), 1 (1 to 25%), 2 (26 to 50%), 3 (51 to 75%) or 4 (76 to 100%) [10]. The total score will be the sum of the scores for the five lobes of both lungs. The study endpoints were first disease-related death (occurring within 30 days of first admission) and second requiring ICU admission as an indicator for disease severity.

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using t test or Mann-Whitney test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. Categorical variables were, on the other hand, compared using chi-square test. To determine the value of quantitative parameters to predict disease outcome, the ROC curve analysis was employed. Also, for weighting each predictive parameter to achieve final scoring system, the multivariable logistic regression modeling was finally used. For the statistical analysis, the statistical software SPSS version 23.0 for windows (IBM, Armonk, New York) was used.

Results

A total of 515 patients were included in the study. The mean age of patients was 56.90 ± 16.37 years in the range of 21 to 89 years and in terms of sex distribution, 64.1% were male and 35.9% were female. In terms of underlying comorbidities, underlying heart disease in 18.4%, history of lung disease in 13.6%, history of diabetes in 7.8% and history of other diseases in 11.7%. In terms of clinical manifestations, the most common symptoms were fever in 90.3%, cough in 72.8%, dyspnea in 39.8%, myalgia in 25.2% and diarrhea in 4.9%. The mean follow-up of patients from the time of admission was 10.85 ± 6.11 days between 1 and 30 days. In this follow-up, the average length of hospital stay was 5.78 ± 4.27 days between 1 and 18 days. During this period, a total of 29.1% were admitted to the ICU. Also, the mortality rate of patients was equal to 28.2%.

First, at the time of admission, 8.7% of patients with CT scan were completely normal. Among other patients with pulmonary involvement, grand glass opacity in 59.2%, consolidation in 29.1%, crazy paving pattern in 7.8%, reverse halo sign in 25.2%, nodular profile in the form of centrilobular air space in 3.9%, bronchiectasis traction between lesions in 32.0% and linear opacities in 46.6%. Regarding the distribution of pulmonary involvement, peripheral distribution was found in 91.2%, axial distribution in 56.3%, peribronchovascular distribution in 20.4%, diffuse distribution in 12.6%, anterior distribution in 65.0% and pericardial distribution in 32.0%. Other observable underlying pulmonary disorders included underlying bronchiectasis in 0.1%, underlying emphysema in 5.8%, pleural effusion in 61.1%, and pulmonary hypertension in 13.6%.

To determine the CTSS score, the mean score of RUL was 2.15 ± 1.28, the mean score of RML was 1.81 ± 1.43, the mean score of RLL was 2.56 ± 1.29, the mean score of LUL was 2.40 ± 1.30 and the mean score of LLL conflict was estimated to be 2.33 ± 1.41. In general, the mean total score of lung involvement was 10.90 ± 5.83.

Comparing pattern and distribution of lesions between survived and non-survived subgroups (Table 1) showed higher prevalence of crazy paving pattern in nun-survived group. Also, non-survived subgroup had higher prevalence of diffuse and pericardial distributions. In the two groups with and without death, the frequency of bronchiectasis was 3.4% and 0.0% ($P = 0.282$), the frequency of emphysema was 13.8%

and 2.7% ($P = 0.030$), the frequency of pleural effusion was 82.8% and 52.7% ($P = 0.005$), and pulmonary hypertension was 20.7% and 10.8% ($P = 0.210$), respectively, indicating differences in the frequency of emphysema and pleural effusion. The mean CTSS score in the two groups was 14.27 ± 5.09 and 9.58 ± 5.59, respectively, which showed a significant difference between the two groups ($P < 0.001$). Based on the analysis of the area under the ROC curve, the evaluation of the CTSS score was considered to have a high value in predicting the occurrence of death (the area under the curve of 0.721, 95% confidence interval between 0.616 and 0.826, $P < 0.001$). Accordingly, a cutoff value of 12.0 with a sensitivity of 79.0% and a specificity of 64.1% will be able to predict the occurrence of death in patients.

Table 1
Comparing CT findings in survived and non-survived groups with Covid-19

Item	Survived group	Non-survived group	P value
Form of lesion			
Ground Glass Opacity	72.4%	54.1%	0.088
Consolidation	24.1%	31.1%	0.485
Crazy paving pattern	17.2%	4.1%	0.020
Reverse halo sign	18.2%	28.4%	0.430
Centrilobular air space	0.0%	5.4%	0.202
Bronchiectasis traction	44.8%	27.0%	0.082
Linear opacities	44.8%	47.4%	0.787
Distribution of lesions			
Peripheral	100%	87.8%	0.059
Axial	69.0%	52.7%	0.184
Peribronchovascular	27.6%	17.6%	0.256
Diffuse	27.6%	6.8%	0.004
Anterior	79.3%	59.5%	0.057
Pericardial	51.7%	24.3%	0.007
Underlying lung disorders			
Bronchiectasis	3.4%	0.0%	0.282
Emphysema	13.8%	2.7%	0.030
Pleural effusion	82.8%	52.7%	0.005
Pulmonary hypertension	20.7%	10.8%	0.210
Mean CTSS score	14.27 ± 5.09	9.58 ± 5.59	0.001

Comparing form of lesions in the two groups with and without ICU admission (Table 2) showed no difference in the prevalence rate of ground glass opacity, consolidation, crazy paving pattern, reverse halo sign, centrilobular air space, or linear opacities. Those requiring ICU admission had higher rate of diffuse axial, anterior, and pericardial distributions as compared to non-ICU admission subgroup. In the two groups with and without ICU hospitalization, the frequency of bronchiectasis was equal to 0.0% and 1.4%, the frequency of emphysema to 13.3% and 2.7% pleural effusion to 76.7% and 54.8% and pulmonary hypertension to 26.7% and 8.2%, respectively. The differences were in the frequency of emphysema, pleural effusions and pulmonary hypertension. The mean CTSS score in the two groups with and without ICU admission was 13.53 ± 4.36 and 9.82 ± 6.04, respectively, which showed a significant difference between the two groups ($P = 0.003$). Based on the analysis of the area under the ROC curve, the evaluation of CTSS score was considered to have a high value in predicting ICU admission (area under the curve was 0.700, 95% confidence interval between 0.594 and 0.803, $P = 0.002$). A cutoff point of 12.0 with a sensitivity of 73.3% and a specificity of 64.4% was able to predict the need for ICU hospitalization. According to multivariable logistic regression model with the presence of death-related correlates (Table 3), crazy paving pattern, diffuse distribution of lesions, CTSS score > 12, the presence of plural effusion or emphysema were the main determinants of COVID-19 related death and should be considered for presenting new scoring system for predicting death following COVID-19 disease. In similar model (Table 4), CTSS score > 12 along with the presence of plural effusion, emphysema, or pulmonary hypertension were the main determinants of requiring ICU admission.

Table 2
Comparing CT findings in groups requiring and no-requiring ICU

Item	Survived group	Non-survived group	P value
Form of lesion			
Ground Glass Opacity	56.7%	60.3%	0.735
Consolidation	40.0%	24.7%	0.119
Crazy paving pattern	13.3%	5.5%	0.333
Reverse halo sign	16.7%	28.8%	0.563
Centrilobular air space	3.3%	4.1%	0.853
Bronchiectasis traction	43.3%	27.4%	0.115
Linear opacities	60.0%	41.1%	0.287
Distribution of lesions			
Peripheral	100%	87.7%	0.056
Axial	80.0%	47.9%	0.003
Peribronchovascular	26.7%	17.8%	0.311
Diffuse	23.3%	8.2%	0.050
Anterior	80.0%	58.9%	0.045
Pericardial	53.3%	23.3%	0.003
Underlying lung disorders			
Bronchiectasis	0.0%	1.4%	0.999
Emphysema	13.3%	2.7%	0.037
Pleural effusion	76.7%	54.8%	0.039
Pulmonary hypertension	26.7%	8.2%	0.024
Mean CTSS score	13.53 ± 4.36	9.82 ± 6.04	0.003

Table 3
Multivariable logistic regression model to determine the main CT-based correlates of death in Covid-19 patients

Item	B	S.E.	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
Crazy paving pattern	1.082	0.417	0.010	2.952	1.303	6.689
Diffuse distribution	1.239	0.341	0.018	2.242	1.150	4.371
Pericardial distribution	0.452	0.271	0.096	1.571	0.923	2.673
CTSS > 12	11.494	0.270	0.038	1.090	0.643	1.849
Pleural effusion	1.140	0.195	0.001	2.405	1.640	3.525
Emphysema	1.179	0.499	0.018	3.250	1.222	8.646
Pulmonary hypertension	0.507	0.298	0.089	1.661	0.926	2.978

Table 4
Multivariable logistic regression model to determine the main CT-based correlates of ICU admission in Covid-19 patients

	B	S.E.	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
					Lower	Upper
Diffuse distribution	-0.126	0.326	0.699	0.882	0.465	1.670
Pericardial distribution	0.278	0.255	0.275	1.321	0.802	2.175
CTSS > 12	1.187	0.262	< 0.001	3.278	1.960	5.480
Pleural effusion	1.153	0.197	< 0.001	2.381	1.619	3.501
Emphysema	1.740	0.432	< 0.001	5.700	2.446	13.279
Pulmonary hypertension	1.175	0.297	< 0.001	3.238	1.808	5.798

Discussion

Predicting the severity of COVID-19 is important in several ways. First, based on clinical evidence, laboratory findings as well as imaging findings, it is possible to predict patient mortality as well as the need for their hospitalization or ICU admission, which is the case in the management of patient reception centers, especially when faced with a new wave of disease will be very important and vital. Second, based on this evidence, it is possible to provide scoring systems for the severity and extent of patients' clinical involvement. What has received special attention in recent months is the use of a combination of clinical findings, laboratory markers, and, in addition, the findings of lung CT scan in the design and delivery of such scoring systems. These systems not only make it possible to determine the extent of involvement of pulmonary pneumonia, but also make it possible to predict the adverse consequences for patients. In assessing the severity and extent of pulmonary involvement, both the type of lung pathology, the distribution of lesions in the pulmonary lobes, and parenchymal lesions, such as interstitial and vascular lesions, should all be considered. In the present study, we aimed to investigate the relationship between the pattern of involvement and the distribution of lung lesions with the severity of clinical involvement and outcome in patients with COVID-19. What was confirmed in the present study was that, firstly, the distribution and severity of pulmonary involvement in CT patients could be of acceptable diagnostic value for predicting mortality as well as the need for ICU hospitalization (a manifestation of the clinical severity of the disease). Among these, the distribution of lesions in the pulmonary lobes, the presence of some underlying pulmonary complications such as emphysema, pleural effusion or pulmonary hypertension, and the severity of pulmonary involvement based on CT score can play an important role in predicting adverse clinical outcome. In this regard, we first found that the existence of evidence of crazy paving pattern, diffuse distribution as well as pericardial lesions in the lung and higher CT score (mostly higher than 12) as well as the incidence of emphysema and pleural effusion can all increase the risk of death and needing ICU wards. On the other hand, diffuse distribution as well as pericardial lesions, higher CT score, and the appearance of emphysema and pleural effusions or pulmonary hypertension will be important predictors of the need for ICU hospitalization or disease severity that were overall used for introducing a new risk stratification approach. Therefore, in order to provide a new scoring system for risk stratification of patients, it is recommended to use the following criteria and in designing such a system, of course, taking into account other clinical features and other laboratory markers: 1) CTSS score above 12, 2) the presence of crazy paving pattern, 3) the presence of diffuse or pericardial distribution pattern, 4) the presence of emphysema, pleural effusion or pulmonary hypertension. However, in different studies, there are differences in the factors associated with the prognosis of the disease. For example, the presence of consolidation has been considered as one of the indicators related to the severity of clinical involvement for which we did not find a significant relationship in the present study. Also, different cut points of CTSS have been mentioned in various studies to predict the severity of disease involvement. The observed differences can be due to differences in study design, differences in the experience of specialists in interpreting CT scan findings, differences in patients' underlying clinical conditions, and even geographical differences. In the study of Francone et al, the CT score was higher in patients with more severe involvement of the disease, so that the CT scores higher than 18 was a strong predictor for mortality in patients [11]. It was similar to our study, but their cut-off point was very different from our finding. In a study by Li et al, the presence of consolidation was much higher in the deceased patients than in the living, although in our study there was no difference in this finding. Also, the mean CT score in deceased patients was much higher than in surviving patients, so that a CT score of 14.5 with a sensitivity of 83.3% and a specificity of 77.3% was a predictor of mortality in these patients [12] which, of course, was the different cut-off point obtained from our study. However, in the study of Raoufi et al, the CTSS index with a cut-off point of 12 with a sensitivity of 75.8% and a specificity of 75.7% was a predictor of patient mortality [13], which, of course, was very close to the cut-off point of our study. Therefore, based on the present study, calculating the CT score along with examining the pattern of involvement (diffuse - pericardial) as well as evidence of emphysema, pleural effusion and pulmonary hypertension in scoring system design will be very useful in predicting the clinical severity of COVID-19 disease.

Conclusion

As a final conclusion, evaluation of the form and pattern of lesion distribution in lung CT has a high value in predicting clinical severity in patients with COVID-19. In this regard, calculating the CT score (score higher than 12) along with observing the pattern of diffuse distribution of lesions and especially associated with other underlying lesions such as emphysema, pleural effusion or pulmonary hypertension can predict patient mortality or will determine the need for hospitalization in the ICU.

Abbreviations

CT: Computed Tomography, COVID -19: Coronavirus Disease 2019, ICU: Intensive Care Units, CTSS: CT severity score, PCR: Polymerase Chain Reaction, SD: Standard Deviation

Declarations

Summary statement

CT scan of the lung in patients with COVID-19 admitted to the ICU is associated with disease severity and mortality.

Authors' contributions

KH N: conceived the original idea, designed the scenarios and approved the final versionthat was submitted, M D, R F and N H: collected the data, M A: carried out the analysis of data.   All the authors met the criteria of authorship based on the recommendations of the international commit-tee of medical journal editors.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. Patients or their legal representatives were informed to participate in this study.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board at the Iran University of Medical Sciences.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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