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Cohort Study

A novel chest CT severity score in COVID-19 and its correlation with severity and prognosis of the lung disease: A retrospective cohort study

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ABSTRACT

Background: HRCT chest has a high sensitivity in the diagnosis of patients with COVID-19 infection. Through our study, we intend to evaluate the diagnostic accuracy and inter-reader variability of a semi-quantitative CT severity score, a novel parameter designed for risk stratification and prognostication of COVID-19 pneumonia with clinical staging of disease.

Methods: It was a single-center retrospective analysis performed on an original cohort of 4180 symptomatic patients with the suspicion of SARS-CoV-2 interstitial pneumonia. Out of 4180, a total of 4004 patients with COVID-19 were confirmed by an RT-PCR. We used an HRCT chest severity score (CT-SS) to evaluate the COVID-19 disease burden on the initial scan obtained at admission. The data were analyzed with IBM SPSS Statistics Version 22.0 Release 2013.

Results: Our study subjects demonstrated the most common clinical features fever, cough, dyspnea, and body aches. Raised CRP levels (CRP >0.5 mg/dL) were found in 81.86% and increased D-dimer levels (>500 ng/mL) were found in 92.3% of patients. The most common radiological findings of the disease included ground-glass opacities, observed in 98.8%. Our study has a sensitivity of 89.2%, a specificity of 94.8%, a positive predictive value (PPV) of 90.6%, and a negative predictive value (NPV) of 94%.

Conclusion: As per our findings, this novel CT scoring system might aid in the risk stratification and the short-term prognostication of patients suffering from COVID-19 pneumonia. This will eventually help in curtailing the extensive burden on the healthcare system amid the current pandemic.

1. Background

Coronavirus (CoV) is a single-stranded, long (30 thousand base pairs) positive-sense RNA virus. It belongs to the coronaviridae family, which is further subdivided into two sub-families named Torovirinae and Coronavirinae [1]. On 31-December 2019, a local hospital reported a cluster of 27 patients with pneumonia of unknown etiology in Wuhan city of the Republic of China. The early clinical manifestations of this pneumonia-like disease included fever, dry cough, and dyspnea. Very little knowledge about transmission and the inability to track the history of exposure lead to a very rapid rate of spread of the virus [2]. The outbreak was declared a global health emergency by WHO on 30-January 2019. The disease began to spread globally at a very high rate. On March 11, 2020, the WHO declared it a pandemic [1].

The clinical manifestations of COVID-19 are very similar to those of severe acute respiratory disorder and Middle East respiratory syndrome. The most common symptoms are fever, non-productive cough, and shortness of breath [3,4]. Severe cases can lead to admission to the intensive care unit for acute respiratory distress syndrome or even death. The management of coronavirus disease highly depends upon the severity of the disease. Mild patients recover without any intervention. In a few cases, they may receive antivirals, symptomatic support, and oxygen therapy. However, severe cases are shifted to intensive care for ventilation support.

Reverse transcriptase-polymerase chain reaction (RT-PCR) and next-generation sequencing are the two gold-standard laboratory investigations for diagnosing COVID-19 infection [5]. But studies have also shown that the sensitivity and specificity of swab testing could be

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insufficient for a single time point. The results may get affected by the person or technical errors [6,7]. The low sensitivity and relatively long turnaround time (TAT) of a polymerase-chain-reaction can lead to the failure to diagnose a large number of COVID-19 patients. Ultimately, it can create a lot of problems in managing those cases.

Various studies have proved that high resolution computed tomography (HRCT) chest has a high sensitivity in the diagnosis of patients with COVID-19 infection. That's the reason why the HRCT chest is routinely done in practical medicine for the management of COVID patients [8]. Typical radiological findings can be found in non-contrast HRCT of almost every patient of COVID disease. These include ground-glass opacities (GGOs), septal thickening, and parenchymal consolidations. The most common distribution pattern of these opacities is peripheral [9,10]. The non-contrast scan is preferred over the contrast scan because the former can have an impact on the interpretation of the pattern of ground-glass opacities. We propose that the HRCT chest can be used to detect the extension of the lung involvement in COVID pneumonia.

The purpose of our study is to assess the diagnostic validity and inter-reader variability of a semi-quantitative CT severity score, a novel parameter designed for risk stratification and prognostication of COVID-19 pneumonia with clinical staging of disease.

2. Method and material

Our research study was a single-center retrospective analysis performed on an original cohort of 4180 patients with clinical suspicion of COVID-19 pneumonia. The study was carried out in Nishtar Hospital, Multan, Pakistan, from January 15, 2021 to February 15, 2022. Out of 4180, a total of 4004 patients with COVID-19 were confirmed by reverse transcriptase-polymerase chain reaction. The research was conducted in accordance with the Declaration of Helsinki. Our work is fully compliant with the STROCSS 2021 criteria [11].

2.1. Inclusion criteria

1. Patients with a fever of $>38^{\circ}$ C and COVID-19 pneumonia suspicion.
2. Patients with throat, cough, and chest pain.
3. Patients with contact history and mild symptoms.
4. Patients who had both HRCT chest and PCR examinations.

2.1.1. Exclusion criteria

1. Patients free from symptoms
2. Patients with other respiratory pathologies like malignancy, atelectasis, or tuberculosis.
3. Patients failed to follow-up.

2.2. Laboratory investigations and disease staging

Baseline investigations and arterial blood gas (ABG) tests were performed for all patients. The following parameters were evaluated: lymphocyte count, D-dimer, C-reactive protein (CRP), serum ferritin and PaO2/FiO2 ratio. We also recorded other key parameters like oxygen saturation (SpO_2) and respiratory frequency.

The disease severity score was evaluated by the criteria provided by the Chinese Center of Disease Control (CDC) [12]. The mild disease included the asymptomatic patients or the patients with mild pneumonia (mild symptoms without shortness of breath; respiratory frequency <30/min; $SpO_2 > 93\%$; PaO_2/FiO_2 ratio ≥ 300 mmHg). The severe disease included the patients presenting with shortness of breath, respiratory frequency ≥ 30/min, $SpO_2 < 93\%$, PaO_2/FiO_2 ratio <300 mmHg, and/or lung infiltrates involving more than 50% of lung parenchyma within 24–48 h of clinical manifestation. The critical disease included patients with adult respiratory distress syndrome (ARDS) or respiratory failure, septic shock, and/or multiple organ dysfunction or failure. For the purposes of this study, two disease groups were made based on disease severity. One is mild disease group, and other is severe disease group in which both severe and critical patients were included.

2.3. Chest CT severity score assessment

A semi-quantitative CT chest severity score (CT-SS) was developed for the assessment of disease burden. This score is based on lung opacifications for extension of the disease in the lungs. A similar method was used previously to describe ground-glass opacity, interstitial opacity, and air trapping, and it was correlated with clinical and laboratory findings in patients with SARS infection [13]. Based on anatomical variability we sub-divided the 18 segments of both lungs into 20 regions. We used an exceptional mathematical based system to validate the groung glass opacities (GGOs) in all of the 20 lung regions. Accordingly, a score of 0 was assigned if parenchymal involvement was 0%, a score of 1 if equal or less than 50%, and a score of 2 if the opacities involved more than 50% of parenchyma of each region. The CT severity score was calculated by summing the individual scored in the 20 lung segments, which may range from 0 to 40 points.

Three diagnostic radiologists, including two radiologists with more than 10 years of experience and a final year radiology resident reviewed all the CT images independently, blinded to the clinical data and laboratory indicators. Two reader pairs were formed. One involved radiologist 1 and final year radiology resident and the second one involved radiologist 2 and final year radiology resident. The window width and level for lung parenchyma in all CT scans were 1200–2000 HU and −600 to −400 HU, respectively.

2.4. CT protocol

Chest CT imaging was performed on a 64-detector CT scanner (Toshiba). All patients were examined in supine position. CT scan had following parameters: X-ray tube parameters - 120 KVp, 350 mAs; pitch - 1.0; rotation time - 0.5sec; section thickness – 5 mm; intersection space – 5 mm.

2.5. Statistical analysis

The data were analyzed with IBM SPSS Statistics Version 22.0 Release 2013. Continuous variables were expressed as mean value ± standard deviation (SD). We used the Mann-Whitney test and the Kruskal-Wallis test for single and multiple comparisons respectively. To compare the consistency of two groups of radiologists in each lung segment, the Weighted Kappa coefficient was used. All measurements were assessed with normality tests. The scores of each lung segment were compared between the mild and severe groups using the Fisher exact test. We used Wilcoxon matched-pairs signed-rank test to compare the scores of both lungs. A p value < 0.05 was considered to be statistically significant.

The number of patients with CT severity score less than 19.5 was 2442 in the Mild group and 132 in the Severe, while the number of patients with CT severity score equal to or greater than 19.5 was 154 and 1276, respectively, resulting in a sensitivity of 89.2%, specificity of 94.8%, positive predictive value (PPV) of 90.6%, and a negative predictive value (NPV) for severe disease of 94%.

3. Results

3.1. Demographic details, clinical presentation and laboratory findings

A total of 4004 patients with a positive RT-PCR test for SARS-CoV-2 were included in this study, 2574 in the Mild group and 1430 in the severe group. There were 2662 males, and 1342 females; the mean age was 58.7 ± 11.3, range 17–82 years. Fever, cough, dyspnea, and, body

aches were the most common clinical symptoms in our study population. We recorded raised CRP levels (CRP >0.5 mg/dL) in 3278/4004 (81.86%) patients with a mean value of 7.7 mg/dL ± 12.3 and increased D-dimer levels (>500 ng/mL) were found in 3696/4004 (92.3%) patients with a mean value of 1682 ng/mL ± 1511. Decreased lymphocyte count was observed in 2464/4004 (61.53%) patients, and decreased PaO2/FiO2 ratio in 2288/4004 (57.14%) patients. The demographic and clinical features of the two populations are listed in Table 1.

3.2. Imaging findings and disease scoring

The inter-reader ICCs for CT-SS was excellent. The kappa coefficient for pair one was 0.812 and for pair 2 was 0.786. For further analysis, the scores provided by one of the two pairs were randomly chosen (Table 2).

The most common radiological findings of the disease included ground glass opacities, observed in 3916 patients (98.8%), followed by septal thickening (crazy paving) (n = 3696; 93.3%) and, bronchial wall thickening (n = 1728; 80%). Related CT features were found as follows: reverse halo sign (n = 1100; 27.77%), bronchodilation (n = 990; 25%), focal atelectasis (n = 704; 17.7%), lung cavitation (n = 418; 10.5%), discrete small nodules (n = 396; 10%), pleural effusion (n = 286; 7.2%), pulmonary fibrosis (n = 154; 3.8%), lymphadenopathy (n = 66; 1.66%), and pneumothorax/pneumomediastinum (n = 88; 2.22%). Two patient did not show any parenchymal involvement at HRCT chest (Table 3).

Overall, the posterior basal segment of the inferior lobes (right, 143/4004 [78.57%]; left, 3476/4004 [86.81%]), the medial basal segment of the inferior lobes (right, 2728/4004 [68.13%]; left, 2860/4004 [71.42%%]), the anterior basal segments of the inferior lobes (right, 2640/4004 [66%]; left, 2904/4004 [72.5%]), and the posterior segments of the superior lobes (right, 2574/4004 [64.28%]; left, 2090/4004 [52.19%]) are the most frequently involved sites in COVID-19 (Fig. 1).

A difference of considerable statistical significance was observed between the Mild and Severe group's lung opacity scoring in each lung region, $P < 0.05$ (Table 4). The total CT-SS was 12.0 (7.0, 12.0) in the Mild group, and 28 (21.60, 31.45) in the Severe group (Figs. 2 and 3).

4. Discussion

An outbreak of coronavirus disease 2019 (COVID-19) infection began in December 2019 in Wuhan, the capital of central China's Hubei province. The coronavirus epidemic was later declared as a global public health emergency by the WHO [1]. The disease have a vast spectrum of clinical manifestations. It ranges from asymptomatic and/or mild presentation to severe disease with intensive care admissions.

The classical radiological features of coronavirus pneumonia include rounded or linear ground-glass opacities (GGOs) [14]. Lesions are multiple, and the most common pattern of distribution is sub-pleural followed by diffuse involvement [15–17]. Some imaging findings of coronavirus disease are similar to those of certain other RNA viral infections, such as para-influenza and respiratory syncytial virus infections [18,19]. Song et al. retrospectively analyzed the HRCT chest images of 51 patients suffering from COVID-19 infection. They showed that 82% of the patients had posterior lung involvement, a finding which is in line with our results [20]. This typical involvement of posterior lung segments is similar to reports on SARS-CoV and MERS-CoV infection [21,22]. In our study, we observed that the lower lobes of both lungs are slightly more involved in disease than the middle and upper ones, without significant differences between the right and left lung. These findings are parallel with other previous analyses [23].

There is no currently available biomarker to triage patients based on the severity of the symptoms and to estimate the prognostication of the disease [24]. In this study, we developed a semi-quantitative scoring method. We used the amount of ground glass opacification involving the 20 segments of both lungs as a surrogate for COVID-19 burden. In our study, CT-SS was much higher in severe cases when compared to mild ones. Most importantly, we determined that a CT-SS threshold of 19.5 could identify severe COVID-19, with a sensitivity of 89.2% and a specificity of 94.8%, resulting in an NPV of 94%. This finding is in line with the results of a previous study done to analyze the sensitivity and specificity of this novel CT scoring method for prognostication of COVID-19 infection [25]. The inter-reader agreement was excellent between our two groups of radiologists. Our study has proved that this simple and relatively straightforward method could help us in identification, risk stratification, triaging, and managing the patients of COVID-19 disease. Ultimately, it will minimize the disease burden and make healthcare resources more accessible.

This retrospective study has several limitations. First, there was no histologic confirmation of the findings. Second, only three radiologists investigated HRCT chest scans. Third, we selected only the first chest CT obtained on admission, which could lead to potential implications for the interpretation of the CT-SS. Fourth, we performed a retrospective

Table 1
Demographic and clinical characteristics of our study population.

Characteristics	Covid-19 Patients (n = 4004)
Gender	
Males	2662/4004 (66.48%)
Females	1342/4004 (33.51%)
Age range (years)	
0-25	132/4004 (3.29%)
26-50	1760/4004 (44%)
51-75	1914/4004 (47.8%)
>75	198/4004 (05%)
Clinical manifestations	
Fever	3762/4004 (94%)
Cough	2354/4004 (58.8%)
Shortness of breath	1848/4004 (46.15%)
Body aches	1276/4004 (31.86%)
Diarrhea	374/4004 (9.3%)
Laboratory findings	
Increased CRP levels	3278/4004 (81.86)
Increased d-dimer levels	3696/4004 (92.3%)
Leukopenia	2662/4004 (66.47%)
Decreased lymphocyte count	2464/4004 (61.53%)
Decrease PaO_2/FiO_2 ratio	2288/4004 (57.14%)
Comorbid conditions	
Hypertension	1298/4004 (32.41%)
Diabetes mellitus	1430/4004 (35.71%)
Lung pathologies	308/4004 (7.7%)
Ischemic heart disease	418/4004 (10.43%)

Table 2
Weighted kappa coefficient between pairs of readers.

Reader pair	k coefficient
Diagnostic radiologist 1- final year radiology resident	0.821
Diagnostic radiologist 2- final year radiology resident	0.786

Table 3
Comparison of radiological features of covid-19 in patients of mild and severe groups.

Radiological findings	Mild group (n = 2574)	Severe group (n = 1430)
Ground glass opacities	2530 (98.29%)	1430 (100%)
Septal thickening	2398 (93.6%)	1298 (90.76%)
Bronchial wall thickening	2002 (77.77%)	1166 (81.5%)
Reverse halo sign	528 (20.51%)	572 (40%)
Bronchodilation	440 (17.1%)	550 (38.46%)
Focal atelectasis	242 (9.4%)	462 (32.3%)
Lung cavitation	22 (0.85%)	396 (27.7%)
Discrete small nodules	22 (0.85%)	374 (26.15%)
Pleural effusion	44 (1.7%)	242 (17%)
Pulmonary fibrosis	00	154 (10.76%)
Lymphadenopathy	00	66 (4.6%)
Pnaumomediastinum/ pneumothorax	00	88 (6.15%)

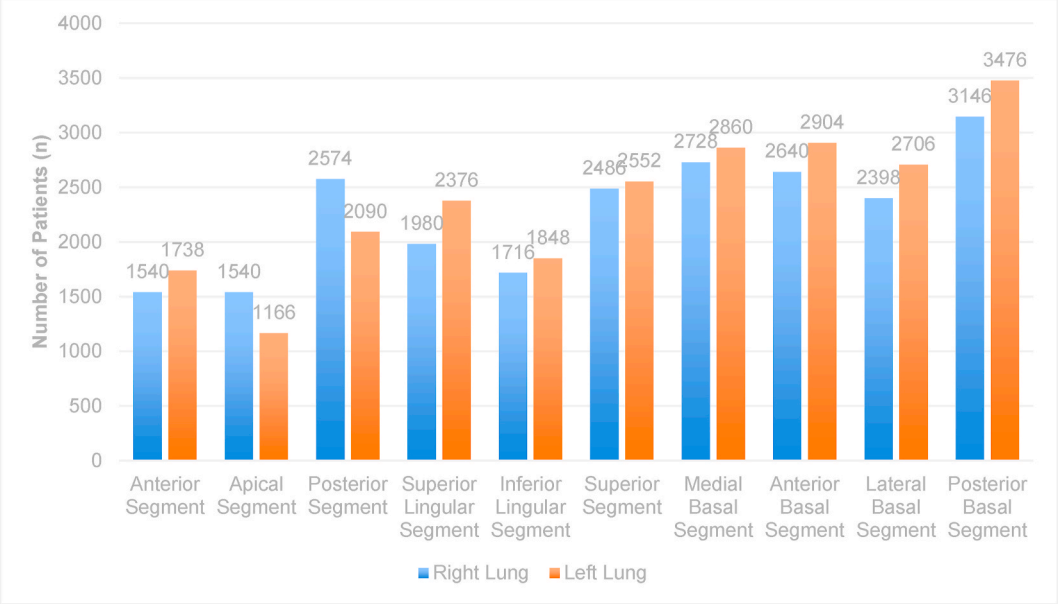

Fig. 1. Comparison of involvement of segments between right and left lung.

Table 4
Comparison of left lung score and right lung score.

Variable	Right lung	Left lung	p value
Mild (n = 2574)	6.0 (3.15, 5.85)	6.0 (3.55, 5.45)	<0.001
Severe (n = 1430)	14 (10.0, 15.8)	15 (10.0, 16.5)	<0.001

analysis in a relatively smaller cohort of patients. Further prospective research with a larger study population is needed to identify the degree of diagnostic consistency of CT-SS in COVID-19 infection.

5. Conclusion

Our study concludes that this novel CT scoring system could help us in risk stratification and short-term prognostication of patients suffering from COVID-19 pneumonia. Various disease parameters like clinical manifestations, laboratory values, and severity are highly co-related with the extent of involvement of the lungs on HRCT. In our study, a score of less than 19 could rule out the severe disease with a negative predictive value of 96%. This method of assessing the severity of the disease could help us decide whether to admit the patient to the hospital or manage in-home isolation settings. It will ultimately minimize the enormous load on the healthcare system nowadays.

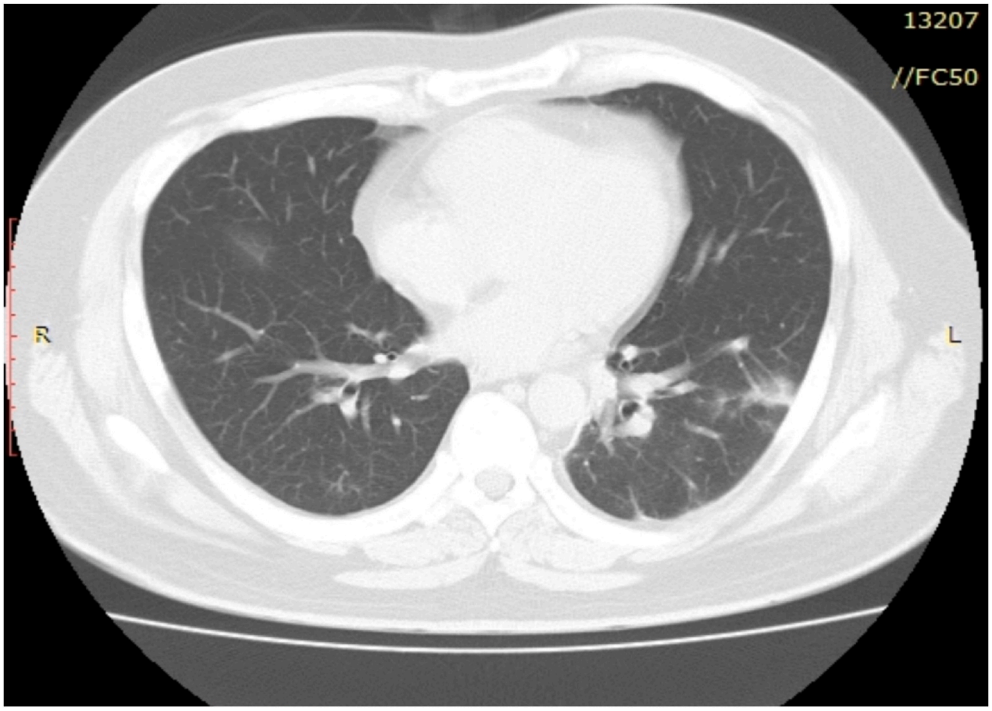

Fig. 2. Non-contrast chest CT images of a 34-year-old man with mild COVID-19 pneumonia. CT scans show very few ground-glass opacities.

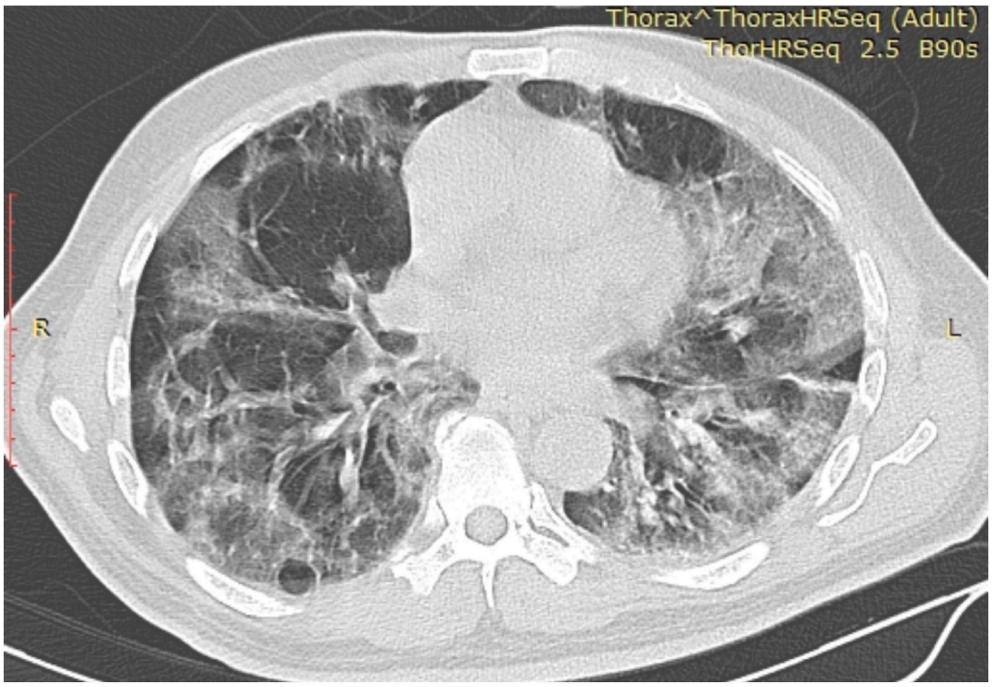

Fig. 3. Non-contrast chest CT images of a 52-year-old man with severe COVID-19 pneumonia. CT scans show multiple ground-glass opacities in multiple lung segments.

Ethical approval

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No funding was received for this research.

Author contribution

HM conceived and designed the study. AS and HM were responsible for data collection and acquisition of data. SY, HM, AY, and HAS analyzed and/or interpreted the data. HM and SY performed the literature review. HM, SY, and AS wrote the initial manuscript. AY and HAS critically revised the manuscript. All authors have approved the final manuscript.

Registration of research studies

1. Name of the registry: NA
2. Unique Identifying number or registration ID: NA
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): NA

Consent

Written informed consent was obtained from the patient for publication of this research paper and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Guarantor

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Provenance and peer review

Not commissioned, externally peer reviewed.

Research questions

- How can we classify COVID-19 pneumonia based on the findings of HRCT?
- What will be the correlation between the severity of lung disease in COVID-19 pneumonia and HRCT severity score?
- Will this scoring system help us in triaging the covid patients?

Declaration of competing interest

No conflict of interest.

Acknowledgment

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104692.

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