

# Association of Computed Tomography Severity Score of COVID-19 Pneumonia with Clinical Severity and Outcome: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Computed Tomography (CT) plays a pivotal role in the diagnosis of Coronavirus Disease-2019 (COVID-19) pneumonia. Various scoring systems have also been proposed for prognostic purposes; but their validation in the Indian setting has not been widely done.

**Aim:** To compare the CT Severity Score (CTSS) of lung involvement with the clinical severity of COVID-19 pneumonia.

**Materials and Methods:** A single centre hospital-based cross-sectional observational study was conducted from October 2020 to April 2021 at Holy Family Hospital, New Delhi, India. Hundred hospitalised Reverse Transcription Polymerase Chain Reaction (RT-PCR) positive COVID-19 pneumonia adult patients underwent thoracic CT scans within 24 hours of hospitalisation for quantification of pulmonary involvement, which were reviewed to obtain the CTSS. The association between CTSS and the clinical profile of the patients (clinical severity of COVID-19 pneumonia at

admission as per Ministry of Health and Family Welfare guidelines, duration of hospitalisation, clinical outcome, and number of co-morbidities) was determined. Fischers-exact test was used for categorical variables and the two sample Student's t-test for continuous variables. A p-value <0.05 was considered significant.

**Results:** Mean age of study participants was 57.8±14.8 years (range 24-90 years); and male to female ratio was 3:2. There was a statistically significant association between the CTSS and clinical severity of COVID-19 pneumonia (p<0.001). Significant association was observed between the CTSS and duration of hospital stay (p-value <0.001). Significant association was also observed between CTSS and clinical outcome of patients (p-value=0.002). Significant association was also observed between CTSS and number of co-morbidities (p-value=0.002).

**Conclusion:** The CTSS had a statistically significant association with the clinical severity of COVID-19 pneumonia, as well as with the duration of hospital stay and the clinical outcome.

**Keywords:** Co-morbidity, Coronavirus disease 2019, Prognosis

## INTRODUCTION

Following the emergence of the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) in Wuhan, China in December 2019, the virus rapidly spread worldwide and was declared a pandemic by the World Health Organisation on 12<sup>th</sup> March 2020. There have been 298 million confirmed cases and over 5 million deaths due to COVID-19 reported till date [1]. In spite of widespread vaccination, it still poses a major health risk with evolutionary mutations in viral spike proteins leading to emergence of newer variants of concern such as the Delta and Omicron variants [2]. The SARS-Cov-2 RT-PCR test performed on respiratory tract specimens is the gold standard for diagnosis of COVID-19 pneumonia. However, owing to various limitations related to sample collection, transportation, type of sample, processing time and performance of diagnostic kit, sensitivity of RT-PCR varies from 60-71% [3,4]. Rapid antigen tests also have similar sensitivity ranging from 68-74% [5].

According to Fleischner Society consensus statement, chest imaging (radiography or CT) is primarily indicated for patients with moderate to severe respiratory symptoms and a high pretest probability of disease; whereas it is not indicated as a COVID-19 screening test for patients with mild respiratory symptoms [6]. Though not a screening tool for detection of COVID-19 pneumonia, imaging may serve as a complementary tool for timely detection of early lung changes in RT-PCR negative patients, which can ensure immediate care to contain disease transmission in the population. Thoracic CT reveals bilateral ground glass opacities and vascular engorgement with lower lobar and posterior predilection in over 70% of cases. Consolidation, nodules, crazy paving pattern, bronchiectasis, halo or reverse halo are less common; whereas cavitating lung lesions, pleural effusions and lymphadenopathy are uncommon in COVID-19

pneumonia [7,8]. A meta-analysis which included six studies comprising 1431 patients revealed a pooled sensitivity of 94.6% and a pooled specificity of 46.0% of chest CT in the detection of COVID-19 pneumonia [9]. In order to standardise the reporting of thoracic CT of patients with moderate to severe symptoms of COVID-19, the COVID working group of the Dutch Radiological Society developed the COVID-19 Reporting and Data System (CO-RADS), in which the likelihood of having COVID-19 infection is graded from very low (CO-RADS category 1) to very high (CO-RADS category 5) [10].

D-dimer, C-reactive protein, serum ferritin, lymphopenia and other biomarkers have been investigated for stratifying COVID-19 patients according to severity for appropriate management [11,12]. Apart from these laboratory markers, thoracic CT can not only aid in the diagnosis of COVID-19 pneumonia, it can also serve as a surrogate marker of its severity. A semiquantitative scoring system was previously employed for quantifying the extent of pulmonary involvement in patients recovering from Severe Acute Respiratory Syndrome (SARS) [13]. Subsequently, with the advent of the COVID-19 pandemic, the same 25-point scoring system was applied by Pan F et al., for assessment of the severity of COVID-19 pneumonia in their retrospective study on the temporal evolution of pulmonary changes on thoracic CT [14]. Another 40-point scoring system was devised by Yang R et al., with a score less than 20 potentially ruling out a severe form of the disease [15]. A different scoring system was proposed by Yuan M et al. combining the extent of pulmonary involvement with specific attenuation patterns (normal, ground-glass, and consolidation). Using this method, a final cumulative score ranging from 0-72 could be obtained, which yielded a sensitivity of 85.6% and a specificity of 84.5% for the prediction of mortality in a population of 27 SARS-CoV-2 patients [16]. In their study to determine the prognostic value

of thoracic CT in COVID-19 pneumonia patients, Colombi D et al. quantified the value of Well Aerated Lung (WAL) Visually (V-WAL) and with Segmentation software (S-WAL); and found V-WAL less than 73% and S-WAL less than 71% were predictors of Intensive Care Unit (ICU) admission or death [17].

Not enough data correlating imaging findings with clinical outcome of Indian patients is available [18-20]; and majority of literature currently available is from China, Europe and USA. Hence, this study was conducted with the primary objectives of comparing the CTSS of lung involvement with the clinical severity of COVID-19 pneumonia; and to predict association between the CTSS with duration of hospital stay and the clinical outcome. As a secondary objective, authors also studied the association of co-morbidities with the CTSS and clinical outcome of COVID-19 patients.

## MATERIALS AND METHODS

A single centre hospital-based cross-sectional observational study was conducted from October 2020 to April 2021 at Holy Family Hospital, New Delhi, India. Ethical clearance from the Institutional Ethical Committee (Reg. No. 240-20118-201-226391) was obtained. Informed written consent was obtained from all participants prior to their inclusion in the study.

Chest CT scans of 100 hospitalised RT-PCR positive COVID-19 pneumonia adult patients were reviewed to obtain an overall CTSS. The association between CTSS and the clinical profile of the patients was determined.

**Inclusion and Exclusion criteria:** Inclusion criteria for the study was RT-PCR positive adult COVID-19 pneumonia patients. Suspected cases of COVID-19 pneumonia who were RT-PCR negative, paediatric COVID-19 patients (age <18 years), patients with negative findings or extensive motion artefacts on chest CT, and those with incomplete clinical data were excluded from the study.

**Sample size calculation:** Sample size was calculated using the formula for cross-sectional observational study:

$N=4PQ/L^2$ ; where N=sample size; P=prevalence of typical COVID-19 findings evaluated by CT ( $p=50\%$  taking the study by Bhandari S et al. as reference); Q=100-P; L=relative error (10%) [21]. Using these values, sample size was calculated to be 100.

## Study Procedure

Clinical severity of COVID-19 in all patients at admission was categorised as mild, moderate or severe as per guidelines issued by Ministry of Health and Family Welfare, Government of India [22]. Patients with uncomplicated upper respiratory tract infection with mild symptoms like fever, cough, sore throat, and without evidence of breathlessness or hypoxia were categorised as mild disease. Patients with pneumonia with clinical features of dyspnoea and/or hypoxia, fever, cough, oxygen saturation ( $SpO_2$ ) between 90-94%, respiratory rate >24 breaths/minute were categorised as moderate disease. Patients with severe pneumonia (pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress,  $SpO_2$  <90%), Acute Respiratory Distress Syndrome (ARDS), sepsis or septic shock were categorised as severe disease.

Baseline laboratory investigations including haemogram, blood sugar, liver and renal function tests, C-Reactive Protein (CRP) and D-dimer levels were recorded. Clinical details in terms of symptomatology, presence of any co-morbidities, management (room air, supplementary oxygen or ventilator), duration of hospital stay, and clinical outcome (death/discharge) of all patients was also recorded.

## CT Acquisition Protocol and Image Interpretation

All patients underwent thoracic CT within 24 hours following hospitalisation for quantification of pulmonary involvement. The CT scan was performed on 128-Slice GE Revolution multidetector CT scanner with a single inspiratory breath hold, without administration

of intravenous contrast medium, and using a low radiation dose protocol (technical parameters: 100 kVp, 10 mAs) to achieve radiation dose of less than 1 mSv. Images were reviewed in lung as well as mediastinal window settings. Presence, location, extent and density of lung parenchymal abnormality was assessed. Lung lesions (ground glass opacity, consolidation) were categorised using Fleischner society glossary of terms for thoracic imaging [23]. Furthermore, other associated abnormalities like pleural effusion, lymphadenopathy and vascular enlargement were assessed. The location of lung lesions was specified with regards to involvement of affected lung in percentage per lobe according to the system proposed by Pan F et al., [14]. The CTSS was calculated by adding scores of all five lung lobes with maximum 25 points [Table/Fig-1]. An overall score of 0-7 was considered as mild, 8-17 as moderate and 18-25 as severe COVID-19 infection [24].

Score	Extent of lobar involvement
0	None
1	<5%
2	5-25%
3	26-49%
4	50-75%
5	>75%
Total score	Sum of 5 lobar scores (range 0-25)

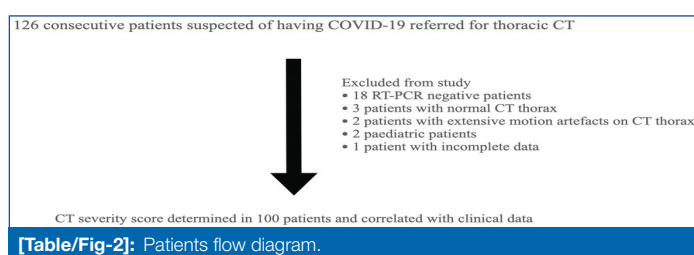
**[Table/Fig-1]:** Semi-quantitative scoring system for pulmonary involvement in COVID-19 pneumonia.

## STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc. Chicago, IL, v. 21.0) software. Continuous variables were expressed as means and standard deviations, whilst categorical variables were expressed as counts and percentages. Statistical calculations were performed using Fischers-exact test for categorical variables and two sample Student's t-test for continuous variables. A p-value <0.05 was considered statistically significant.

## RESULTS

This study comprised of 100 hospitalised RT-PCR positive COVID-19 pneumonia adult patients. Flow of patients in the study is depicted in [Table/Fig-2].



**[Table/Fig-2]:** Patients flow diagram.

Mean age of the patients was  $57.8 \pm 14.8$  years (range 24-90 years); and the male to female ratio was 3:2. Based on clinical assessment, it was observed that 32% patients had mild disease, 48% patients had moderate disease, and 20% patients had severe disease. All patients with clinically mild disease (32%) were managed on room air; and all patients with clinically moderate disease (48%) needed supplemental oxygen. Of patients with clinically severe disease, 13 (13%) were managed with ventilatory support, whereas the remaining 7 (7%) were managed with supplemental oxygen alone. The demographic and clinical profile of study participants is summarised in [Table/Fig-3]; whereas their imaging findings are summarised in [Table/Fig-4].

Association of CTSS with clinical parameters of COVID-19 pneumonia: There was a statistically significant association between CTSS and clinical severity of COVID-19 pneumonia ( $p < 0.001$ ). Mean CTSS of patients with clinically severe disease was 18.52; with clinically

Variables	n (%)
<b>Age</b>	
<40 Years	11 (11%)
40-49 Years	21 (21%)
50-59 Years	20 (20%)
60-69 Years	25 (25%)
>70 Years	23 (23%)
<b>Gender</b>	
Male	60 (60%)
Female	40 (40%)
<b>Symptoms<sup>†</sup></b>	
Fever	80 (80%)
Cough	75 (75%)
Breathlessness	52 (52%)
Myalgia	35 (35%)
Diarrhoea	11 (11%)
Anosmia	8 (8%)
None	2 (2%)
<b>Underlying comorbidities<sup>†</sup></b>	
Hypertension	54 (54%)
Diabetes mellitus	46 (46%)
Chronic kidney disease	5 (5%)
Chronic liver disease	4 (4%)
Coronary artery disease	11 (11%)
Stroke	1 (1%)
<b>Laboratory parameters (Mean±SD    Range)</b>	
Haemoglobin (g/dL)	12.49±1.78  8.2-17.3
Random blood sugar (mg/dL)	165.6±73.12  76-474
<b>Liver function tests</b>	
Alanine aminotransferase (U/L)	48.85±26.97  11-156
Aspartate aminotransferase (U/L)	47.36±37.51  5-294
<b>Renal function tests</b>	
Blood urea (mg/dL)	35.96±26.42  11-178
Serum creatinine (mg/dL)	1.27±1.87  0.5-16
Lymphocyte count (×10 <sup>3</sup> /L)	8.03±4.4  2.4-24
C-reactive protein (mg/L)	6.66±7.1  0.2-36.2
D-dimer (mcg/mL)	974.3±1112    169-6700
<b>Clinical severity</b>	
Mild	32 (32%)
Moderate	48 (48%)
Severe	20 (20%)
<b>Management</b>	
On room air	32 (32%)
Supplemental oxygenation	55 (55%)
Ventilatory support	13 (13%)
<b>Duration of hospital stay</b>	
≤7 days	29 (29%)
8-14 days	50 (50%)
15-42 days	21 (21%)
<b>Clinical outcome</b>	
Discharge	89 (89%)
Death	11 (11%)

**[Table/Fig-3]:** Demographic and clinical profile of study participants.

<sup>†</sup>Other symptoms included sore throat; gastrointestinal symptoms (loose motions, abdominal pain or distension, gastrointestinal bleed); dizziness and syncope, and no symptoms; <sup>‡</sup>The number of symptoms and comorbidities exceeds the total number of patients due to overlapping features

moderate disease was 12.74; and with clinically mild disease was 8.24. The mean CTSS of clinically mild disease fell outside the range

Variables	Mild (n=20)*	Moderate (n=57)*	Severe (n=23)*	Total
<b>CT pattern</b>				
Ground glass opacity	20	57	22	99
Consolidation	4	28	20	52
Crazy paving	0	7	15	22
<b>Distribution of lung lesions</b>				
Subpleural	15	25	3	43
Random	4	26	3	33
Diffuse	1	7	16	24
<b>Lobar involvement</b>				
Right upper lobe	5	31	14	50
Right middle lobe	2	17	9	28
Right lower lobe	4	29	17	50
Left upper lobe	5	33	15	53
Left lower lobe	4	28	18	50
<b>Ancillary features</b>				
Vascular enlargement	0	7	12	19
Reverse halo sign	0	4	3	7
Pleural effusion	1	5	4	10
Lymphadenopathy	5	6	3	14

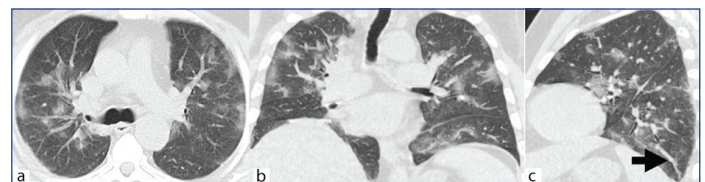
**[Table/Fig-4]:** Computed tomography features of study participants.

\*The number of computed tomography features exceed number of patients (n) in each category due to overlapping features

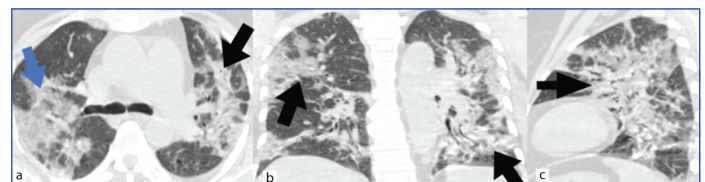
of 0-7 as 12 of these patients had moderate CTSS. Cases of varying severity as per CTSS are illustrated in [Tables/Fig-5-7].

Clinical outcome had a statistically significant association with chronic kidney disease (p-value=0.035) but not with any other specific type of co-morbidity as depicted in [Table/Fig-8].

Significant association was observed between CTSS and duration of hospital stay (p<0.001). Significant association was also observed between CTSS and clinical outcome (p-value=0.002) [Table/Fig-9].



**[Table/Fig-5]:** 33-year-old male with fever and cough for 4 days and no comorbidities. Axial section (a), coronal (b) and sagittal reformats (c) of CT thorax in lung window show patchy ground glass opacities in both lungs; with vascular enlargement in posterior segment of left lower lobe (black arrow) (CT severity score 6-mild COVID-19 pneumonia).



**[Table/Fig-6]:** 46-year-old hypertensive male with fever, cough and breathlessness for 2 days. Axial section (a), coronal (b) and sagittal reformats (c) of CT thorax in lung window show ground glass opacification (blue arrow) and consolidation (black arrows) in bilateral lungs (CT severity score 14-moderate COVID-19 pneumonia).



**[Table/Fig-7]:** 59-year-old diabetic and hypertensive female with fever and cough for 6 days. Axial section (a), coronal (b) and sagittal reformats (c) of CT thorax in lung window show extensive ground glass opacities (blue arrows) and consolidation (black arrows) in bilateral lungs (CT severity score 20-severe COVID-19 pneumonia).

Co-morbidities	Clinical outcome		Chi-square	p-value
	Death (n=11)*	Discharge (n=89)*		
Diabetes mellitus	4	42	0.508	0.476
Chronic kidney disease	2	3	4.451	0.035
Hypertension	5	49	0.413	0.521
Chronic liver disease	1	3	0.794	0.373
Stroke	1	1	3.126	0.077
Coronary artery disease	1	10	0.051	0.821

**[Table/Fig-8]:** Association of clinical outcome with various comorbidities.

\*Data are number of patients. The number of comorbidities exceeds the number of deaths/discharges (n) as some patients had more than one comorbidity

Clinical parameter		CT Severity, n (%)			p-value
		Mild (n=20)*	Moderate (n=57)*	Severe (n=23)*	
Clinical severity	Mild (n=32)	19 (95)	12 (21.1)	1 (4.3)	<0.001†
	Moderate (n=48)	1 (5)	43 (75.4)	4 (17.4)	
	Severe (n=20)	0	2 (3.5)	18 (78.3)	
Hospital stay (Days)	Mean±SD	6.2±2.821	11.1±5.588	16.3±8.581	<0.001†
Clinical outcome	Death	0 (0.0)	4 (7.0)	7 (30.4)	0.002†
	Discharge	20 (100)	53 (93.0)	16 (69.6)	
No. of co-morbidities	None	8 (40)	16 (28.1)	1 (4.4)	0.002†
	Single	6 (30)	26 (45.6)	7 (30.4)	
	Double	4 (20)	13 (22.8)	7 (30.4)	
	Multiple	2 (10)	2 (3.5)	8 (34.8)	

**[Table/Fig-9]:** Association of CT severity with clinical severity of COVID-19 pneumonia, the clinical outcome, associated co-morbidities and duration of hospital stay of the study patients.

\*Data are the number of patients; while the number in parentheses are the percentages; †p-value determined using Chi-square test; ‡p-value determined using Analysis of Variance (ANOVA) test

## DISCUSSION

Mean age of patients in the present study was 57.8±14.86 years (range 24-90 years). People aged 60-69 years were the most common affected age group constituting 25% cases; young patients were less commonly afflicted with patients <40 years comprising only 11% of cases. There was also a slight male predilection. Similar observations were made by several authors [21,25,26].

In the present study, patient care management was determined by the clinical severity of the disease. 32% were managed conservatively at room air, 55% required oxygen supplementation and 13% patients required ventilator support. Saeed GA et al., reported that 71.5% patients did not require oxygen support, 21.5% needed oxygen supplementation by various means such as nasal cannula or face mask, and only 7% required intubation. However, they had a greater proportion of patients with mild disease severity compared to our study [24]. In another study it was reported that out of 470 patients, 60.6% were managed with oxygen supplementation and 32.6% required mechanical ventilation [27]. These variations are accounted for by heterogeneity in patient populations in different studies.

We observed a significant association between clinical severity of COVID-19 pneumonia and CT severity of lung involvement ( $p < 0.001$ ) implying that CTSS accurately predicted the severity of disease in the majority of the cases. Our results were in concordance with those of other studies, as several other authors have also reported significant association between clinical severity and CT severity index of COVID-19 patients [25,28-32]. Abdollahi I et al., found CT score >19 to be predictive of severe disease and ICU admission [25]. The median CTSS was significantly higher in severely ill as compared to moderately ill patients (13 and 10 respectively;  $p < 0.001$ ) in a study by Pouw W et al., in which they used a 40-point scoring system. However, they only included moderate or severely ill cases; mild

cases were not categorised separately in their study [29]. Therefore, apart from the assessment of clinical parameters, CTSS can be treated as a reliable prognostic tool to determine the degree of severity of COVID-19 pneumonia.

In present study, the median duration of hospital stay was 9 days, with an interquartile range (IQR) of 3-41 days. El-Jawhari A et al., reported similar results with a median hospital stay of eight days (IQR 1-37 days) [27]. In a systematic review regarding length of hospital stay of COVID-19 patients, the median length of hospital stay ranged from 4-53 days [33]. The authors also analysed the association between patients' duration of hospital stay and CTSS and observed that as the severity of the disease increases, there is every likelihood that hospital stay will get prolonged. Several other authors have also reported the direct association between hospital stay and severity of disease [29,34,35]. For instance, Pouw N et al., reported a significant association between disease severity and length of hospital stay ( $p < 0.001$ ); the median length of hospital stay for severely ill patients was 9 days (IQR 4-23 days) compared to 6 days (IQR 3-12 days) for moderately ill patients [29].

The in-hospital mortality was 11% in the present study, which falls between the in-hospital death rate of 4.3-28% reported in various studies [27,29,36-38]. The authors observed a significant association between CTSS and clinical outcome; with mortality being highest amongst those with CTSS >17. In their retrospective study of 46 patients of COVID-19 pneumonia, Lei Q et al., also reported that a high CTSS and diffuse pulmonary involvement was predictive of poorer prognosis and higher mortality. Median CTSS of patients who succumbed to the disease in their study was 20; whereas it was six for the patients who recovered ( $p < 0.005$ ) [39]. In another study, CT score >19 was found to be predictive of mortality (odds ratio-1.84) [25].

The clinical symptomatology and underlying co-morbidities in our patients was in line with what had been observed in other studies [21,40]. In a meta-analysis on COVID-19, the prevalence of diabetes, hypertension and cardio-cerebrovascular disease was found to be maximum [41]. In the present study, it was observed that clinical outcome has a significant association with the number of co-morbidities ( $p$ -value=0.004). Other authors have also demonstrated that co-morbidities not only affect the disease severity but also elevate its mortality rate [42-44]. Ejaz H et al., in a comprehensive review, reported that co-morbidities such as hypertension, diabetes and chronic obstructive pulmonary disease increase the mortality amongst COVID-19 patients. They postulated this to be due to upregulation of Angiotensin Converting Enzyme-2 (ACE-2) receptors in certain co-morbid conditions; which is utilised by the virus to gain entry into host cells [45]. Rather than the type of co-morbidity, the number of underlying co-morbidities was found to be a more important determinant of the CTSS as well as the eventual clinical outcome in our study. Thus, risk of mortality would be much greater if patients have multiple co-morbidities as compared to a single co-morbidity.

## Limitation(s)

The sample size was small and CT scan was done only at a single time-point; follow-up scans were not included in the study. As this was a hospital based study and majority of patients with clinically mild disease underwent home isolation, this category of patients were under-represented. Though oxygen saturation of all patients was regularly monitored in the wards, correlation of SpO<sub>2</sub> levels with the CTSS was not determined. Lastly, the study was conducted during the second wave of the COVID-19 pandemic when vaccination drive was just commencing. Hence, applicability of CTSS to newer strains of SARS-CoV-2 and following widespread vaccination campaigns needs to be validated.

## CONCLUSION(S)

A 25-point CTSS corroborates well with the clinical severity of COVID-19 pneumonia. Statistically significant association was

also seen between CTSS and duration of hospital stay; as well as between CTSS and the clinical outcome. Thus, this scoring system can be considered a reliable prognostic tool to assess severity of COVID-19 pneumonia.

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