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Original Article

Radiology Section

Prediction of Clinical Requirement of Tocilizumab Injection in COVID-19 Patients with High Chest CT Severity Score- A Retrospective Analysis

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ABSTRACT

Introduction: The ongoing Coronavirus Disease 2019 (COVID-19) pandemic has spread rapidly across the globe. Tocilizumab is a recombinant monoclonal antibody to Interleukin-6 (IL-6) receptor. An increasing number of studies across the world is reporting the use of tocilizumab in treating COVID-19 patients or at risk of developing cytokine storm. Apart from clinical and laboratory parameters, High Resolution Computed Tomographic (HRCT) chest scan is a promising tool to identify patients very early in the course of COVID-19 disease.

Aim: To find whether high chest CT Severity Score (CTSS) on HRCT thorax scan predict the clinical requirement of tocilizumab injection in COVID-19 patients.

Materials and Methods: In this retrospective study, during the period from May 2020 to July, 2020, 250 patients with confirmed Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) diagnosed with COVID-19 in first or repeat sample and who also underwent HRCT scan of the chest, were assigned chest CTSS. From the data obtained, patients were categorised into two groups based on mild and severe CTSS. Patients with higher CTSS have a higher future possibility of developing the cytokine storm and hence the requirement of tocilizumab can be reliably predicted. All statistical analysis was performed in IBM Statistical Package for the Social Sciences (SPSS) version 20.

Results: Out of a total of 250 patients, 72 patients were given tocilizumab injection. The average CTSS was 29.8±6.38 in the tocilizumab injection group. Only 8% of patients with mild CTSS received tocilizumab injection while 60% of patients with severe CTSS received tocilizumab injection ($p<0.001$). Out of 72 patients who received tocilizumab injection, 16.7% had mild CTSS while 83.3% had severe CTSS ($p<0.001$). Average values of inflammatory markers like C-Reactive Protein (CRP), D-Dimer, Ferritin, Lactic De-Hydrogenase (LDH), and IL-6; were significantly higher in severe CTSS and tocilizumab group ($p<0.001$).

Conclusion: CTSS may be used as a new decisive tool in triaging in-hospital COVID-19 patients. Categorising patients in mild and severe CTSS early in the disease course, even before the marked worsening of laboratory parameters and development of cytokine storm may help initiate early treatment and thereby save many lives.

Keywords: Coronavirus disease 2019, Cytokine storm, Inflammatory markers, Pandemic, Recombinant antibody

INTRODUCTION

The ongoing COVID-19 pandemic has spread rapidly across the globe. The novel coronavirus SARS-CoV-2 is the culprit. The first pneumonia cases were identified in Wuhan, the capital city of Hubei province (China), in December 2019 [1]. As of January 11 2021, 91,328,321 cases and 1,953,182 deaths have been reported across the globe, and India is one of the worst-hit countries currently [2].

The clinical spectrum varies widely from asymptomatic, mild Upper Respiratory Tract Infection (URTI) to severe pneumonia which may progress to Acute Respiratory Distress Syndrome (ARDS) with respiratory failure requiring oxygenation support or intubation [3,4].

Imaging plays a vital role in the diagnosis and monitoring changes during treatment. In highly suspected subjects with a negative result of Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR), HRCT scan of the chest is the modality of choice [5,6]. HRCT is a very sensitive radiological modality for the diagnosis of lung involvement in COVID-19, with varied radiological patterns in the disease course [7,8]. Though CT, being limited by specificity (inability to differentiate different viruses), confirmatory diagnosis requires nasopharyngeal swabs and virus RNA extraction by RT-PCR [9,10].

Several CT scoring systems have emerged and research is ongoing to assess the clinical and prognostic implications of severe lung involvement on CT [11]. Visual assessment or Artificial Intelligence (AI) aided quantitative analysis of the CT exam can be used for this purpose.

Tocilizumab is a recombinant monoclonal antibody to IL-6 receptor of the host cells [12,13]. Till now, an increasing number of studies across the world have reported the use of tocilizumab in treating COVID-19 patients or at risk of developing cytokine storm [14,15]. Many of them have shown promising results in proving that treatment with tocilizumab, might reduce the risk of invasive mechanical ventilation or death in patients with severe COVID-19 pneumonia [16].

The purpose of this study is to find an answer to a question that can high chest CTSS predict the clinical requirement of tocilizumab injection in COVID-19 subjects later in the course of the disease? Thus, able to triage the high-risk patients early in the course of the disease even before laboratory and clinical parameters start to worsen.

MATERIALS AND METHODS

A retrospective, cross-sectional analysis of the hospital medical records of 250 hospitalised patients between May 2020 to July 2020 with confirmed RT-PCR diagnosis of COVID-19 on first or repeat samples was conducted in Tertiary care centre, Gujarat, India. Ethical approval from the institutional ethical committee was taken (UNMICRC/ALLIED/2020/01). Data was analysed in August 2020 and September 2020. The data of 250 patients was collected from May 2020 to July 2020.

Inclusion criteria: A total of 250 patients with severe pneumonia clinically and who also underwent an HRCT scan of the chest were included in the study.

Exclusion criteria: The patients who had high chest CTSS but were not able to receive tocilizumab due to contraindications like co-existent infection, history of severe allergic reactions to monoclonal antibodies, active symptomatic gastrointestinal tract conditions that might predispose patients to bowel perforation, severe haematological, renal, or liver function impairments. Those patients with high CTSS but died before the tocilizumab injection were also excluded.

Severe pneumonia was defined as at least one of the following: the presence of a respiratory rate of 30 or more breaths per minute, peripheral blood oxygen saturation (SpO_2) of less than 93% in room air and a ratio of arterial oxygen partial pressure (PaO_2) to fractional inspired oxygen (FiO_2) of less than 300 mm Hg in room air, this is according to Chinese management guidelines for COVID-19 (version 6.0) [3,17].

All CT examinations were performed in the second week from symptoms onset, ranging from day 8 to day 10. Patients' demographics and laboratory findings were also collected.

Chest CT Analysis and Scoring System

All patients underwent a 128 slice SOMATOM Definition AS+(Siemens Healthcare, Germany) CT scanner. The parameters were set at 120 kVp; 100-200 mAs; pitch, 1-1.2; and collimation, 128×0.6. All images were viewed with both lung (width, 1200 HU; level, -600 HU) and mediastinal (width, 350 HU; level, 50 HU) window settings.

Various CT scoring systems are available for severity scoring of COVID-19 pneumonia depending on the varying degrees of lobar or segmental volume involvements. In lobar scoring system, five lung lobes are assigned a score of 0, 1, 2, 3 or 4 depending upon the percentage of lobar involvement and classified as none (0%), minimal (1-25%), mild (26-50%), moderate (51-75%), or severe (76-100%). The total score is the sum of the five lobe scores (range from 0 to 20). The segmental scoring system divides segments of both lungs into 20 regions, only the ground glass or consolidative lung opacities were considered for evaluation of the 20 lung regions while fibrotic or atelectatic bands were excluded [18]. Scores of 0, 1, and 2 were assigned respectively for parenchymal opacification of 0%, less than 50%, or equal or more than 50% of each region.

The CTSS was defined as the sum of the individual scores in the 20 segments of lung (10 on either side). The total score may range from 0 to 40 points. The individual scores in each lung, as well as the total CTSS were higher in severe COVID-19 when compared with mild cases ($p<0.05$). In the study by Yang et al., [18], the requisite CTSS threshold for identifying severe COVID-19 was 19.5 (area under the curve, 0.892), sensitivity and specificity being 83.3% and 94%, respectively.

According to consensus by two experienced radiologists, the segmental scoring system was chosen over the lobar system. The segmental scoring system was found to be simpler, less subjective, and more reliable to reproduce as compared to lobar system. All the CT images were reviewed independently by two experienced radiologists, who were blinded to the demographics, clinical data and laboratory indicators. For the ease of interpretation, a cut off of 20 was finalised (instead of 19.5 in the study by Yang R et al., [18]), a score of <20 being considered as mild and score ≥20 being considered as severe. The final score considered was the average of the scores given by two independent radiologists. The scoring performa used is as shown in [Table/Fig-1].

A standard protocol was devised by the team of pulmonologists and intensive care specialists of the institute for tocilizumab injection. Patients who showed SpO_2 of less than 93% and a PaO_2/FiO_2 ratio of less than 300 mm Hg in room air or a more than 30% decrease in their PaO_2/FiO_2 ratio in the previous 24 hour during hospitalisation, were given tocilizumab injection. As per institutional protocol, patient was administered intravenous tocilizumab at a dose of 8 mg/kg body weight (up to a maximum of 800 mg) [19].

Lobe of lung	Segment of lobe
Right upper lobe	Apical segment
	Anterior segment
	Posterior segment
Right middle lobe	Medial segment
	Lateral segment
Right lower lobe	Superior segment
	Anterior basal segment
	Medial basal segment
	Lateral basal segment
	Posterior basal segment
Left upper lobe	Apical segment
	Anterior segment
	Posterior segment
Left lingular segment	Superior segment
	Inferior segment
Left lower lobe	Superior segment
	Anterior basal segment
	Medial basal segment
	Lateral basal segment
	Posterior basal segment
Total score	
Scores	**Interpretation**
0	No involvement
1	<50% segment involvement
2	>50% segment involvement
Mild	<20
Severe	≥20
Minimum score=0, Maximum score=40	

[Table/Fig-1]: Chest CT Severity Score (CTSS).

STATISTICAL ANALYSIS

All statistical analysis was performed in IBM SPSS version 20. Quantitative variables were expressed as the mean±standard deviation (SD) and qualitative variables were expressed as a percentage (%). A comparison of parametric values between two groups was performed using the independent sample t-test. Categorical variables were compared using the chi-square test. A nominal significance was taken as a two-tailed p-value <0.05.

RESULTS

Out of a total of 250 patients, 175 patients were males and 75 patients were females. Out of 72 patients who were given tocilizumab injection, 56 were males and 16 were females. The average age of the patients was 56.88±13.68 years in whole study while it was 59.42±11.96 years in the tocilizumab injection group.

The average CTSS was 19.58±8.84. It was 29.8±6.38 in the tocilizumab injection group. Out of 72 patients who received tocilizumab injection, 12 belong to mild score group with the average score being 17.58±1.44 and 60 belong to severe score group with the average score being 32.31±3.43. From mild CTSS group, only 8% of patients received tocilizumab injection while from severe CTSS group, 60% of patients received tocilizumab injection ($p<0.001$). Gender, age and CTSS parameters in mild and severe group and tocilizumab injection group are shown in [Table/Fig-2].

CTSS groups and tocilizumab injection association are shown in [Table/Fig-3,4]. Average values of CRP, Ferritin, LDH, and IL-6 were significantly higher in severe CTSS and tocilizumab group (p <0.001). All parameters are summarised in [Table/Fig-5-7].

Variables	Mild CTSS group (n=150)	Severe CTSS group (n=150)	Total (n=250)	Tocilizumab injection group (n=72)
Gender, M/F	105/45	70/30	175/75	56/16
Age (mean±SD) (range) age in years	54.25±14.24	60.81±11.8	56.88±13.68	59.42±11.96
CTSS (mean±SD) (range)	13.34±3.8	28.93±5.23	19.58±8.84	29.86±6.38

[Table/Fig-2]: Gender, age and CTSS parameters in mild and severe group and tocilizumab injection group.

CTSS	Tocilizumab injection given	Tocilizumab injection not given	p-value
n (%)	72 (28.8)	178 (71.2)	
Mild (<20)	12 (16.7 %)	138 (77.5 %)	<0.0001*
Severe (≥20)	60 (83.3 %)	40 (22.5 %)	

[Table/Fig-3]: CTSS groups and tocilizumab injection association.
*<0.05 statistically significant, Chi-square test used

Drug	Mild N=150/250 (60%)	Severe N=100/250 (40%)	p-value
n (%)	150 (60)	100 (40)	
Tocilizumab	12 (8%)	60 (60%)	<0.0001*

[Table/Fig-4]: Tocilizumab injection and CTSS groups' numbers association.
*<0.05 statistically significant, Chi-square test used

Variables	Tocilizumab given with mild CTSS	Tocilizumab given with severe CTSS	p-value
n (%)	12 (16.7)	60 (83.3)	
CRP (mg/L) mean±SD (range)	76.13±35.45 (34.13-143.97)	88.90±73.6 (8.27-320)	0.56
Ferritin (ng/mL) mean±SD (range)	518.34±326.52 (91.1-1000)	1359.85±405.59 (581-1994)	<0.0001*
LDH (U/L) mean±SD (range)	264.67±46.24 (196-350)	432.22±78.1 (301-551)	<0.0001*
D-Dimer (ng/mL) mean±SD (range)	570.83±212.56 (218-1000)	1031.59±1811.76 (159.97-10000)	0.39
IL-6 (pg/mL) mean±SD (range)	96.36±57.95 (40.10-224.5)	246.12±102.51 (85-436)	<0.0001*

[Table/Fig-5]: Blood parameters and tocilizumab injection group with mild-severe CTSS association.
<0.05 statistically significant, Independent sample t-test used The range which is given in bracket is Range in our study population

Variables	Mild group	Severe group	p-value
n (%)	150 (60)	100 (40)	
CRP (mg/L) mean±SD (range)	22.33±19.08 (7-143.97)	60.66±66.66 (8.27-320)	<0.0001*
Ferritin (ng/mL) mean±SD (range)	141.35±149.62 (12.4-1000)	909.28±638.1 (140-1994)	<0.0001*
LDH (U/L) mean±SD (range)	199.81±37.58 (140-350)	353.91±115.56 (185-551)	<0.0001*
D-Dimer (ng/mL) mean±SD (range)	366.51±120.87 (200.30-1000)	812.03-±1436.39 (156.87-10000)	0.0002*
IL-6 (pg/mL) mean±SD (range)	19.47±28.19 (5-224)	154.91±137.45 (7-436)	<0.0001*

[Table/Fig-6]: Blood parameters and CTSS groups association.
*<0.05 statistically significant, Independent sample t-test used

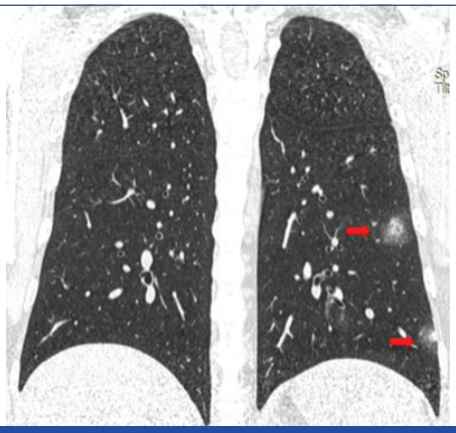
Variables	Tocilizumab injection given	Tocilizumab injection not given	p-value
n (%)	72 (28.8)	178 (71.2)	
CRP (mg/L) mean±SD (range)	86.77±68.69 (8.27-320)	17.80±4.43 (7-32.92)	<0.0001*
Ferritin (ng/mL) mean±SD (range)	1219.6±502.95 (91.10-1994)	136.63±73.06 (12.40-320)	<0.0001*
LDH (U/L) mean±SD (range)	404.29±97.32 (196-551)	203.67±35.38 (140-283)	<0.0001*
D-Dimer (ng/mL) mean±SD (range)	954.79±1662.70 (159.97-10000)	378.84±168.97 (156.87-1674)	0.0002*
IL-6 (pg/mL) mean±SD (range)	221.16±111.41 (40.10-436)	13.98±6.57 (5-34)	<0.0001*
CTSS mean±SD (range)	29.86±6.38 (14-39)	15.42±5.76 (1-35)	<0.0001*
Male	56 (77.8)	119 (66.9)	0.07
Female	16 (22.2)	59 (33.1)	

[Table/Fig-7]: Blood parameters and tocilizumab injection- no injection group association.
*<0.05 statistically significant, Independent sample t-test used

DISCUSSION

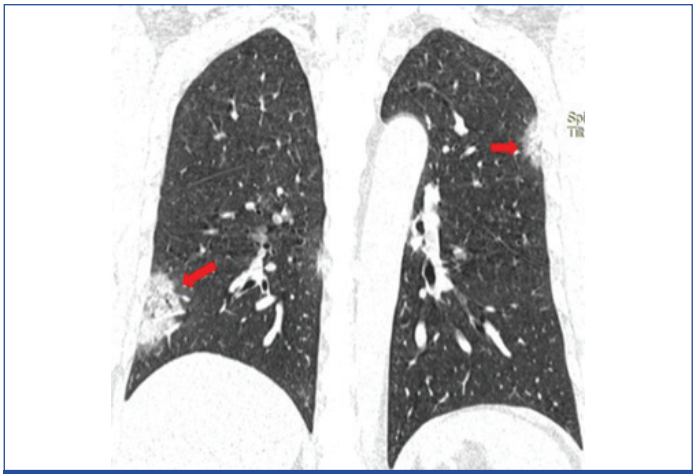
The rapid rate with which the pandemic is spreading not only in India but across the globe has created panic in the health care system. Flooding of the hospitals with patients, scarcity of Intensive Care Unit (ICU) beds, increased demand for oxygen units, and ventilators are major concerns especially in developing and overpopulated countries like India. Thus, triaging is the key to better patient management and outcome.

Chest radiographs, though being a low-cost examination modality, are limited by low sensitivity in early diagnosis of suspected COVID-19 patients. [20-22]. A High Resolution CT scan of the chest has high sensitivity in the early diagnosis of lung involvement in COVID-19 patients [Table/Fig-8] [23-25]. Various CT severity scoring systems have emerged on HRCT. Assessment can be done subjectively by visual method. Many AI based automated volume quantification tools are also now available.

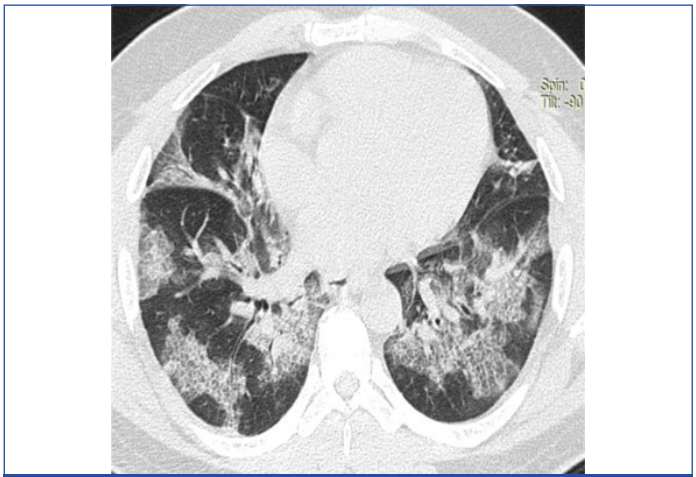


[Table/Fig-8]: Mild COVID-19 pneumonia. Coronal lung window CT image showing focal rounded ground-glass opacities in the lower lobe of the left lung. CTSS was three in the same patient.

The typical imaging manifestations of early COVID-19 are patchy, rounded, peripheral segmental, or subsegmental ground-glass opacities, with or without consolidation [Table/Fig-9,10] [22]. Based on typical CT findings proposed in various studies, Yuan M et al., have proposed a scoring method to screen patients based on the admittance CT scan [11]. Yang R et al., in their study devised a semi-quantitative scoring method using the amount of lung opacification involving 20 lung regions as a surrogate for COVID-19 burden [18]. More recently, Li K et al., also described a visual, quantitative analysis of lung damage, based on the degrees of parenchymal loss, which correlated with a score of clinical severity [26]. The CTSS was higher in severe cases of COVID-19 pneumonia when compared to mild cases and the same were the results of their study. This study adhered to the threshold of 19.5 to identify severe COVID-19 as proposed in their study. The segmental scoring system was chosen over the lobar system due to simplicity, less subjectivity, and more reliable reproducibility by visual quantitative evaluation. This relatively undemanding method could help early triaging and reliably predict the future possibility of developing cytokine storm and hence



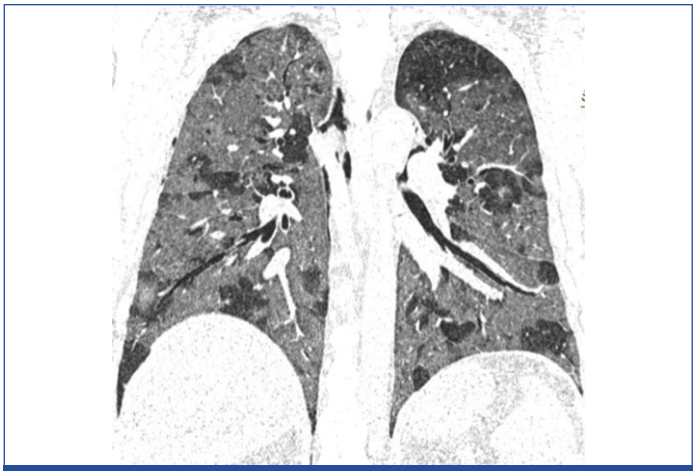
[Table/Fig-9]: Mild COVID-19 pneumonia. Coronal lung window CT image showing focal rounded consolidation with surrounded ground-glass opacities in the lower lobe of the right lung and upper lobe of the left lung. CTSS was seven in the same patient.



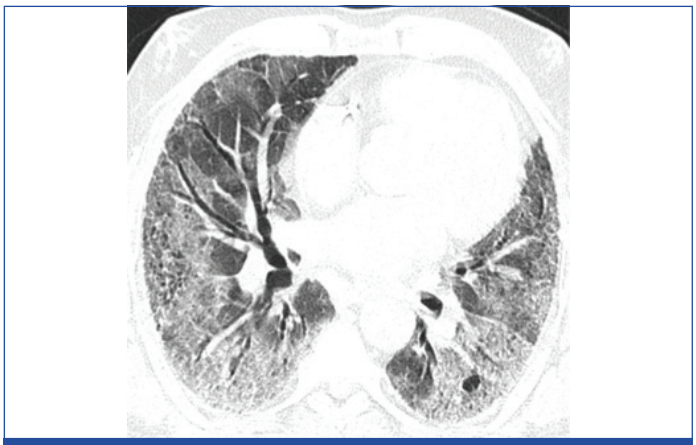
[Table/Fig-10]: Severe COVID-19 pneumonia. Axial lung window CT image showing multifocal ground-glass opacities and interstitial septal thickening creating crazy-paving appearance. CTSS was 29 in the same patient.

the need for tocilizumab injection, particularly in circumstances of restricted availability of healthcare assets.

Currently, laboratory blood parameters and clinical oxygen requirements guide the management of patients with severe COVID-19 pneumonia. A significant high risk of developing ARDS and cytokine storm in patients with high CTSS was found [Table/Fig-11,12]. By categorising patients based on mild and severe CTSS, the future possibility of cytokine storm and hence the requirement of tocilizumab can be reliably predicted. Lanza E et al., have studied a similar concept and showed that quantitative chest CT analysis in COVID-19 predicts the need for future oxygenation support and intubation [27]. Similar kind of



[Table/Fig-11]: Severe COVID-19 pneumonia. Coronal lung window CT image showing diffuse ground-glass opacities and tractional dilatation of few bronchi. CTSS was 36 in the same patient.



[Table/Fig-12]: Severe COVID-19 pneumonia with Acute Respiratory Distress Syndrome (ARDS). Axial lung window CT image showing diffuse ground-glass opacities and interstitial septal thickening creating crazy-paving appearance and tractional dilatation of bronchi.

study conducted by our institute also showed correlation of high chest CTSS with clinical requirement of oxygen [28].

Limitation(s)

It was a retrospective analysis co-morbid conditions and clinical information of the patients were not combined. This may explain a few of the patients with mild CTSS ending up with tocilizumab injection. CTSS is based on the assumption that lung opacities represent COVID-19 disease burden but histopathological confirmation of the same is lacking. CTSS considered was an average of only two experienced radiologists (independent blinded analysis). A single CT study of in-hospital patients done in the second week of symptoms onset was analysed. The data was retrieved from medical records, hence there may have been a human error of perception and memory in providing the exact day of symptoms onset. Also, follow-up scans were not considered. The segmental scoring system was chosen over the lobar scoring system based on departmental protocol decision. Analysis through AI has been proven to be more precise over visual manual analysis, but there is limited availability and high cost of AI and also the manual method fairly serves the purpose of the intended study. Team of pulmonologists and intensive care specialists of the institute decided which patients were to be given the tocilizumab injection, based on the standard protocol. Validity of CTSS still needs to be determined by external validation studies with multicenter larger cohorts.

CONCLUSION(S)

CTSS serves as a new guiding tool in triaging in-hospital COVID-19 subjects. Categorising patients in mild and severe CTSS early in the disease course, even before the marked worsening of laboratory parameters and development of cytokine storm may save energy, health resources, help to triage severe patients, and above all may save many lives.

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REFERENCES

[1] Guan W, Ni ZY, Hu Y, Liang C, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382:1708-20. https://doi.org/ 10.1056/NEJMoa2002032.
[2] COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU).coronavirus.jhu.edu.
[3] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Published: March 11, 2020. Doi: https://doi.org/10.1016/S0140-6736(20)30566-3.

[4] Poston JT, Patel BK, Davis AM. Management of critically ill adults with COVID-19. JAMA 2020;323(18):1839-41. PMID: 32215647. https://doi.org/10.1001/jama.2020. 4914.
[5] Huang P, Liu T, Huang L, Liu H, Lei M, Xu W, et al. Use of Chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology. 2020;295(1):22-23. Published Online: Feb 12, 2020. https: // doi.org /10.1148 / radiol.2020200330.
[6] Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J, et al. Chest CT for typical 2019-nCoV pneumonia: Relationship to negative RT-PCR testing. Radiology. 2020;296(2):E41-45.
[7] Shi H, Han X, Jiang N, Jiang N, Cao Y, Alwalid O, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis. 2020;20:425-34.
[8] Chung M, Bernheim A, Mei X, Zhang N, Huang M, Zeng X, et al. MD CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology. 2020;295(1):202-07.
[9] Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): Role of chest CT in diagnosis and management. AJR Am J Roentgenol. 2020;214(6):1280-86. Doi: 10.2214/AJR.20.22954. Epub 2020 Mar 4. PMID: 32130038.
[10] Lescure FX, Bouadma L, Nguyen D, Parisey M, Wicky PH, Behillil S, et al. Clinical and virological data of the first cases of COVID-19 in Europe: A case series. Lancet Infect Dis. 2020;20(6):697-706. https://doi.org/10.1016/S1473-3099(20) 30200-0.
[11] Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PLoS One. 2020;15(3):e0230548. Published 2020 Mar 19. Doi: 10.1371/journal.pone.0230548.
[12] Hennigan S, Kavanaugh A. Interleukin-6 inhibitors in the treatment of rheumatoid arthritis. Ther Clin Risk Manag. 2008;4:767-75.
[13] Swerdlow DI, Holmes MV, Kuchenbaecker KB, Engmann JEL, Shah T, Sofat R, et al. The interleukin-6 receptor as a target for prevention of coronary heart disease: A mendelian randomization analysis. Lancet. 2012;379:1214-24.
[14] Klopfenstein T, Zayet S, Lohse A, Balblanc JC, Badie J, Royer PY, et al. Tocilizumab therapy reduced intensive care unit admissions and/or mortality in COVID-19 patients. Med Mal Infect. 2020;50(5):397-400; published online May 6. Doi: 10.1016/j.medmal.2020.05.001.
[15] Toniati P, Piva S, Cattalini M, Garrafa E, Regola F, Castelli F, et al. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy. Autoimmun Rev 2020;19(7):102568. published online May 3. Doi: 10.1016/j.autrev.2020.102568.
[16] Guaraldi G, Meschiari M, Cozzi-Lepri A, Milic J, Tonelli R, Menozzi M, et al. Tocilizumab in patients with severe COVID-19: A retrospective cohort study. Lancet Rheumatol 2020;2(8):E474-84. AUGUST 01, 2020 Published:June 24, 2020. Doi: https://doi.org/10.1016/S2665-9913(20)30173-9.
[17] National Health Commission of the People's Republic of China. Chinese management guideline for COVID-19 (version 6.0). Feb 19, 2020.
[18] Yang R, Li X, Liu H, Zhen Y, Zhang X, Xiong Q, et al. Chest CT Severity Score: An imaging tool for assessing severe COVID-19. Radiology- Cardiothoracic Imaging, RSNA- Radiology Society of North America. Published Online: Mar 30, 2020, https://doi.org/10.1148/ryct.2020200047.
[19] Le RQ, Li L, Yuan W, Shord SS, Nie L, Habtemariam BA, et al. FDA approval summary: Tocilizumab for treatment of chimeric antigen receptor t cell-induced severe or life-threatening cytokine release syndrome. Oncologist. 2018;23:943-47.
[20] Bandirali M, Sconfienza LM, Serra R, Brembilla R, Albano D, Pregliasco FE, et al. Chest X-ray findings in asymptomatic and minimally symptomatic quarantined patients in Codogno, Italy during COVID-19 Pandemic. Radiology. 2020;295(3):E7.
[21] Wong HYF, Lam HYS, Fong AHT, Leung ST, Chin TWY, Lo CSY, et al (2019) Frequency and distribution of chest radiographic findings in COVID-19 positive patients. Radiology. 2020;296(2):E72-78.
[22] Ng MY, Lee EY, Yang J, Yang F, Li X, Wang H, et al. Imaging profile of the COVID-19 infection: Radiologic findings and literature review. Radiology: Cardiothoracic Imaging. 2020;2:e200034.
[23] Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: A report of 1014 cases. Radiology. 2020;296(2):E32-40.
[24] Revel MP, Parkar AP, Prosch H, Silva M, Sverzellati N, Gleeson F, et al. COVID-19 patients and the radiology department-advice from the European Society of Radiology (ESR) and the European Society of Thoracic Imaging (ESTI). Eur Radiol. 2020. https://doi.org/10.1007/s00330-020-06865-y.
[25] Paul NS, Roberts H, Butany J, Chung TB, Gold W, Mehta S, et al. Radiologic pattern of disease in patients with severe acute respiratory syndrome: The Toronto experience. RadioGraphics. 2004;24(2):553-63.
[26] Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, et al. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol. https://doi.org/10.1007/s00330-020-06817-6.
[27] Lanza E, Muglia R, Bolengo I, Santonocito OG, Lisi C, Angelotti G, et al. Quantitative chest CT analysis in COVID-19 to predict the need for oxygenation support and intubation. Eur Radiol. 2020;30:6770-78. https://doi.org/10.1007/s00330-020-07013-2.
[28] Rana Y, Patel D, Sheth M, Chhodvadiya S, Patel S, Garachh M, et al. Chest CT severity score to forecast clinical requirement of oxygen support in Covid-19 patients. Int J Radiol Diagn Imaging. 2021;4(1):103-09. Doi: 10.33545/26644436.2021.v4.i1b.170.

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