

Introduction of a Radiologic Severity Index for the 2019 Novel Corona Virus (COVID-19)

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Abstract

Background: Given the limited number of beds in intensive care units, establishing a system that can predict the outcome in COVID19 positive patients based on imaging plays an important role in using resources efficiently. Therefore this study was conducted to design an optimal scoring system related to the severity of COVID19 cases for distinguishing severe from non-severe patients.

Materials and Methods: In this cross-sectional retrospective study, 82 patients with a definite diagnosis of COVID-19 infection, who had at least one chest CT scan in hospital course were enrolled.

To assess the severity of pulmonary parenchymal involvement, we semi-quantitatively evaluated the extent and nature of abnormalities. The area of lung involvement was scored in three levels based on a 0-4 grading scale. Also, we established a 4-point scoring system for defining the nature of lung abnormalities. The two scores were multiplied by each other. A final radiologic severity score was determined after adding together the scores of all levels.

Result: Of all cases, fifty-three (64.6%) were male with an average age of age 53.75. Among the patients in our study, 7 (8.5%) had severe disease and the mortality rate was 7.2%. The mean (\pm standard deviation) of the radiologic severity score was 34.3(\pm 18.4) in the severe group and 11.3(\pm 11.4) in the non-sever group. (P-value <0.05). Also, we found a significant reverse relationship between our severity score and O₂ saturation (P-value <0.05).

Conclusion: The radiologic severity score demonstrated a significant correlation with the patients' mortality and severity of illness in COVID-19 patients.

Introduction

On 11th March 2020, the World Health Organization (WHO) announced Corona-virus disease (COVID-19) as a pandemic (1). Due to the fast global spread, until April 2nd, 2020, COVID-19 is affecting 203 countries and territories all over the world with over 944,000 confirmed cases and over 47,000 deaths (2).

Our knowledge about COVID-19 is limited. Chen. et al reported an incubation period of up to 14 days (3). The clinical manifestations vary from mild symptoms including fever, cough, sore throat and myalgia to more severe presentations such as pulmonary edema, acute respiratory distress syndrome (ARDS) and multiple organ failure (4-7).

COVID-19 has become a huge burden and a global health emergency with over 20% critical patients and mortality around 3% (8). Given the limited number of beds in intensive care units (9, 10), establishing a system that can predict the outcome in COVID19 positive patients based on para clinical data can play an important role in using resources efficiently.

Like previous corona-viruses, including Middle East respiratory syndrome coronavirus (MERS) in 2012 and severe acute respiratory syndrome caused by corona-virus (SARS-COV) in 2002, COVID-19 can also

lead to ARDS as a main cause of death(11, 12). Due to the short interval between onset of symptoms and the development of ARDS in COVID-19 pneumonia, early diagnosis is essential for better management (13).

Chest CT plays a key role in the early diagnosis of infected patients. Typical findings including ground-glass opacity, consolidation, and linear opacities are the most common findings in chest CT of COVID-19 positive patients (14, 15). Also, one of the main methods for distinguishing severe and critical cases from milder cases is based upon the evaluation of disease progression by chest [computed tomography](#) (CT) in patients.

This study aims to compare the clinical condition and pulmonary involvement in CT scan of confirmed COVID-19 patients to develop a scoring system related to the severity of this disease for distinguishing severe from non-severe patients.

Method

Study design and participants

In this cross-sectional retrospective study, patients with a definite diagnosis of COVID-19 infection were recruited at the two main referral hospitals for COVID-19 from February through March 2020.

Inclusion criteria were as follows: A) having a proper history; B) Positive real-time PCR of SARS-CoV-2; C) having at least one non-contrast chest CT scan

We studied the demographic, clinical, laboratory and radiologic findings of the patients. The data from the patients were kept confidential through codes.

Computerized Tomography Scans

Non-contrast CT scan was performed in a supine position during full inspiration. Scanning was extending from thoracic inlet to the upper abdomen. The technical parameter included: 8 slice scanner (GE Medical Systems, Milwaukee, WI, and USA), 120Kvp, thickness of 1.25-2mm, 1.25 mm interval.

Imaging evaluation

The primary chest CT scan was reviewed independently by four radiologists', three of whom (SS, PI, SJ) were board-certified in general diagnostic radiology with approximately eight to fifteen years of practice experience and one in training (YE with four years of practice experience). The radiologists were blind to the primary impression, clinical symptoms, and the patient's outcome and undertook the classification and categorization of scans. The CT findings were arbitrarily considered to be one of these four categories as ground-glass opacity (GGO), consolidation, crazy paving, and nodular opacities.

The definitions of these findings were determined based on the Fleischer Society guidelines (16). Consolidation and GGO were defined as hazy areas of increased attenuation with and without

obscuration of the underlying vasculature, respectively. GGO with intra-lobular lines were defined as crazy paving and nodular opacities were identified when focal round opacities either solid or GGOs with a diameter less than 3 cm.

To assess the severity of pulmonary parenchymal involvement, we quantified the extent and nature of abnormalities. For this purpose, the area of lung involvement was scored in the axial CT images based on the method described previously by Ooi et al in 2004 for the severe acute respiratory syndrome (SARS) (17). In this method each lung was assessed in three levels; upper (above the carina), middle (below the carina up to the upper limit of the inferior pulmonary vein), and lower (below the inferior pulmonary vein). Also, the right and left lung were evaluated separately and summed up to conclude the final score of each level.

The percentage of lung involvement in each level was evaluated independently and categorized as follows: 0 as normal, 1 as < 25% abnormality, 2 as 25–49% abnormality, 3 as 50–74% abnormality, and 4 as \geq 75% of the pulmonary cross-section CT scan (Table.1).

The nature of abnormalities can also determine the severity of lung involvement (18, 19). In this regard, we arbitrarily established a 4-point scoring system for defining the pattern of lung abnormalities in CT scans that summarized in Table 2.

Then, the two scores (extent and nature of abnormality) were multiplied by each other (Figure1). After adding together the scores of all 6 levels (3 levels in each side), a final radiologic severity score (RSS) for parenchymal involvement with values ranging from 0 to 96 was determined for each patient (Figure 2-4).

Eventually, the final score was determined by consensus between all four radiologists.

Eventually, this severity score was compared between severe and non-severe patients according to American Thoracic Society guidelines for community-acquired pneumonia (20).

Statistical analysis

The collected data was summarized as means (\pm SD), and categorical data are presented as the count (percentage). Unpaired Student's t-test, chi-square test, or Fisher's exact test was used to compare the RSS of COVID-19 patients as appropriate. A P. value of less than 0.05 considered indicating statistical significance. All the statistical analyses were performed by the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 26.0.

Result

During the study period, 113 patients with confirmed COVID-19 PCR were registered at our clinical sites, which 82 cases with at least one chest CT scan were enrolled for the purpose of our study. Among the selected patients, fifty-three (64.6%) were male and twenty-nine (35.4%) were female. The mean \pm SD of

age was 53.75 ± 1.56 [Min = 20, Max = 89]. Only 20% of cases reported a clear history of contact with infected COVID-19 cases.

Seven patients were admitted in ICU with a mean age of 59.29 ± 8.5 years and 6 patients died during hospitalization with a mean age of 57 ± 1.9 years. Among the patients in our study, 7 (8.5%) had severe disease and the mortality rate was 7.2% (6 out of 82 patients). There was no significant difference between the severe and non-severe groups with respect to the patients' age. (P.value = 0.77)

Underlying comorbidity diseases were collected from the patients' history, including hypertension, cardiovascular disease, diabetes, and chronic obstructive pulmonary disease. Based on our results 36% of the non-severe patients and 57.1% of the severe patients had underlying comorbidity diseases, however, no significant differences were observed between the two groups (P=0.417).

The mean interval between onset of symptoms and first chest CT scans was 6.7 days (range: 1-22 days). Among the patients, six (7.3%) had a normal chest CT scan. The predominant CT findings were GGO (94%), consolidation (58.5%) and crazy paving (48.5%). Also, the right lower lobe (89.5%) and left lower lobe (86.5%) were the most involved part.

The mean (\pm standard deviation) of RSS was $34.3 (\pm 18.4)$ in the severe group and $11.3 (\pm 11.4)$ in the non-severe group (P-value <0.05). There was also a significant correlation between RSS of the first CT scan and both the clinically severe group (<0.05, Z=-3.5) and the mortality group (<0.05, Z=-3.5).

Receiver operating characteristic (ROC) analysis was used to assess the relation between RSS and the patients' disease severity and mortality. The area under the curve stated 0.900 (95% confidence interval: 0.819, 0.983) for the prediction of severe cases and 0.784 (interval: 0.527, 1.000) for prediction of death (Figure 5).

Also, considering area under ROC curve, we suggested 13.5 as optimal cut-point in radiologic severity score with specificity of 72% and sensitivity of 100% for the prediction of severe group (95% confidence interval= 0.819-0.983;P-value =0.00) and 30.5 with specificity of 93% and sensitivity of 66% for the prediction of mortality group (95% confidence interval= 0.527-1.000; P-value: 0.021).

Statistically, we found a significant reverse relationship between our severity score and O_2 saturation (O_2 sat), which was measured by pulse oximeter during the first examination (P-value <0.05) (Figure 6). However, no significant relation was found between the RSS and CRP or lymphocyte count (Table 3).

Discussion

A variety of clinical manifestations can be caused by coronaviruses family ranging from asymptomatic to severe illness. Previously, SARS and MERS which come from the same family as COVID-19 had caused epidemics throughout several countries in the last decades. However, the novel corona 2019 virus has

caused pandemic unlike others and infected more people due to its high contagious characteristics (13, 14, 21-23).

Given the highly contagious nature of the disease and limited resources, COVID19 infection poses a huge impact on the health care systems. As a result, early diagnosis is critical for disease treatment and control.

In the current study, the mean age of patients was 53.7 years and the majority of them were males (64%). Among them, 8.5% were severely ill and the mortality rate among hospitalized patients was 7.3%. Among the initial CT scan findings, the most frequent was GGO that is consistent with other studies (24, 25).

Our RSS demonstrated a significant correlation with the patients' mortality and severity of illness. Consistent with prior studies, we suggest that CT could be used to evaluate the severity and prognosis of the disease (26). We also achieved a cut-off point of 30.5 with sensitivity and specificity of 66% and 93% respectively for mortality and also a cut-off of 13.5 with sensitivity and specificity 100% and 72% respectively for the severity of illness. However, due to the small sample size of our study and the skepticism of the outcome of the patients, further studies on larger samples are needed for application in clinical practice. One of the advantages of our index is in the consideration of both the nature and extent of lung involvement in a more feasible manner.

In addition, we found a significant reverse relation between our score and O₂- saturation that can be a helpful point in practice.

Li et al. (27) designed a scoring system that ranged from 0 to 25 based on the percentage of each lung lobe involvement and reported the sensitivity and specificity of 80.0% and 82.8% respectively based on a cut-off of 7. Similarly, Bernheim et al. (28) and Pan et al. (29) also reported a scoring system in their studies which included only the extension of abnormality in each lung lobes to assess changes in pulmonary involvement during the course of COVID-19 pneumonia, however, the correlation between score and clinical condition was not evaluated.

Another study used the mean pulmonary inflammation index (PII) to assess the severity of involvement, focusing on the distribution and size of abnormality. They reported a significant relationship between PII and clinical symptoms with lymphocyte counts and CRP (26).

Yuan et al. (30) described the extension of abnormality using a modified version of Feng et al. (31) that was published in 2014 for avian influenza H7N9 pneumonia. They used a 3-point scale: 3 as consolidation, 2 as ground-glass attenuation, and 1 as normal attenuation. The results showed that the median CT score of the mortality group was higher compared to their survival group. However, assigned cut-off points of their study achieved a higher sensitivity but lower specificity (85.6% and 84.5% versus 66% and 93%, respectively) for evaluating the patients' mortality. As mentioned earlier, in many cases consolidation and GGO cannot be easily differentiated which we resolved this issue with an intermediate score in our indexing score.

Yang et al. also suggested a 3-point scoring scale but in 20 regions of the lung achieved a sensitivity and specificity of 83.3% and 94% in predicting the severity of the illness (32).

There were some limitations in our study. While highly accurate in our study population, our cut-offs were achieved based on a small sample size, with a smaller number of severe/critical patients. For more reliable accurate cut points, further studies with larger sample sizes are warranted. Also, the fact that most of our patients were already hospitalized at the time of the CT scan makes the results less applicable to the unadmitted COVID-19 patients. In the end, none of the patients had a lung biopsy or autopsy to reflect the histopathological changes.

Conclusion

This study provided a straightforward semi-quantitative method for evaluating and managing COVID-19 patients based on the initial chest CT scan. Such approaches could have importance in triage and assessing the patients in high-volume centers, especially during outbreaks when resources and other diagnostic tests such as PCR are limited. Although a significant correlation with the prognosis and severity of the disease was achieved, further studies in higher volume settings and comparing with clinical features are needed for applying this index in clinical practice.

Declarations

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none to declare

Statement of data access and integrity

The authors declare that they had full access to all of the data in this study and the authors take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Authors Contribution

Mehrzad Lotfi, and Mohsen Moghadami designed the study. Pouya Iranpour, Yasaman Emami, and Seyed Hamed Jafari reviewed and interpreted the radiological images. Alireza Mirahmadizadeh carried out the statistical analysis. Keivan Ranjbar, Amirhossein Erfani, Mehrdad Emami, and Reza Shahriarirad carried out the manuscript preparation. All authors proofread the final version of the manuscript.

Ethical statement

This study was conducted with the approval of the Shiraz University of Medical Sciences Review Board and informed consent was collected from the patients in our study.

Conflict of interest

The authors declare no conflict of interest

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Tables

Table 1. Scoring system based on the extent of lung involvement in each region of the patients CT-scan

percentage of lung involvement	Score
0	0
1-24%	1
25-49%	2
50-74%	3
≥75%	4

Table 2. Scoring system based on the nature of involvement in each region of the patients CT-scan

Pattern of involvement in each level	Score
Normal lung parenchyma	1
At least 75% GGO	2
Combination of GGO and consolidation ;on a condition that each of them has less than 75% involvement	3
At least 75% consolidation	4

Table 3. Pearson Correlation between radiological severity score and CRP, O₂ saturation (O₂_Sat) and lymphocyte count.

* indicates P.value

Severity score	1			
CRP	0.078	1		
Lymph count	-0.174	-0.07	1	
O ₂ _Sat	-0.414	-0.45	-0.46	1
	<0.05*	0.65*	0.65*	
	Severity score	CRP	Lymph count	O ₂ _Sat

Figures

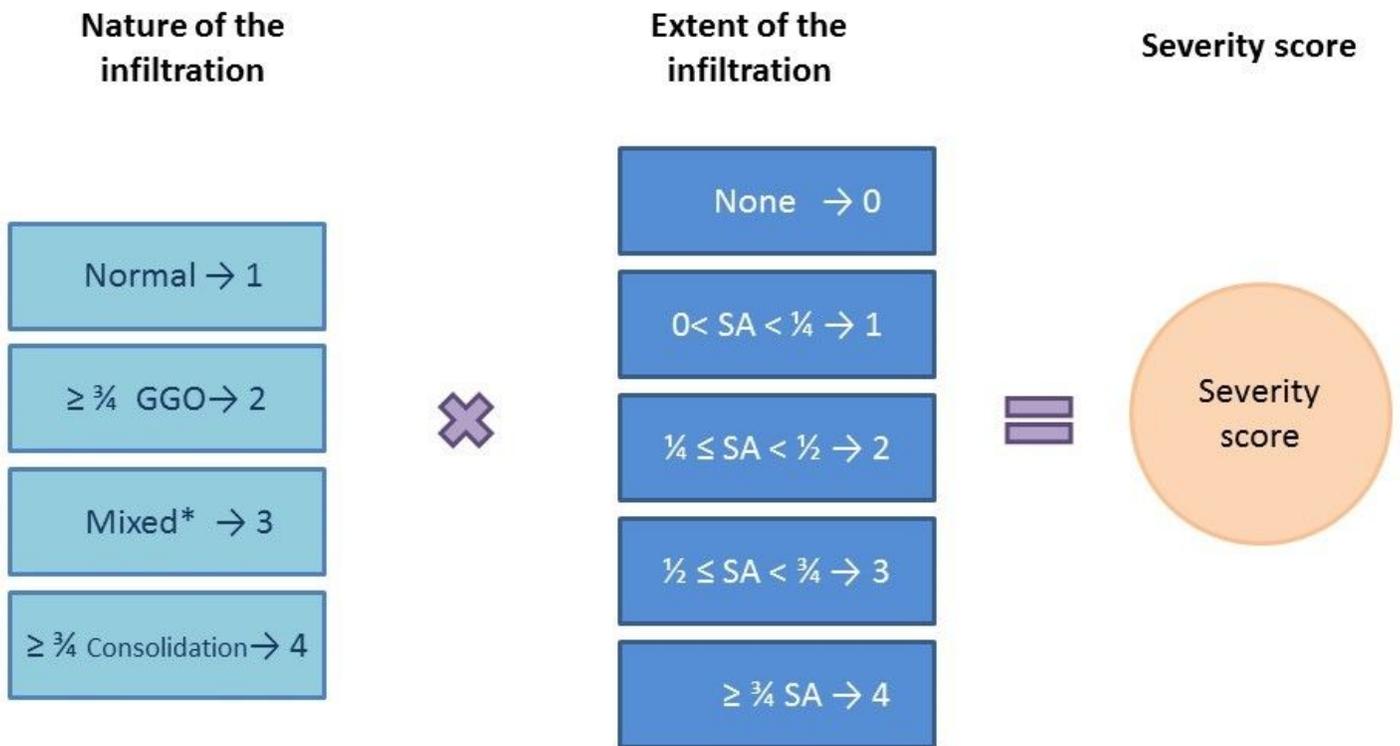


Figure 1

Schematic image for calculating the radiological severity score in each region; GGO: Ground Glass Opacity; SA: Segmental Area * Combination of GGO and consolidation; considering that each type has less than 75% involvement

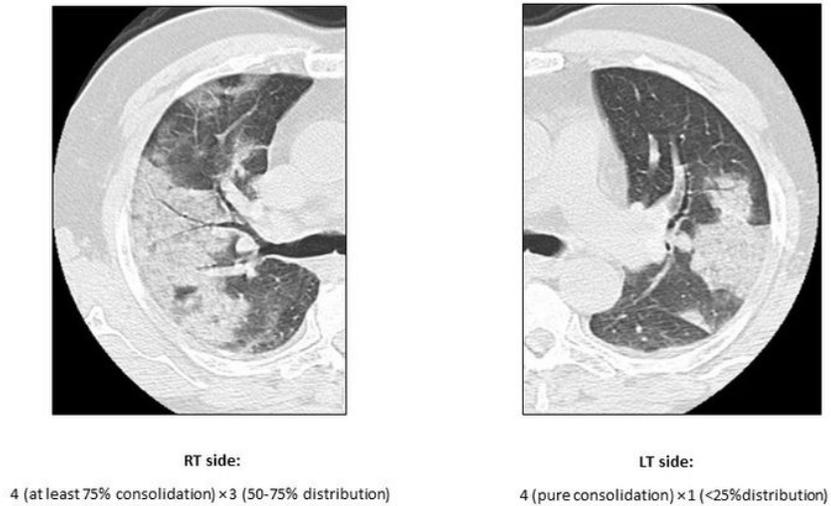


Figure 2

A sample scoring on CT images of a 61 years old man at the level of carina (Middle level): The combination of right and left score makes a final score of each level; which is 16 for this level

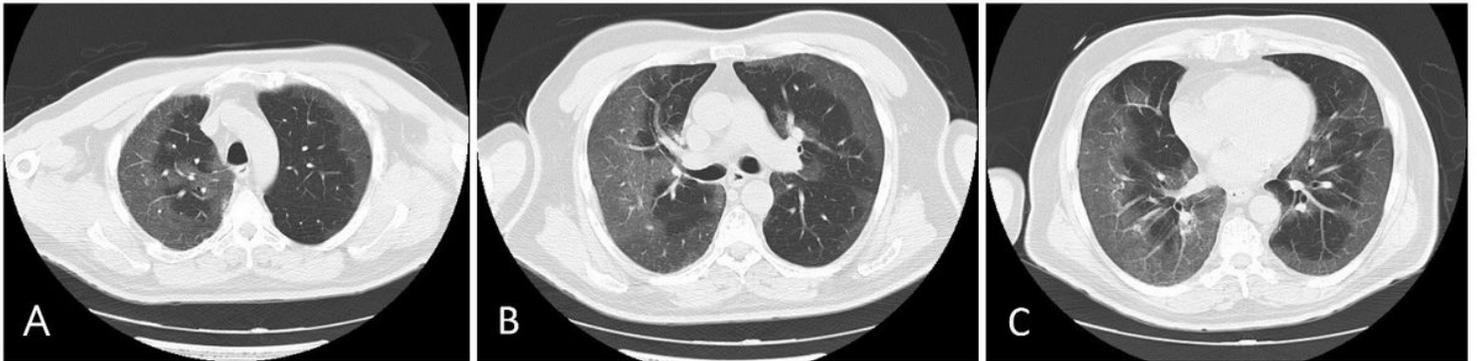


Figure 3

A sample scoring on CT images of a 64 years old man with a total severity score of 28. It was calculated as: for upper level (A), right side(6): 2 [pure GGO] × 3 [50–75% distribution] + left side(2): 2 [pure GGO] × 1 [< 25% distribution]; for middle level (B), right side(4): 2[pure GGO] × 2 [25– 50% distribution] + left side(6): 2 [pure GGO] × 3 [50–75% distribution]; and for lower level (C), right side(6): 2 [pure GGO] × 3 [50-75% distribution] + left side(4): 2 [pure GGO] × 2 [25-50% distribution].



Figure 4

A sample scoring on CT images of a 63 years old man with a total severity score of 38. It was calculated as: for upper level (A), right side(6):3 [Mixed consolidation and GGO] × 2 [25–50% distribution] + left side(4): 2 [at least 75% GGO] × 2 [25%-50% distribution]; for middle level (B), right side(6): 3 [Mixed consolidation and GGO] × 2 [25–50% distribution]+ left side(6): 2 [at least 75% GGO] × 3 [50%-75% distribution]; and for lower level (C),right side(8): 4 [at least 75% consolidation] × 2 [25-50% distribution] + left side(8): 4 [at least 75% consolidation] × 2 [25-50% distribution].

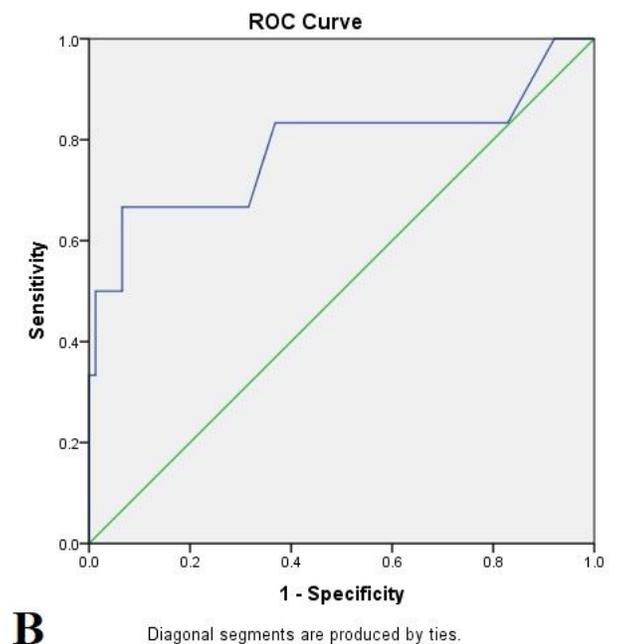
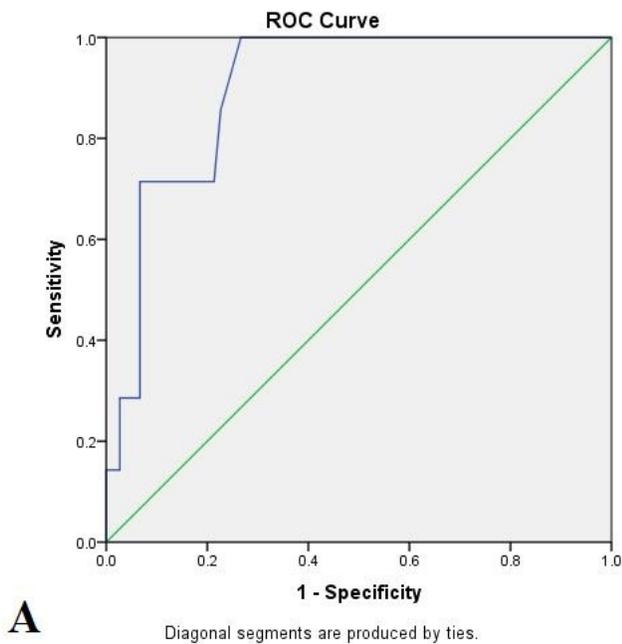


Figure 5

ROC analysis of the CT score for prediction of (A) severe group; N=82, AUC 0.900 and (B) mortality, N= 82; AUC = 0.784

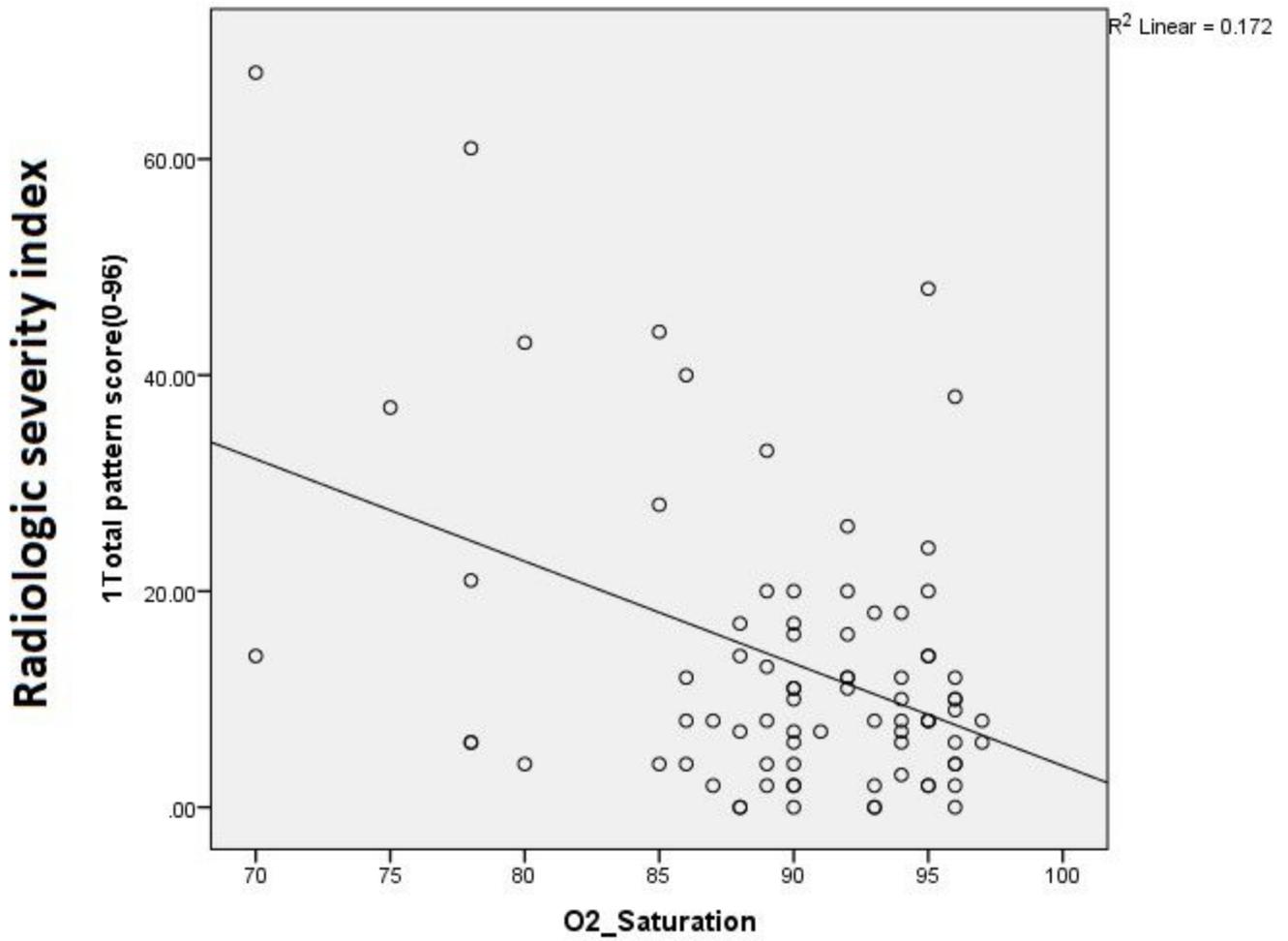


Figure 6

Scatter chart based on radiology severity index and O2 saturation, demonstrating a reverse relation, R2=0.172