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Chest Computed Tomography Severity Score to Predict Adverse Outcomes of Patients with COVID-19

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ABSTRACT

Background: The novel coronavirus disease 2019 (COVID-19) continues to wreak havoc worldwide. This study assessed the ability of chest computed tomography (CT) severity score (CSS) to predict intensive care unit (ICU) admission and mortality in patients with COVID-19 pneumonia.

Materials and Methods: A total of 192 consecutive patients with COVID-19 pneumonia aged more than 20 years and typical CT findings and reverse-transcription polymerase chain reaction positive admitted in a tertiary hospital were included. Clinical symptoms at admission and short-term outcome were obtained. A semi-quantitative scoring system was used to evaluate the parenchymal involvement. The association between CSS, disease severity, and outcomes were evaluated. Prediction of CSS was assessed with the area under the receiver-operating characteristic (ROC) curves.

Results: The incidence of admission to ICU was 22.8% in men and 14.1% in women. CSS was related to ICU admission and mortality. Areas under the ROC curves were 0.764 for total CSS. Using a stepwise binary logistic regression model, gender, age, oxygen saturation, and CSS had a significant independent relationship with ICU admission and death. Patients with CSS ≥12.5 had about four-time risk of ICU admission and death (odds ratio 1.66, 95% confidence interval 1.66 – 9.25). The multivariate regression analysis showed the superiority of CSS over other clinical information and co-morbidities.

Conclusion: CSS was a strong predictor of progression to ICU admission and death and there was a substantial role of non-contrast chest CT imaging in the presence of typical features for COVID-19 pneumonia as a reliable predictor of clinical severity and patient's outcome.

Keywords: Chest CT; COVID-19; Prognosis; SARS-CoV-2; CT severity score

INTRODUCTION

The coronavirus disease 2019 (COVID-19) caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was a newly emerging disease with high

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Conflict of Interest

No conflicts of interest.

Author contributions

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infectiousness and mortality. It belongs to the same family of viruses as the SARS-CoV and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), which caused serious outbreaks in 2003 and 2012, respectively [[1,](#page-8-0) [2\]](#page-8-1). The disease has originated in December 2019 in Wuhan, the capital of the Hubei province in China [[3](#page-8-2)], and has been spreading at a rapid rate worldwide, causing the World Health Organization (WHO) to declare it a pandemic [\[4](#page-8-3)]. Since the number of infected patients continues to increase rapidly, there is a need for better diagnosis and treatment of COVID-19 to overcome this pandemic [\[5\]](#page-9-0). The disease is mild and self-limiting in most patients, but in some patients, it is severe and fatal. Deciding which patients are at high risk of severe disease or mortality is an essential part of understanding this disease.

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Non-contrast chest computed tomography (CT) scan was found to be a useful diagnostic instrument for screening COVID-19 pneumonia. The most prevalent CT imaging findings consist of ground-glass opacities (GGO) with or without consolidation as the indicator of viral pneumonia, which mainly tends to be bilateral and poses a peripheral location accompanied by lower lobe predominance [[6](#page-9-1), [7\]](#page-9-2). There is scarce data available on the prognostic application of chest CT scans.

Governments and societies are now fighting with numerous stimulating problems, including people and medical personnel panic, lack of cheap, accessible, and sensitive diagnostic methods, limited hospital capacities and intensive care unit (ICU) beds, and insufficient public preventive tools, which engendered a significant psycho-socioeconomic burden on communities. Therefore, most diagnostic attempts are now focused on predicting the severity and prognosis of the disease as the main issue of challenge among clinicians. Some studies have suggested that old age, the presence of co-morbidities, the need for mechanical ventilation, interleukin-6, higher serum levels of D-dimer, lactate dehydrogenase, procalcitonin, and C-reactive protein, lymphocyte count, and features from CT scoring as predictors of severity and prognosis of COVID-19 [[8](#page-9-3)[–10\]](#page-9-4). Appropriate and clear prognostic imaging and clinical models could help choose patients with poorer outcomes, which need hospital care from those that can be managed as an outpatient. This strategy also helps decrease the admission load of patients in the healthcare centers and the greatest reduction in mortality rate. This study assessed the prognostic value of chest CT severity score (CSS) to predict the severity of symptoms and outcomes among patients with typical CT findings.

MATERIALS AND METHODS

1. Patients

From March 21, 2020 to August 14, 2020 a total of 192 consecutive patients (>20 years old) with classic symptoms of COVID-19 pneumonia and positive reverse transcriptasepolymerase chain reaction (RT-PCR) test attending in tertiary referral hospital, which is affiliated to Isfahan University of Medical Sciences, Iran, were included. The inclusion criteria were consisting of all patients with respiratory symptoms favoring COVID-19 diagnosis in similarity with WHO interim guideline, available laboratory data, RT-PCR positive test, and at least one of the following criteria: oxygen (O_2) saturation ≤93%, tachypnea (respiratory rate ≥22 breaths/min), tachycardia (pulse rate >100/min), and hypotension (systolic blood pressure ≤100 mmHg) according to the Iranian national COVID-19 protocol [[11\]](#page-9-5). Patients whose initial scans were not highly suggestive of COVID-19 and those assessed in the emergency room but not admitted, or those that died in the emergency room, were excluded.

All the included patients had undergone non-contrast chest CT imaging within the first 24 hours of hospitalization and an RT-PCR test was performed for all patients. The average (standard deviation [SD]) number of days between hospitalization and CT scan was 1.13 (1.2) days and the time gap between initial clinical assessment, laboratory test sampling, and scans was about 24 hours for all enrolled patients. Demographic and clinical data on admission were collected from patient's records.

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2. Ethics statement

Ethical approval was obtained from the Isfahan University of Medical Sciences ethical committee, compliant with the Declaration of Helsinki (approval no. IR.MUI.MED. REC.1399.164). This study was based on routine medical procedures, and additional written consent was not essential. The data were processed and analyzed by official medical personnel only and were anonymized and de-identified before analysis.

3. Clinical symptoms

Clinical symptoms were extracted from patients' records documented at admission time. According to WHO classification, established based on admission time's clinical data, we classified patients into mild and severe pneumonia groups. Severe pneumonia is defined by the presence of respiratory rate >30 breaths/min, severe respiratory distress, or $O₂$ Saturation ≤93% with fever or suspected respiratory infection. Non-severe pneumonia and independence from supplemental oxygen administration were considered mild cases [[12](#page-9-6)].

4. Chest CT imaging

All chest CT images were non-contrast and performed during inspiratory breath-hold at the supine position using a 16-detector-row CT scanner (Philips Brilliance 16, Philips Medical Systems, Best, the Netherlands) with the following default settings: 120 kVp , $100 - 200 \text{ mAs}$, all the imaging data were reconstructed with a slice thickness of 1.5 mm and interval of 0.75 mm. All chest CT images were assessed independently and blindly by two board-certificated radiologists with more than five years of experience in chest CT interpretation, who were blind to the clinical and laboratory data. However, if there were any cases with inter-observational disagreement, the third radiologist with 15 years of experience made the final decision. The CT findings were classified using the Radiology Society of North America consensus statement on Reporting Chest CT findings Related to COVID-19 [\[13](#page-9-7)]. Chest CT images were assessed for the presence of ground-glass opacities (GGOs), consolidation, GGOs with consolidation, centrilobular nodules, septal thickening, perilobular opacities, reticular pattern, architectural distortion, subpleural bands, traction bronchiectasis, bronchial wall thickening, mediastinalhilar lymphadenopathy, and pleural and pericardial effusion [\[14](#page-9-8)].

To evaluate the extent of pulmonary parenchymal involvement, we used a semi-quantitative scoring system previously used by others [[15,](#page-9-9) [16](#page-9-10)] using a system previously described for severity of acute respiratory distress syndrome on thin section lung CT scan [\[17](#page-9-11)]. Briefly, each lung was divided into three regions, (1) upper (above the level of the carina), (2) middle (between the carina and inferior pulmonary vein), and (3) lower (below the level of the inferior pulmonary vein). Each region of the lung was evaluated in terms of the percentage of involvement on a scale of $0 - 4$: 0, no involvement; 1) less than 25%; 2) 25% to less than 50%; 3) 50% to less than 75%; and 4) 75% or greater involvement. Overall CT scores was the summation of scores from all 6 lung regions. Then, the total CSS calculated to be a number in the range of 0 (representative of no involvement) to 24 (indicative of diffuse interstitial involvement) and assigned for each patient.

5. Short-term outcome

Patients were divided into two groups: the patients with a poor prognosis who received ICU care or died during the hospitalization period and those with a good prognosis who were discharged without ICU care.

6. Discharge criteria

Discharge criteria were defined as the improvement of chest X-ray findings and clinical symptoms, the absence of fever for at least three days' period, and O₂ saturation of more than 93% without mechanical ventilation.

7. Statistical analysis

Continuous and categorical variables are expressed as means with standard error (SE) of the mean or 95% confidence intervals (CIs) and percentages, respectively, unless otherwise specified. Statistical methods used included the Student's *t*-test, Chi-square test, or Fisher's exact test, one-way analysis of variance followed by the one-way post hoc Tukey test, and stepwise binary logistic regression. Spearman's rho partial correlation analyses adjusting for age were performed to determine the linear relationship between $O₂$ saturation, respiratory rate, and CSS. Age-standardized means were considered and compared using general linear models. To estimate the predictors of disease short-term outcomes a stepwise binary logistic regression was used with the SPSS for Windows (SPSS Inc., Chicago, IL, USA). Variable age, respiratory rate, and $O₂$ saturation were entered in models as a continuous variable, whereas gender, hypertension, diabetes, cardiovascular, chronic respiratory, and chronic kidney disease were entered in models as categorical. CSS was entered in the model both as categorical and continuous. The ability of CSS to predict short-term outcomes was examined by the receiver- operating characteristic (ROC) curve and their respective areas under the curve, in which sensitivity is plotted as a function of 1-specificity. The area under the curve (AUC) above 0.7 was considered to be useful, while an AUC between 0.8 and 0.9 indicated good diagnostic accuracy.

RESULTS

Out of the 192 patients (114 men and 78 women, mean [SE] age 57.5 [1.11] year), 36 were ICU admitted (18.8%) and unfortunately, 10 (5.2%) died. The incidence of admission to ICU was 22.8% in men and 14.1% in women. Patients with good prognosis had a mean (SE) age of 54.7 (1.28) years, while ICU admitted and deceased patients had mean (SE) age of 68.5 (2.19) and 74.0 (3.44) years, respectively. One patient died before ICU admission. **[Table 1](#page-4-0)** shows the differences in the distribution of age, age-adjusted mean CSS, and clinical findings among patients who were discharged without ICU care, and those who received ICU care or died. Those who received ICU care or died during the hospitalization period were older and had higher age-adjusted total CSS, right upper, middle, lower, and left upper and lower lobe CSS, and lower O₂ saturation than those who were discharged without ICU care (P <0.001). The mean (SE) CSS was 9.7 (0.45) in the good prognosis group and 14.4 (0.90) in the poor prognosis group. The difference was statistically significant (*P* <0.001). 88 (56.8%) men were in the good prognosis group and 26 (70.3%) men in the poor prognosis group (*P* <0.05). The participants of each group were classified into mild and severe pneumonia subgroups by means of admission time symptom severity. As expected, those in the poor prognosis group had more severe pneumonia than participants with a good prognosis (*P* <0.05). The presence of hypertension as the main co-morbidity affecting severity and prognosis of disease was

Table 1. Age, Age-adjusted means (SE) and proportions of selected characteristics between 37 patients with COVID-19 pneumonia who admitted to ICU or died and 155 who did not admit to ICU and discharge alive

Age-adjusted means were calculated using general linear models. Patients with a good prognosis were discharged without ICU care and those who received ICU care or died during hospitalization period considered as poor prognosis.

^aP <0.001, ^bP <0.01, ^cP <0.05.

SE, standard error; COVID-19, coronavirus disease 2019; ICU, intensive care unit; CI, confidence interval.

compared between groups and no significant difference was detected between the good prognosis and poor prognosis groups (*P* >0.05). Other co-morbidities also compared between the two groups and were not statistically different, except cardiovascular disease, which was higher in the ICU admitted group (P <0.01).

1. Chest CT findings

Chest CT findings are illustrated in **[Table 2](#page-4-1)**. GGO and consolidation was the most common finding in both groups and the second most common finding was pure GGO. The GGO

Patients with a good prognosis were discharged without ICU care and those who received ICU care or died during hospitalization period considered as poor prognosis.

a *P* <0.05, b *P* <0.001.

CT, computed tomography; COVID-19, coronavirus disease 2019; ICU; intensive care unit; GGO, ground-glass opacities; CI, confidence interval.

rate was higher in the ICU care and consolidation was higher in those with good prognosis. Parenchymal abnormalities were distributed bilaterally in 166 patients (86.4%) (113 patients (72.9%) in the good prognosis group and 36 patients (97.3%) in the ICU care group), whereas unilateral involvement was seen in 43 patients (22.3%) (42 patients (27.1%) in good prognosis group and one patients (2.7%) in ICU care group. The lower zones (50.6%, 86 patients) were the most frequently involved sites in both groups. In the transverse plane, the lung abnormalities mostly showed peripheral (62.0%, 106 patients) involvement in both groups. No significant difference was found in the respiratory rate between the two groups.

2. ROC curve analysis

The ROC curves for predicting poor prognosis for total CSS, right upper lobe, right middle lobe, right lower lobe, left upper lobe, and left lower lobe CSS in terms of disease severity are shown in **[Figure 1](#page-5-0)**. The areas under the ROC curves were 0.764 (95% confidence interval [CI]: 0.682, 0.847) for total CSS, 0.721 (95% CI: 0.629, 0.814) for the right upper lobe, 0.596 (95% CI: 0.483, 0.709) for the right middle lobe, 0.730 (95% CI: 0.642, 0.818) for the right lower lobe, 0.726 (95% CI: 0.634, 0.818) for the left upper lobe, and 0.776 (95% CI: 0.691, 0.860) for the left lower lobe CSS indicating a useful discrimination for patients with higher risk of ICU care and mortality. All CSS subgroups were significant predictors of future risk of ICU admission and mortality (*P* <0.001). Total CSS had areas slightly but not significantly larger than that of subgroup CSSs. However, in these patients with COVID-19 pneumonia, the subgroup CSS was similar to predict future risk of ICU admission. The optimal total CSS threshold for identifying poor prognosis was 12.5, with 66.7% sensitivity and 73.0% specificity.

All six subgroup CSSs were highly correlated with each other and the strongest Pearson correlation coefficients were found between total CSS and left lower lobe CSS and the weakest ones were between the right middle lobe and left lower lobe CSS (**[Table 3](#page-6-0)**).

3. Logistic regression analysis

To determine the independent associations of poor prognosis (short-term outcomes) a forward stepwise binary logistic regression was performed to test nine variables: age,

Figure 1. Receiver operating characteristic curves for total severity score, the right upper lobe (RUL), right middle lobe (RML), right lower lobe (RLL), left upper lobe (LUL) and left lower lobe (LLL) severity score for predicting ICU admission or death in patients with COVID-19 pneumonia. The estimates of the area under the ROC curves and their 95% CIs are shown.

COVID-19, coronavirus disease 2019; ROC, receiver-operating characteristic; CI, confidence interval.

a *P* <0.001.

CSS, computed tomography CT severity score.

gender, hypertension, respiratory rate, $O₂$ saturation, diabetes, chronic respiratory disease, cardiovascular disease, and chronic kidney disease. **[Table 4](#page-6-1)** shows the results of the ageadjusted and multivariate analysis. Older patients were significantly more frequent in the poor prognosis group $(P<0.001)$. Of radiologic findings, in the age-adjusted model, CSS ≥ 12.5 (OR [95% CI] 4.49 [1.96, 10.29], *P* <0.001) could predict poor prognosis. All variables with a *P* <0.1 in the age-adjusted analysis were entered into a multivariate model to independently predict outcome measures and measure their association. Patients with poor prognosis were more likely than those of good prognosis to be older (OR [95% CI] 1.04 [1.01, 1.06], per year increase, *P* <0.01), be men (OR [95% CI] 2.16 [1.01, 4.66], *P* <0.05), have lower O2 saturation (OR [95% CI] 0.94 [0.89, 0.99], *P* <0.05) and to have higher total CSS (OR [95% CI] 3.93 [1.66, 9.29], *P* <0.001). Total CSS ≥12.5 was a stronger odds ratio to predict poor prognosis. When in multivariate analysis CSS considered as continues variable the association remained statistically significant (OR [95% CI] 1.24 [1.05, 1.46], *P* <0.05). Age-adjusted CSS was inversely correlated with O₂ saturation (r = −0.408, *P* <0.001) but no correlation with respiratory rate $(r = 0.115, P > 0.05)$.

^aOdds ratio (with 95% CI) calculated using binary logistic regression.

^bP <0.05, ^cP <0.01, ^dP <0.001.

ICU; intensive care unit; CI, confidence interval; CT, computed tomography.

DISCUSSION

Hospitalized patients with COVID-19 may eventually need admission to ICU. This study showed the ability of CSS to predict ICU admission and mortality in 192 hospitalized patients with COVID-19 pneumonia, RT-PCR positive, and typical CT imaging findings, further emphasizing the utility of CSS in predicting adverse outcomes. A CSS was equal or greater than 12.5 had a sensitivity of 66.7% and specificity of 73.0% for ICU care and mortality. CSS ≥12.5 in patients with COVID-19 pneumonia predicts admission to ICU with an OR (95% CI) of 3.93 (1.66, 9.29). Age, gender, and lower $O₂$ saturation are weaker ICU admission risk predictor than CSS. Similar to our findings, Khosravi et al. [\[18\]](#page-9-12) and Abbasi B et al. [[19](#page-9-13)] have shown that CSS was well associated with ICU admission, intubation, and mortality. Yang et al. [\[20](#page-9-14)] also designated a similar study with 102 patients using different CT-scoring methods that also giving proof for quantitative CT evaluation as an accurate predictive scale of clinical severity. A study of chest CT findings in relation to COVID-19 clinical conditions by Zhao et al. [\[9](#page-9-15)] was done using another method of CT scoring, which demonstrated a significantly higher extent of pulmonary parenchymal involvement in severe and fatal types of the disease than those with mild and common types.

CSS was significantly higher in patients with severe symptoms than those who presented with mild symptoms at the time of admission. Such a quantitative evaluation has been applied in relation to clinical classification by Li et al. [[21\]](#page-9-16), and the same results have yielded.

Consistent with prior studies [[22\]](#page-10-0), the present study found similarly increasing the ICU admission and mortality with increasing age, decreasing $O₂$ saturation, and in men in the patients with COVID-19 pneumonia.

Similar to previous studies [[19](#page-9-13), [23-](#page-10-1)[25\]](#page-10-2), most of our patients had bilateral pulmonary involvement, with GGO, consolidation, or both being the most frequent abnormality. The most frequently involved anatomical location in this study were lower zones. The distribution of the lesions was not shown to be associated with a poor prognosis.

Finally, to compare the performance of CT findings to diagnose the short-term outcome with clinical information at admissions, such as $O₂$ saturation and respiratory rate and co-morbidities several logistics regression models were implemented, which showed the superiority of CSS over other clinical information and co-morbidities.

Our findings highlight the substantial role of non-contrast chest CT imaging and CSS in the presence of typical features for COVID-19 pneumonia as a reliable predictor of clinical severity and patient's outcome. Our results suggested that more emphasis should be placed on the value of serial chest CT scans in early diagnosis and evaluation of disease progression. Patients with higher CSS may benefit from early ICU admission and can help inpatient discharging in the emergency departments, especially in settings with limited ICU beds.

We used a semi-quantitative scoring method previously used by others [[10,](#page-9-4) [15,](#page-9-9) [18,](#page-9-12) [19](#page-9-13)] to score the degree of involvement. However, there is little data available on the association of ICU care and mortality outcomes (which have higher cost and burden for the healthcare system) with initial CT findings in COVID-19 pneumonia. Other scoring systems have also been proposed to predict the prognosis of patients with COVID-19 pneumonia. Pan et al. proposed a scoring system based on the number of lobes and percentages of involvement in

each lobe [\[26](#page-10-3)]. Colombi et al. [\[27](#page-10-4)] used a software-based calculation of aerated lung volume to predict ICU admission or death. Ufuk et al. [\[28](#page-10-5)] used the area of pectoralis major muscles in CT scans to predict the severity of the COVID-19 pneumonia outcomes. Yuan et al. [\[29\]](#page-10-6) have proposed a scoring system based on the type of abnormality and the area involved by each type with reliable results in predicting mortality. However, the semi-quantitative scoring method used in this study can be easily implemented in clinical practice.

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Our study has some limitations. This study was a single-center study with a relatively small number of cases and a small number of patients with severe symptoms. Therefore, other studies including multicenter prospective studies with larger populations with a higher number of individuals with severe symptoms, employing consecutive RT-PCR assays and follow-up genomic kinetic assessment will be more generalizable and add value to our achievements in a more comprehensive study. Because there was no information about the body weight and height of patients we cannot evaluate whether the increased overweight / obesity risk was mediated by ICU care and mortality. Due to RT-PCR kit shortages in the initial days of the COVID-19 epidemic in Iran, RT-PCR testing was not repeated in RT-PCR negative patients and we excluded these patients from the study. Also, nasopharyngeal sampling errors due to the anxiety and overly protective measures in the first few weeks had increased the rate of false-negative RT-PCR results. While the design of the study may limit its generalizability to other populations, these findings are meaningful in that they are specifically applicable to urban Iranian patients with COVID-19 pneumonia.

In summary, our findings revealed that CT images and CSS can predict ICU admission and mortality in patients with COVID-19 pneumonia. Clinicians and radiologists can use CSS as a measure of disease severity and an indicator of poor prognosis, including the need for mechanical ventilation. Also, our findings showed the superiority of CT findings over other clinical information and co-morbidities in predicting the short-term outcome. Further efforts are needed to predict the value and reliability of CSS using large prospective studies.

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