ORIGINAL RESEARCH

Association of Chest Computed Tomography Severity Score with Oxygen Requirement D-dimer CRP and Comorbidities in Patients with COVID-19 Infection

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Abstract

Objective: Chest CT has higher sensitivity in comparison to reverse transcription-polymerase chain reaction (RT-PCR) for COVID-19 diagnosis. We aim to identify the association of CT severity scores (CTSS) with lab markers and the need for oxygen.

Methods: Cross-sectional observational study of 104 COVID-19 RT-PCR positive hospitalized patients. Patients underwent pulmonary CT, and their CTSS was calculated. SpO2, D-dimer and C-reactive protein (CRP) were also measured. The data was then collected and analyzed.

Results: CT Severity Score (CTSS) was higher in patients above 50 years of age and males, though statistically insignificant. CTSS was positively correlated with D-dimer ($p = 0.048$) and oxygen requirement (0.000). However, HbA1C was lower in patients with higher CTSS.

Conclusion: High CTSS correlates well with oxygen requirement, low SpO2, and high D-dimer but not with CRP and HbA1C. Our data suggest that CTSS can help predict disease outcomes by assessing disease severity.

Keywords: COVID-19, CT severity score, Hypoxia, SpO2, SARS-CoV-2.

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Introduction

Since December 2019, a series of cases of unknown pneumonia with similar clinical manifestations suggesting viral pneumonia appeared in Wuhan, China. A new type of coronavirus was isolated from the lower respiratory tract named coronavirus-2, (SARS-CoV-2).[1] The disease soon surpassed China and involved almost the entire world.[2] On 30th January 2020, the World Health Organization (WHO) declared the transmission of coronavirus the sixth public health emergency of international concern. On 22nd February 2020, the WHO called the disease caused by coronavirus COVID-19 and on 11th March 2020, the WHO formally announced that COVID-19 is a pandemic.

The incubation period of COVID-19 is 3–7 days (<14 days), and its mortality rate is around 2.3%. Most of the patients have mild symptoms and have a good prognosis, but a minority have severe pneumonia, acute respiratory distress syndrome (ARDS), multiple organ failure, and die because of coronavirus. Mortality in critically ill patients is high, and the risk of disease increases in the elderly population and patients with comorbidities such as cardiovascular disease, hypertension, diabetes, lung diseases, and cancer.

The disease varies from mild to moderate to critical. The mild disease causes either no symptoms or mild coughing and fever with loss of smell and taste, whereas moderate disease causes dyspnea, hypoxemia, and changes in imaging with low oxygen on a pulse oximeter. The critical disease leads to respiratory failure, shock, and multiorgan failure.

To diagnose COVID-19, RT-PCR COVID-19 test and HRCT chest are available. In RT-PCR, a predetermined number of cycles of amplification of target (e.g., SARS-Cov-2) nucleic acid occur. If a target is present in the specimen, then each round of amplification results in a doubling of the amount of target present in the sample. The cycle threshold value (Ct value) is used to know the viral load in the sample; the samples are taken from the nasopharynx and oropharynx. Lower the CT value. The PCR test is very specific but has a lower sensitivity of 65–95%, which means that the test can be negative even when the patient is infected.[3] Patient has to wait for the test results for up to 24 hours while CT results are available right away.

Imaging plays an important role in the diagnosis of highly suspected cases. CT has a higher sensitivity but lower specificity and can play a role in the diagnosis and treatment of the disease. Many cases with CT changes of COVID-19 are RT-PCR negative, but treatment needs to be started as per protocol based on CT findings.

Common CT findings are ground-glass opacities with a posterior predominance, commonly located in the inferior lobe of the right lung, crazy paving, vascular dilatation, traction bronchiectasis subdural bands, and architectural distortion.[4–8]

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CT involvement score has also been developed to assess the severity of lung involvement. CT severity score can be calculated by scoring according to the percentage of each of the five lobes' involvement.[9–12] A score of 1 represents <5% involvement, a score of two represents 5–10% involvement, a score of 3 represents 26–49% involvement, a score of 4 represents 50–75% involvement, and a score of five represents >75% involvement of the lobe. The total CT score is the sum of the individual lobar scores and can range from 0 (no involvement) to 25 (maximum involvement).

Advanced stage disease is associated with significantly increased ground glass opacities plus a reticular pattern (crazy paving), vacuolar sign, fibrotic streaks, air bronchogram, bronchus distortion, subpleural line or a subpleural transparent line, pleural effusion.[13,14]

D-dimer is the degradation product of cross-linked fibrin. It reflects the ongoing activation of the hemostatic system. Healthy individuals have minimal D-dimer levels. Levels also depend on the procedure used, so the cut-offs are different for different labs. Malignancy, trauma, postsurgical treatment, liver diseases, heart diseases, lipemia, high triglyceride, high bilirubin, presence of RA factor and hemolysis falsely increase D-dimer. It increases in most of the COVID-19 patients and signifies micro thrombosis and fibrin degradation.

C-reactive protein is an acute-phase reactant produced by the liver, and its level increases when a condition causes inflammation in the body and follows IL-6 secretion by macrophages and T cells. It assists in complement binding to foreign and damaged cells and enhances phagocytosis by macrophages. It's important for innate immunity as an early defense system against infections. It is one of the most important markers which increases early and is important for deciding prognosis.

Pulse oximetry is a noninvasive test that measures oxygen saturation in the capillary blood and is within 2% accuracy. It measures the changing absorbance at each of the wavelengths allowing it to determine the absorbances due to the pulsating arterial blood alone, excluding venous blood. Oxygen saturation may decrease, and supplemental oxygen may be required in COVID-19 patients with extensive lungs involvement, which can be seen in the chest CT.

The aim of this retrospective study was to determine the correlation between a chest CT based semiquantitative score of pulmonary involvement and the need for oxygen based on SpO2. We also aim to identify the association of CTSS with lab markers like D-dimer, CRP, and comorbidities.

Materials and Methods

This is a cross-sectional study. The approval from the institutional ethics committee was taken before starting the study. Patients who were above 18 years of age, tested positive for COVID by RT-PCR, were able to give written informed consent, whose samples were sent for lab markers including CRP and D-dimer, who underwent CT Chest, and whose measurements of capillary oxygen saturation using finger pulse oximetry were available, were included in the study. Patients whose data was incomplete, for whom investigations had not been done or who refused to give informed consent were excluded from the study.

COVID-19 RT-PCR was tested by RNA amplification using the ABI 7500 Fast Dx RT-PCR machine. The Ct value was also measured. At presentation, a detailed history of the patient was taken, and baseline investigations, inflammatory markers and a chest HRCT were done. Later on, the treatment of the patients was started according to the prevailing national guidelines.

The pulmonary CT scan was performed for all patients, and slice thickness of 0.625–5 mm was taken by Siemens Go Now 16 slice in supine position with deep inspiration. The CT images were reconstructed, and two experienced radiologists examined the scan and calculated the severity score. To calculate the CTSS according to the anatomical structure of the lungs, five lobes were given a score according to the percentage involvement of the lobes, minimum being 0/25 and maximum being 25/25.

The samples were sent for D-dimer and CRP to the central labs for measurements. The capillary blood oxygen saturation was also collected from pulse oximetry by using the same brand's pulse oximeter for all patients.

Study Design

This study was planned and executed by the researchers of Mahatma Gandhi Medical College and Hospital located in the city of Jaipur in India. Of all COVID-19 RT-PCR positive patients admitted to the hospital during this pandemic between September 2020 and December 2020, around 104 patients were randomly selected for the study.

Statistics

The data was captured on Google Forms, and a Google sheet was prepared for it. The data was then processed in Microsoft Excel. Finally, the data was interpreted and analyzed by a statistician.

The processing of the data was done in Microsoft Excel. The analysis started with a calculation of descriptive statistics of the data such as the number of patients with comorbidities, number of patients showing various symptoms of COVID-19, number of patients with their lab reports, markers such as D-dimer and CRP and the severity score of patients' HRCT chest. One hundred four patients were included in the study.

Results

Of the 104 patients included in this study, 75 (72.11%) were males, and 29 (27.88%) were females. Twenty-five patients were <50 years of age (24.03%), and 79 patients were >50 years of age (75.96%). A total of 31 patients had a CTSS <8, 53 patients had a CTSS between 8 and 14, whereas only 20 patients had a CTSS above 14. The difference in CTSS according to age was not statistically significant (Table 1).

A total of 26 patients required inhalational oxygen out of 104 patients anytime during their stay in the hospital. Only three patients with CTSS <8 required oxygen, whereas 14 patients with CTSS >14 required oxygen, with this difference being statistically significant (p-value: 0.000).

Among patients with oxygen saturation between 90 and 94%, there were 13 patients with CTSS <8 and 19 patients with CTSS >14. Among patients with SpO2 >94%, 18 patients had CTSS <8, while only one patient had CTSS >14, with this difference being statistically significant (p-value: 0.000) (Table 2).

We evaluated CTSS and its association with lab markers, mainly D-dimer and CRP. The mean D-dimer in patients with CTSS <8 was 349.22 ± 1005.12. In patients with CTSS between 8 and 14, it was 475.03 ± 1111.02, whereas, in patients with CTSS >14, it was 1089.25 ± 1131.44, which was statistically significant (p-value: 0.048). So higher the CTSS higher was the D-dimer.

While looking for the association between CTSS and CRP, we observed CRP 35.18 ± 58.07 in patients with CTSS <8, 47.38 ± 61.67 in patients with CTSS between 8 and 14, and 74.69 ± 60.07 in those with CTSS >14. Though CRP was high in patients with CTSS >14, it was statistically insignificant (0.076) (Table 3).

While evaluating the association between the glycemic status of patients and CTSS, we observed random blood sugar 167.78 ± 76.71 in patients with CTSS <8, 171.79 ± 85.15 in patients with CTSS between 8 and 14 groups, and 175.6 ± 85.59 in those with CTSS >14. It is evident from Table 4 that random blood sugar was higher in those with CTSS >14 in comparison to those with CTSS <8, but this difference was statistically insignificant (p-value: 0.946). Whereas HbA1C of 6.31 ± 1.32 was observed in patients with CTSS <8, it was 6.94 ± 1.309 in patients with CTSS between 8 and 14 group and was 6.21 ± 1.32 in those with CTSS >14. An inverse relationship was therefore found between CTSS and HbA1C in our study, and this relationship was statistically significant (p-value: 0.037) (Table 4).

In our study, we did not find a statistically significant association between any of the comorbidities with CTSS (Table 5).

Discussion

Most of the COVID-19 patients develop only mild grade fever, cough, body ache, loss of taste, and smell, and do not require hospitalization, but a few patients develop severe symptoms and multisystem involvement, which is common in elderly patients, patients with comorbidities and patients who already have a progressed disease at the time of admission. Stratifying patients for treatment according to severity becomes important in resource limited situations, especially during the COVID-19 pandemic. It also helps in predicting the prognosis of COVID-19 patients.

The objective of this study was to identify the factors associated with severe disease and poor prognosis so that the patients can be treated according to the severity of the disease. This also helps in predicting outcomes based on expected prognosis.

Our study involved 104 randomly selected patients admitted to the hospital. There were 79 patients >50 years of age, and 16 patients had a CTSS of >14. Though a greater number of patients above 50 years of age had a CTSS of >14, this difference was not statistically significant (p-value: 0.582). Similarly, there was no statistically significant difference in CTSS for males and females, indicating that gender is not an independent risk factor for disease severity.[15] Zhichao F et al. found that older age increased neutrophil-lymphocyte ratio, and increased CTSS on admission were independent risk factors for clinical progression in moderate

Table 1: CTSS according to age and gender (Chi-square test)

		CTSS <8 N = 31	*CTSS 8–14 N = 53*	*CTSS >14 N = 20*	*Chi-square (df)*	*p-value*
Age	<50 years	10	11	4	1.08^2	0.582
	>50 years	21	42	16		
Gender	Male	20	39	16	1.565^2	0.457
	Female	11	14	4		

CTSS; Chest tomography severity score

Table 2: Oxygen requirement and SpO2 according to CTSS (Chi square test)

		CTSS <8 N = 31	*CTSS 8–14 N = 53*	*CTSS >14 N = 20*	*Chi-square (df)*	*p-value*
Oxygen requirement	Yes	3	9	14		
	No	28	44	6	27.299^2	0.000
SpO2	90–94%	13	33	19	14.608^2	0.000
	>94%	18	20	1		

CTSS; Chest tomography severity score, SpO2; oxygen saturation

Table 3: D-dimer and CRP relationship with CTSS (ANOVA)

		CTSS <8 N = 31	*CTSS 8–14 N = 53*	*CTSS >14 N = 20*	*p-value*
D-dimer	Mean	349.22	475.03	1089.25	0.048
	SD	1005.12	1111.02	1131.44	
CRP	Mean	35.18	47.38	74.69	0.076
	SD	58.07	61.67	60.07	

CTSS; Chest tomography severity score, CRP; C reactive protein

Table 4: Random blood sugar and HbA1C relation with CTSS (ANOVA)

		CTSS less <8 N = 31	*CTSS 8–14 N = 53*	*CTSS >14 N = 20*	*p-value*
Random blood sugar	Mean	167.78	171.79	175.6	0.946
	SD	76.71	85.15	85.59	
HbA1C	Mean	6.31	6.94	6.21	0.037
	SD	1.32	1.309	1.32	

CTSS; Chest tomography severity score

Table 5: Association of CTSS and with comorbidities

	CTSS <8	*CTSS 8–14*	*CTSS >14*	*Chi-square test (df)*	*p-value*
HT N = 38	13	13	12	2.773^4	0.597
Hypothyroidism N = 12	6	3	3		
CAD and CKD N = 7	2	4	1		

COVID-19 patients. They also concluded that chest CT has the potential to predict the risk of progression and disease severity early.

Our data showed that patients with a CTSS of >14 had supplemental oxygen requirements, and this difference was statistically significant (*p*-value 0.000). We also found a significant inverse relationship between CTSS and oxygen saturation (SpO2) (*p*-value 0.000). Aalinezhad M et al. found a significant inverse relationship between CTSS and capillary oxygen saturation. They also found an important role of previous comorbidities in determining CTSS.[16] Xie et al. showed an association between hypoxemia and mortality in patients with COVID-19. Therefore, our patients with CTSS >14 had hypoxemia, required supplemental oxygen, and were at a higher risk of morbidity and mortality.[17]

Inflammatory markers such as D-dimer and C reactive protein were higher in patients with higher CTSS. The D-dimer in this group was significantly higher in comparison to the group with low CTSS (*p*-value 0.048). Though the CRP was higher in the high CTSS group it was not statistically significant (*p*-value: 0.076).[18]

COVID-19 patients may have higher blood sugar levels because of various reasons, like pre-existing borderline diabetes, drugs or stress, the action of the virus on ACE 2 receptors on various organs or worsening of pre-existing diabetes.[19] In our study, patients with higher CTSS, had higher random blood sugar levels, but the difference was not statistically significant (*p*-value: 0.946). However, our data showed an inverse relationship between HbA1C and high CTSS, contrary to the studies which showed higher CTSS in diabetic patients. This may be because of the smaller sample size of our study. (*p*-value: 0.037)

We also analyzed the relationship of CTSS with preexisting comorbidities like hypertension, chronic kidney disease, coronary artery disease, and hypothyroidism, and we did not find any statistically significant correlation. This also needs to be seen in the light of the smaller number of patients with comorbidities in our study.

Our study was conducted at a single tertiary center, and no doctors or patients were blinded. A large multicenter study with a higher number of subjects may be helpful in concluding the role of age, gender, viral load, comorbidities, CTSS, and different biomarkers in determining the severity & outcome of COVID-19 disease.

Conclusion

Our study showed that there was no significant gender difference in patients with or without higher CTSS. Patients with higher CTSS required oxygen and had hypoxia with lower SpO2 and had an inverse relationship with it. Higher CTSS were also associated with higher inflammatory markers and D-dimer, which signifies thrombosis in these patients. Our data failed to show the relationship between HbA1C and higher CTSS. Some of our findings were in line with previous studies, whereas some of them were not. These results may help in the clinical management of COVID-19 patients by determining severity and prognosis with the help of CTSS, especially in settings with limited critical care resources.

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