Maximum chest CT score predicts progression to severe illness in patients with COVID-19: a retrospective study from Wuhan, China

Jianwei Xiao
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Xiang Li
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Yuanliang Xie
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Zengfa Huang
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Yi Ding
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Shengchao Zhao
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Pei Yang
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Dan Du
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Bin Liu
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
Xiang Wang (✉ wangxiangwhch1971@163.com)
The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology
https://orcid.org/0000-0002-0105-9755

Research article

Keywords: Chest CT, COVID-19, COPD, ROC, CT scores, multivariate regression

Posted Date: August 26th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-51054/v1

Version of Record: A version of this preprint was published on December 11th, 2020. See the published version at https://doi.org/10.1186/s12879-020-05683-3.

Abstract

Background: We investigated the clinical course and imaging findings of hospitalized patients who were initially diagnosed with moderate COVID-19 symptoms to identify risk factors associated with progression to severe/critical symptoms.

Methods: This study was a retrospective single-center study at The Central Hospital of Wuhan. 243 patients with confirmed COVID19 pneumonia were enrolled in the analysis, of which 40 patients progressed from moderate to severe/critical symptoms during follow up. Demographic, clinical, laboratory and radiological data were extracted from electronic medical records and compared between moderate and severe/critical symptom types. Univariable and multivariable logistic regressions were used to identify the risk factors associated with symptom progression.

Results: Patients with severe/critical symptoms were older (p□0.001) and more often male (p=0.046). We found that the combination of chronic obstructive pulmonary disease and high maximum CT scores was associated with disease progression. Maximum CT scores (≥11) had the greatest predictive value for disease progression. The area under the receiver operating characteristic curve (ROC) was 0.861 (*95% CI*: 0.811-0.902).

Conclusions: Maximum CT scores and COPD are associated with patient deterioration. Maximum CT scores (≥11) are associated with severe illness.

Background

Worldwide there have been 234,073 confirmed cases and 9,840 deaths resulting from novel coronavirus 2019 (COVID-19) infection as of March 19, 2020. The rate of overall case-fatality was about 2.3% across China. Although few deaths were found in mild COVID-19 patients, the rate of case-fatality was obviously elevated among critical ill patients. Nevertheless, what factors influence the prognosis of COVID-19 patients has not been clearly clarified [1, 2].

The onset of COVID-19 is associated with symptoms such as fever, cough, and myalgia. The case definition adopted in China and elsewhere includes further stratification of cases as mild, moderate, and severe/critical [3]. More than 80% of the laboratory confirmed cases in China (including both non-pneumonia and pneumonia cases) were mild-to-moderate types [4]. A fifth of these cases progressed to a severe or critical stage, with the highest case fatality rate of 4.47% in Wuhan before March 2020 [5]. Most previous studies have only focused on the general epidemiological findings, clinical characteristics, and outcomes of patients with COVID-19 [2, 6, 7]. However, few studies have investigated the clinical findings in patients who progress from moderate to severe/critical type symptoms.

In this study, we did a comprehensive analysis of the clinical course and imaging findings of 243 hospitalized COVID-19 patients who initially presented with moderate type symptoms. These patients were admitted to the isolation ward of the Central Hospital of Wuhan, which is very close to the seafood

market and one of the first hospitals in Wuhan to admit COVID-19 patients. We aimed to identify risk factors associated with progression from moderate to severe/critical type symptoms.

Methods

Study design and participants

This was a retrospective single-center study at The Central Hospital of Wuhan. The study was approved by The Central Hospital of Wuhan Ethics Committee (No.2020421), and written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

Patients who were diagnosed with COVID-19 based on WHO interim guidelines were enrolled consecutively from December 25 to February 16, 2020 [8]. Based on the new coronavirus pneumonia diagnosis and treatment protocols (version 6) developed by the National Health Commission of the People's Republic of China (http://www.nhc.gov.cn/), the clinical classification of COVID-19 is as follows: moderate types include those with fever, respiratory tract involvement, and other symptoms, as well as imaging findings of pneumonia; severe types meet any of the following: (1) respiratory distress with a respiratory rate ≥ 30 beats/min; (2) oxygen saturation ≤ 93% at rest; and (3), arterial blood oxygen partial pressure (PaO_2)/oxygen concentration (FiO_2) ≤ 300 mm Hg (1 mm Hg = 0.133 kPa); critical types meet any of the following conditions: (1) respiratory failure requiring mechanical ventilation; (2) occurrence of shock; (3) ICU admission for combined organ failure.

Data Collection

Epidemiological, clinical, laboratory, radiological characteristics, and outcome data were extracted from electronic medical records. The data were reviewed by two physicians, and a third physician adjudicated the difference in interpretation between the two primary researchers. Fever was defined as axillary temperature higher than 37.3 °C. Epidemiological, clinical, and laboratory data were defined as the results of the first consultation or examination in the electronic medical records. The initial chest CT was defined as the first chest CT examination of admission.

CT Image Acquisition

Chest CT scans were performed with the patient in a supine position and using a single inspiratory phase on one of the four CT systems (Bright Speed Elite, GE, America; Philips Ingenuity Core128, Philips Medical Systems, Best, the Netherlands; uCT 760, United Imaging, China; SOMATOM Definition AS, Siemens Healthineers, Germany). The following main parameters were used: tube voltage = 120 kVp; automatic tube current modulation (20–130 mAs); matrix = 512 × 512; FOV = 350 mm × 350 mm – 370 mm × 370 mm; pitch = 0.75–1.25 mm; slice thickness = 1-1.5 mm. The reconstructed images were automatically sent to the corresponding post-processing workstation and picture archiving and communication systems (PACS) for multiplanar reconstruction post-processing.

Chest CT Evaluation

All chest CT images were independently analyzed, and the features were scored by a senior thoracic radiologist with more than 20 years of experience who was blinded to clinical and laboratory findings. A previous semi-quantitative scoring system was performed to estimate the pulmonary involvement of lesions on the basis of the area involved [9]. Each of the 5 lung lobes was visually scored from 0 to 5, as follows: 0, no involvement; 1, < 5% area involvement; 2, 5%-25% area involvement; 3, 26%-49% area involvement; 4, 50%-75% area involvement; and 5, > 75% area involvement. The total CT score was the sum of the scores of the 5 lung lobes (0–25).

Follow-up Chest CTs

After admission, patients were re-examined for chest CT examination. The endpoint of this study was the development of severe/critical illness. We excluded patients transferred from other medical institutions and those transferred out from our hospital. We also excluded fatalities. All patients in our study recovered. From the day of illness onset, follow-up chest CTs were performed anytime from day 3 to day 60.

Statistical Analyses

Continuous variables are presented as mean ± SD or median (IQR), depending on the normality of distribution. Categorical variables are presented as frequencies and percentages. Continuous variables were compared between the moderate type group and the severe/critical type group using a two-sample t-test or Mann-Whitney U test. Categorical variables were compared using a chi-square test or Fisher's exact test as appropriate. Univariable and multivariable logistic regression models were used to explore the risk factors associated with severe/critical symptom type progression from moderate symptom types. Using the new coronavirus pneumonia diagnosis protocols as the standard of reference, diagnostic performance with the highest CT score of severe/critical type progression was determined using analyses of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and area under the curve (AUC). 95% confidence intervals (CIs) are also reported. Diagnostic ability was illustrated using a receiver operating characteristic curve (ROC). A two-tailed p 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 18 (SPSS, Inc., Chicago, IL).

Results

A total of 457 adult patients diagnosed with COVID-19 were admitted to our hospital from December 25, 2019 to February 16, 2020. There were 191 patients still hospitalized or not confirmed by SARS-CoV-2 RNA detection or death before our final follow-up, and they were excluded from analysis. We also excluded 7 patients who were diagnosed with severe/critical type symptoms on admission. Sixteen patients were excluded because their medical records were not available. In total, 243 patients with confirmed COVID19 pneumonia were enrolled in the analysis. Forty patients progressed from having moderate symptoms to severe/critical symptoms during follow-up. The mean age of the 243 patients was 47 years, with a range of 20 to 89 years. One hundred thirty-eight (56.8%) were female (Table 1). The

patients with severe/critical symptoms were older (p□0.001) and more likely male (p = 0.046) than patients with moderate type symptoms. The most common symptoms at onset were fever (83.5%) and cough (63.8%), followed by weakness (45.7%) and sputum (28.8%). Chest tightness was more likely to occur in patients with severe/critical symptoms (42.5%) than in patients with moderate type symptoms (p = 0.002). Patients in the severe/critical symptom type group had significantly higher mean levels of D-dimer (2.1 ± 4 vs. 0.8 ± 1.6 mg/L, p□0.001), C-reactive protein (3.6 ± 3.2 vs. 2 ± 3 mg/L, p = 0.038), α-hydroxybutyrate dehydrogenase (247 ± 352 vs. 142 ± 57 U/L, p□0.001), lactate dehydrogenase (251 ± 119 vs. 185 ± 79 U/L, p = 0.002), creatine kinase, (273 ± 636 vs. 120 ± 172 U/L, p□0.001), and creatinine (211 ± 449 vs. 67 ± 43 μmol/L, p□0.001) than patients in the moderate type group. The neutrophil-to-lymphocyte ratio was also significantly higher in the severe/critical type group (NLR, 10.6 ± 7.7 vs 3.7 ± 3.9, p□0.001). Other laboratory findings did not significantly differ between the two groups. In comparison with patients in the moderate type group, patients in the severe/critical type group were more likely to have underlying hypertension (15, 37.5% vs. 30, 14.8%), chronic obstructive pulmonary disease (COPD) (5, 12.5% vs. 5, 2.5%) and chronic kidney disease (6, 15% vs. 4, 2%).

Table 1
Clinical characteristics, laboratory findings and imaging features of 243 COVID-19 patients

	Total (n = 243)	Moderate Type (n = 203)	Severe/Critical Type (n = 40)	P value
Characteristics				
Age, years	47.0 (20–89)	44.7 (20–87)	58.7 (28–89)	0.001
60	175 (72)	154 (75.9)	21 (52.5)	0.003
≥ 60	68 (28)	49 (24.1)	19 (47.5)	
Sex				0.046
Male	105 (43.2)	82 (40.4)	23 (57.5)	
Female	138 (56.8)	121 (59.6)	17 (42.5)	
Symptoms				
Fever	185 (83.5)	158 (77.8)	27 (67.5)	0.161
Cough	155 (63.8)	130 (64)	25 (62.5)	0.853
Sputum	70 (28.8)	56 (27.6)	14 (35)	0.344
Weakness	111 (45.7)	90 (44.3)	21 (54.5)	0.343
Diarrhoea	21 (8.6)	18 (8.9)	3 (7.5)	0.779
Nausea/Vomitting	20 (8.2)	14 (6.9)	6 (15)	0.088
Chest tightness	57 (23.5)	40 (19.7)	17 (42.5)	0.002
Dyspnea	12 (4.9)	9 (4.4)	3 (7.5)	0.413
Myalgia	66 (27.2)	58 (28.6)	8 (20)	0.265

Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.

	Total (n = 243)	Moderate Type (n = 203)	Severe/Critical Type (n = 40)	P value
Chill	41 (16.9)	36 (17.7)	5 (12.5)	0.419
Conjunctival congestion	1 (0.4)	1 (0.5)	0	0.835
Dizziness	45 (18.5)	37 (18.2)	8 (20)	0.792
Laboratory findings				
White blood cell count, × 109/L	5 (2.1)	4.8 (1.9)	5.9 (2.8)	0.006
10	236 (97.1)	199 (98)	37 (92.5)	0.056
≥ 10	7 (2.9	4 (2)	3 (7.5)	
Lymphocyte count, × 109/L	1.2 (0.6)	1.2 (0.6)	0.9 (0.4)	0.07
1	110 (45.3)	87 (42.9)	23 (57.5)	0.089
≥ 1	133 (54.7)	116 (57.1)	17 (42.5)	
Monocyte count, × 109/L	0.4 (0.2)	0.4 (0.2)	0.4 (0.3)	0.02
0.5	187 (77)	158 (77.8)	29 (72.5)	0.464
≥ 0.5	56 (23)	45 (22.2)	11 (27.5)	
Platelet, × 109/L	182 (66)	183 (66)	172 (67)	0.414
100	19 (7.8)	15 (7.4)	4 (10)	0.574
≥ 100	224 (92.2)	188 (92.6)	36 (90)	
Haemoglobin, g/L	133 (26)	133 (28)	131 (19)	0.924
D-dimer, mg/L	1 (2.2)	0.8 (1.6)	2.1 (4)	0.001

Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.

	Total (n = 243)	Moderate Type (n = 203)	Severe/Critical Type (n = 40)	P value
1	199 (81.9)	173 (85.2)	26 (65)	0.002
≥ 1	44 (18.1)	30 (14.8)	14 (35)	
C-reactive protein, mg/L	2.3 (3.1)	2 (3)	3.6 (3.2)	0.038
1	121 (49.8)	107 (52.7)	14 (35)	0.041
≥ 1	122 (50.2)	96 (47.3)	26 (65)	
α-hydroxybutyrate dehydrogenase, U/L	161 (161)	142 (57)	247 (352)	0.001
180	195 (80.2)	173 (85.2)	22 (55)	0.001
≥ 180	48 (19.8)	30 (14.8)	18 (45)	
Lactate dehydrogenase, U/L	197 (91)	185 (79)	251 (119)	0.002
250	199 (81.9)	178 (87.7)	21 (52.5)	0.001
≥ 250	44 (18.1)	25 (12.3)	19 (47.5)	
Creatine kinase, U/L	148 (313)	120 (172)	273 (636)	0.001
190	214 (88.1)	184 (90.6)	30 (75)	0.005
≥ 190	29 (11.9)	19 (9.4)	10 (25)	
Alanine aminotransferase, U/L	30 (45)	30 (48)	31 (26)	0.662
Aspartate aminotransferase, U/L	28 (23)	27 (22)	34 (25)	0.526
γ-glutamyltransferase, U/L	37 (52)	34 (50)	54 (60)	0.07

Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.

	Total (n = 243)	Moderate Type (n = 203)	Severe/Critical Type (n = 40)	P value
Blood urea nitrogen, mmol/L	7.1 (28)	6.7 (30)	9.2 (11)	0.744
Creatinine, μmol/L	90.7 (192)	67 (43)	211 (449)	0.001
97	226 (93)	193 (95.1)	33 (82.5)	0.004
≥ 97	17 (7)	10 (4.9)	7 (17.5)	
Procalcitonin, ng/mL	0.1 (0.2)	0.09 (0.18)	0.16 (0.28)	0.135
Brain natriuretic peptide	420 (2587)	69 (109)	1532 (5210)	0.001
NLR	3.9 (4.2)	3.7 (3.9)	10.6 (7.7)	0.001
Comorbidities				
Any	97 (40.2)	70 (34.8)	27 (67.5)	0.001
Hypertension	45 (18.5)	30 (14.8)	15 (37.5)	0.001
Diabetes	24 (9.9)	18 (8.9)	6 (15)	0.235
Hyperlipemia	10 (4.1)	8 (3.9)	2 (5)	0.671
Chronic obstructive pulmonary disease	10 (4.1)	5 (2.5)	5 (12.5)	0.003
Chronic pulmonary disease	12 (4.9)	8 (3.9)	4 (10)	0.116
Cerebrovascular disease	1 (0.4)	1 (0.5)	0	0.036
Chronic kidney disease	10 (4.1)	4 (2)	6 (15)	0.002
Fatty liver	12 (5)	9 (4.5)	3 (7.5)	0.316
Hepatitis	6 (2.5)	3 (1.5)	3 (7.5)	0.058
Malignancy	9 (3.7)	8 (4)	1 (2.5)	0.656

Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.

	Total (n = 243)	Moderate Type (n = 203)	Severe/Critical Type (n = 40)	P value
Surgery history	34 (14)	27 (13.3)	7 (17.5)	0.484
Imaging features				
Initial CT score, median (IQR)	3 (0–15)	3 (0–15)	3 (1–15)	0.112
Maximum CT score, median (IQR)	8 (0–28)	7 (0–20)	14 (3–28)	0.001
Others				
Onset of symptom to hospital, median (IQR), days	4 (2–7)	4 (2–7)	4 (2–7)	0.733
Hospital stay, median (IQR), days	19 (13–25)	18 (13–24)	22 (18.5–28.5)	0.001
Time from illness onset to highest CT score, median (IQR), days	10 (6–13)	9 (6–12)	13 (8-17.8)	0.001
Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.				

All patients had abnormal CT imaging features (Fig. 1). There were no significant differences in the initial CT scores between the moderate type group and severe/critical type group (p = 0.112). Patients in the severe/critical type group had significantly higher median maximum CT scores (14, IQR 3–28 vs. 7, IQR 0–20; p0.001) than the moderate type group. There was no significant difference in the median time from onset of symptoms to hospitalization between the moderate type group and the severe/critical type group (p = 0.733). In comparison with patients in the moderate type group, patients in the severe/critical type group had longer hospital stays (22, IQR 18.5–28.5 vs. 18, IQR 13–24; p0.001) and a longer time from illness onset to high CT score (13, IQR 8-17.8 vs. 9, IQR 6–12; p0.001) (Fig. 2).

Using univariable analysis, the calculated odds of progression to the severe/critical type group was found to be higher in patients having any comorbidity, including hypertension and COPD. Age (≥ 60 years), sex (male), chest tightness, levels of D-dimer (≥ 1 mg/L), C-reactive protein (≥ 1 mg/L), α-hydroxybutyrate dehydrogenase (≥ 180 U/L), lactate dehydrogenase (≥ 250 U/L), creatine kinase (≥ 190 U/L), creatinine (≥ 97 μmol/L), NLR, and highest CT score were also associated with disease progression. The length of the hospital stays and time from illness onset to the time of the highest CT score were also associated with disease progression. A collinearity analysis showed no collinearity between variables. We included

these variables in the multivariable logistic regression analysis. We found that the combination of COPD (*OR* = 9.06, *95% CI* [1.30-63.36]; p = 0.026) and a higher maximum CT score (*OR* = 1.39, *95% CI* [1.21–1.60]; p□0.001) were associated with disease progression (Table 2).

Table 2
Risk factors associated with deterioration

	Univariable *OR (95% CI)*	*P* value	Multivariable *OR (95% CI)*	*P* value
Characteristics				
Age, years				
60	1 (ref)		1 (ref)	
≥ 60	2.84 (1.41–5.72)	0.003	1.48 (0.54–4.05)	0.444
Sex (vs female)	2.00 (1.01–3.97)	0.048		
Symptoms	0			
Chest tightness	3.01 (1.47–6.16)	0.003	0.85 (0.32–2.78)	0.918
Laboratory findings				
White blood cell count, × 109/L				
10	1 (ref)			
≥ 10	1.03 (0.87–18.77)	0.075		
Lymphocyte count, × 109/L				
1	1 (ref)			
≥ 1	0.55 (0.28–1.10)	0.092		
Monocyte count, × 109/L				
0.5	1 (ref)			
≥ 0.5	1.33 (0.62–2.87)	0.47		
D-dimer, mg/L				
1	1 (ref)		1 (ref)	
≥ 1	3.11 (1.46–6.62)	0.003	1.82 (0.62 – 0.21)	0.388
C-reactive protein, mg/L				

Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.

	Univariable *OR (95% CI)*	*P* value	Multivariable *OR (95% CI)*	*P* value
1	1 (ref)			
≥ 1	2.07 (1.02–4.19)	0.043	0.62 (0.21–1.84)	0.276
α-hydroxybutyrate dehydrogenase, U/L				
180	1 (ref)			
≥ 180	4.72 (2.27–9.83)	0.001		
Lactate dehydrogenase, U/L				
250	1 (ref)			
≥ 250	6.44 (3.05–13.62)	0.001		
Creatine kinase, U/L				
190	1 (ref)		1 (ref)	
≥ 190	3.23 (1.37–7.61)	0.007	1.20 (0.31–4.63)	0.792
Creatinine, μmol/L				
97	1 (ref)		1 (ref)	
≥ 97	4.09 (1.46–11.51)	0.008	2.43 0.56–10.50)	0.235
NLR	1.13 (1.04–1.23)	0.003	1.09 (0.98–1.21	0.105
Comorbidities (vs no)				
Any	3.89 (1.89–8.01)	0.001	1.95 (0.58–6.51)	0.278
Hypertension	3.46 (1.64–7.31)	0.001	0.67 (0.17–2.61)	0.567
Chronic obstructive pulmonary disease	5.66 (1.56–20.56)	0.008	9.06 1.30-63.36)	0.26
Imaging features				
Initial CT score, median (IQR)	1.07 (0.97–1.17)	0.184		

Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.

	Univariable *OR (95% CI)*	*P* value	Multivariable *OR (95% CI)*	*P* value
Maximum CT score, median (IQR)	1.40 (1.26–1.56)	0.001	1.39 (1.21–1.60)	0.001
Others				
Onset of symptom to hospital, median (IQR), days	1.03 (0.94–1.13)	0.507		
Hospital stay, median (IQR), days	1.07 (1.03–1.12)	0.002		
Time from illness onset to highest CT score, median (IQR), days	1.15 (1.07–1.23)	0.001		
Data are mean (SD), median (IQR), n (%) or n/N (%). NLR, Neutrophil Lymphocyte Ratio.				

Using receiver operating characteristic curve (ROC) analysis, an optimal cutoff value of a maximum CT score of 11 with a sensitivity of 85% (*95% CI*: 70.2%-94.3%) and specificity of 78.3% (*95% CI*: 72%-83.8%) was shown to be predictive of disease progression (Fig. 3). The area under the ROC was 0.861 (*95% CI*: 0.811–0.902).

Discussion

This retrospective study identified high CT scores and COPD as risk factors for deterioration in hospitalized patients with COVID-19 in Wuhan, China. Additionally, being older and male, having chest tightness, hypertension, and elevated levels of D-dimer, C-reactive protein, α-hydroxybutyrate dehydrogenase, lactate dehydrogenase, creatine kinase, creatinine, and NLR were associated with progression to severe or critical COVID-19 illness.

Recently, Zhou *et al.* demonstrated that older age is associated with death in hospitalized COVID-19 patients in a retrospective, multicenter cohort study of 191 patients [10]. Other studies have also shown that older age (> 65 years) is associated with poorer clinical outcome in patients with COVID-19 [6, 11, 12]. The present study confirmed that more severely or critically ill patients were older (60 years) than patients with moderate type COVID-19 symptoms. The age-dependent risk has also been seen in previous studies of SARS and MERS [12, 13]. However, in this current study, older age was not shown to be an independent predictor of deterioration in hospitalized patients with COVID-19. The difference between the present and previous studies may be partly due to the different outcomes. The current study was aimed at the progress of moderate type patients with COVID-19 who eventually recovered, rather than died. Furthermore, we had a relatively small sample size for the severe or critical group.

Chest CT is the routine imaging modality for clinical diagnosis of patients with COVID-19 pneumonia in the Hubei Province. It may help to screen patients with suspected COVID-19 symptoms, especially those with a negative RT-PCR result at the early stages of the disease [14]. In order to comprehensively evaluate the CT features of COVID-19 pneumonia, a semi-quantitative scoring system has been developed to quantitatively estimate the severity of inflammation based on quantifying the extent of pulmonary abnormalities (including ground-glass opacities, consolidations, or other fuzzy interstitial opacities)[9]. Using this method, no significant differences of initial CT scores have been found between moderate type and severe/critical type groups. A recent study showed that CT scores in severe-critical type groups were significantly higher than those in the moderate type groups [15]. This may be explained by the fact that patients with COVID-19 in the present study were all of the moderate type initially. With the progression of COVID-19, there were significant differences in the highest CT scores between moderate type and severe/critical type groups. Moreover, using multivariable analysis, the maximum CT score indices were found to be an important independent predictor of deterioration of patients who progressed from moderate type symptoms to severe/critical type symptoms. Furthermore, ROC analysis showed an optimal cutoff value of a maximum score CT index of 11 (sensitivity of 85% and specificity of 78.3%) to predict deterioration. We hope that this maximum score CT index may be used to identify patients at earlier stages of COVID-19 who may potentially progress to severe/critical stage symptoms from moderate type symptoms. Patients with this maximum score CT index will then receive more aggressive treatment and close monitoring. However, the efficacy of such an approach remains to be validated in multi-center and large sample studies in the future.

Lung complications, especially COPD, are common in patients with pneumonia. According to a national cross-sectional study, the total number of patients with COPD in China approximates 100 million [16]. Most of the recent studies have shown no significant differences in COPD between patients with COVID-19 in non-severe types and severe types [1, 7, 17–19]. In the current study, COPD was more common in the severe/critical type group than those in the moderate type group, a finding which agreed with results reported by Guan *et al* [6]. In addition, COPD has been found to be associated with the deterioration of patients with COVID-19. It should be noted that all studies to date, including our study, have used small sample sizes of COVID-19 patients with COPD. The potential impact of COPD on the disease outcomes of patients with COVID-19 requires further observation and research.

Our study has some limitations. First, not all laboratory tests were done in all patients, including the measurement of levels of α-hydroxybutyrate dehydrogenase, lactate dehydrogenase, creatine kinase, procalcitonin and brain natriuretic peptide. Therefore, their roles might be underestimated in predicting disease progression. In addition, we did not analyze the changes in laboratory findings in the process of the disease progression or patient recovery. Some of these results might also contribute to the deterioration in some patients. Second, this was a retrospective study from a single center with a relatively small sample size and a certain selection bias, as some patients were transferred to other medical institution through government decree. Thus, comparisons of clinical characteristics, laboratory findings, and imaging features may be skewed. Third, the semi-quantitative methods for measuring

COVID-19 pneumonia lesions may be somwhat subjectivie. Last, infants, children and adolescents were not included in the present study, and an effort should be made to include these groups in future studies.

Conclusions

Maximum CT score index and COPD were identified as risk factors which may be used to predict COVID-19 disease progression. A maximum CT score ≥ 11 is associated with development of severe illness.

Abbreviations

COVID19: Coronavirus Disease 2019; CT: Computed Tomography; COPD: Chronic obstructive pulmonary disease; ROC: Receiver operating characteristic curve; NLR: Neutrophil Lymphocyte Ratio; IQR: Interquartile range; AUC: Area under the curve; CI: Confidence interval; PACS: Picture archiving and communication systems; ICU: Intensive Care Unit

Declarations

Availability of data and materials

As the current manuscript describes the study protocol and no other data, we do not have any raw data to share at the moment.

Ethics approval and consent to participate

The study was approved by The Central Hospital of Wuhan Ethics Committee (No.2020421), and written informed consent was waived by the Ethics Commission of the designated hospital for emerging infectious diseases.

Consent for publication

Not applicable.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

JWX and XW conceived and designed the study. YD, SCZ, PY, DD and BL collected the data. JWX and XL wrote the paper. YLX and ZFH analyzed the data, and XW reviewed and edited the manuscript. All authors read and approved the manuscript and agree to be accountable for all aspects of the research.

Acknowledgments

Not applicable.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X et al: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020, 395(10223):497-506.
2. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y et al: Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020, 395(10223):507-513.
3. Yang G, Wang Y, Zeng Y, Gao GF, Liang X, Zhou M, Wan X, Yu S, Jiang Y, Naghavi M et al: Rapid health transition in China, 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet 2013, 381(9882):1987-2015.
4. Diseases NCfC: Report on cardiovascular diseases in China. 2014.
5. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, Ma K, Xu D, Yu H, Wang H et al: Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020, 368:m1091.
6. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC et al: Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020.
7. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, Li SB, Wang HY, Zhang S, Gao HN et al: Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ 2020, 368:m606.
8. DALYs GBD, Collaborators H: Global, regional, and national disability-adjusted life-years (DALYs) for 315 diseases and injuries and healthy life expectancy (HALE), 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016, 388(10053):1603-1658.
9. Chang YC, Yu CJ, Chang SC, Galvin JR, Liu HM, Hsiao CH, Kuo PH, Chen KY, Franks TJ, Huang KM et al: Pulmonary sequelae in convalescent patients after severe acute respiratory syndrome: evaluation with thin-section CT. Radiology 2005, 236(3):1067-1075.
10. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X et al: Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020, 395(10229):1054-1062.
11. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y et al: Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020.
12. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M et al: Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020.
13. Hong KH, Choi JP, Hong SH, Lee J, Kwon JS, Kim SM, Park SY, Rhee JY, Kim BN, Choi HJ et al: Predictors of mortality in Middle East respiratory syndrome (MERS). Thorax 2018, 73(3):286-289.

14. Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J: Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. Radiology 2020:200343.
15. Li K, Fang Y, Li W, Pan C, Qin P, Zhong Y, Liu X, Huang M, Liao Y, Li S: CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol 2020.
16. Wang C, Xu J, Yang L, Xu Y, Zhang X, Bai C, Kang J, Ran P, Shen H, Wen F et al: Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. Lancet 2018, 391(10131):1706-1717.
17. Wang L, He W, Yu X, Hu D, Bao M, Liu H, Zhou J, Jiang H: Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up. J Infect 2020.
18. Liu W, Tao ZW, Lei W, Ming-Li Y, Kui L, Ling Z, Shuang W, Yan D, Jing L, Liu HG et al: Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chin Med J (Engl) 2020.
19. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, Akdis CA, Gao YD: Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy 2020.

Figures

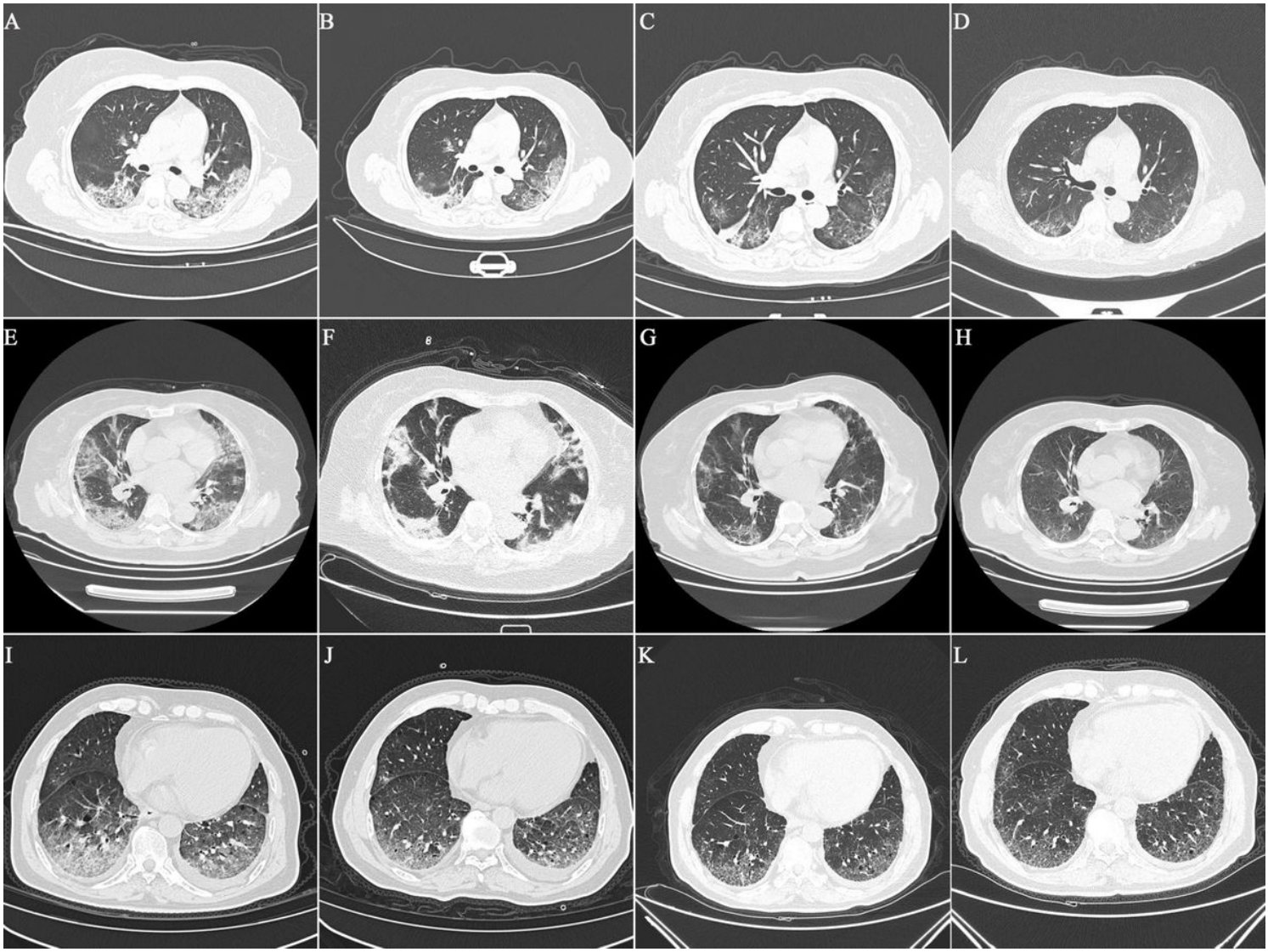

Figure 1

CT images in moderate type group (A-D), severe type group (E-H), and critical type group (I-L).

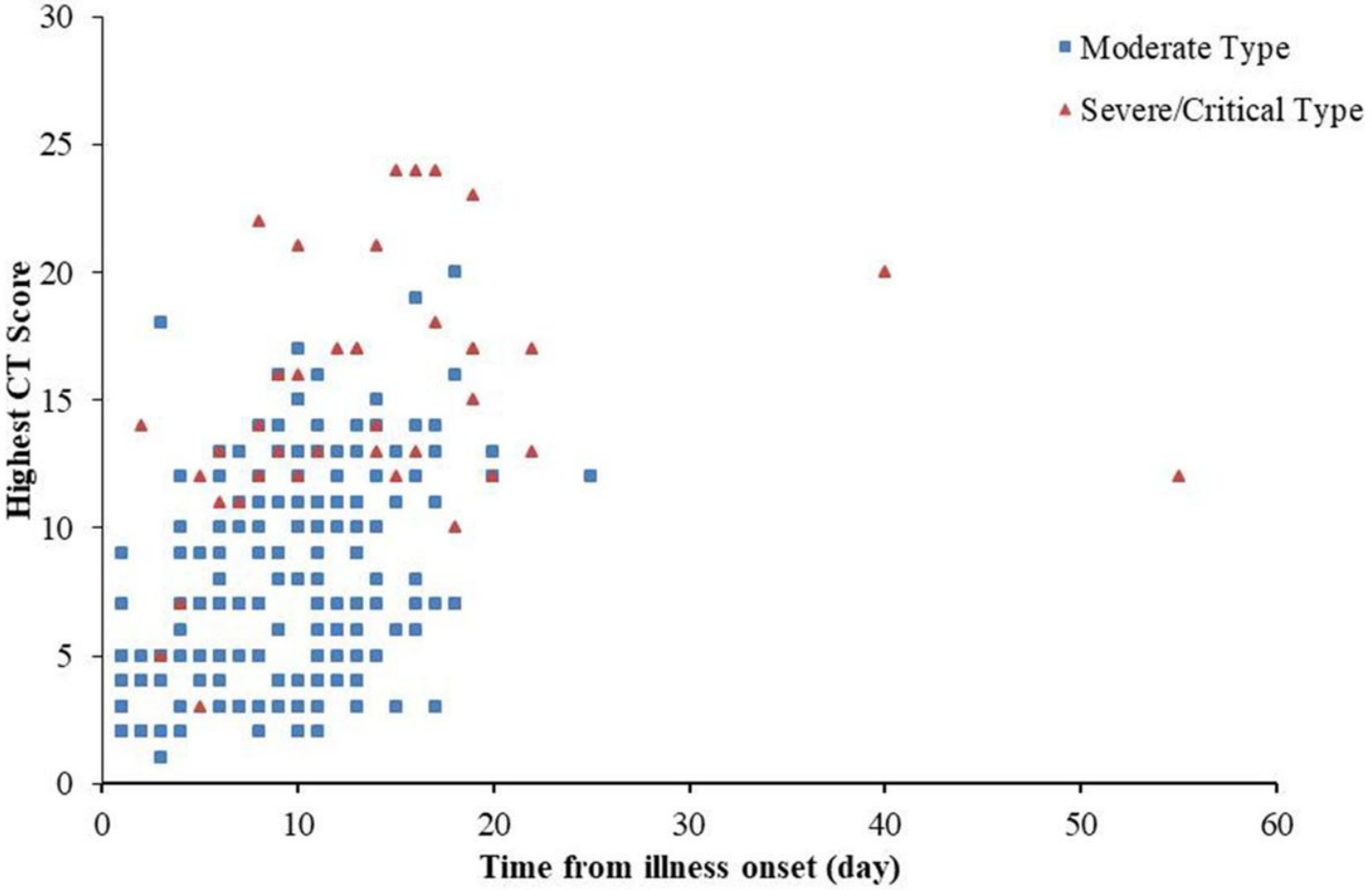

Figure 2

Scatter diagram of maximum CT score with time from illness onset in two groups.

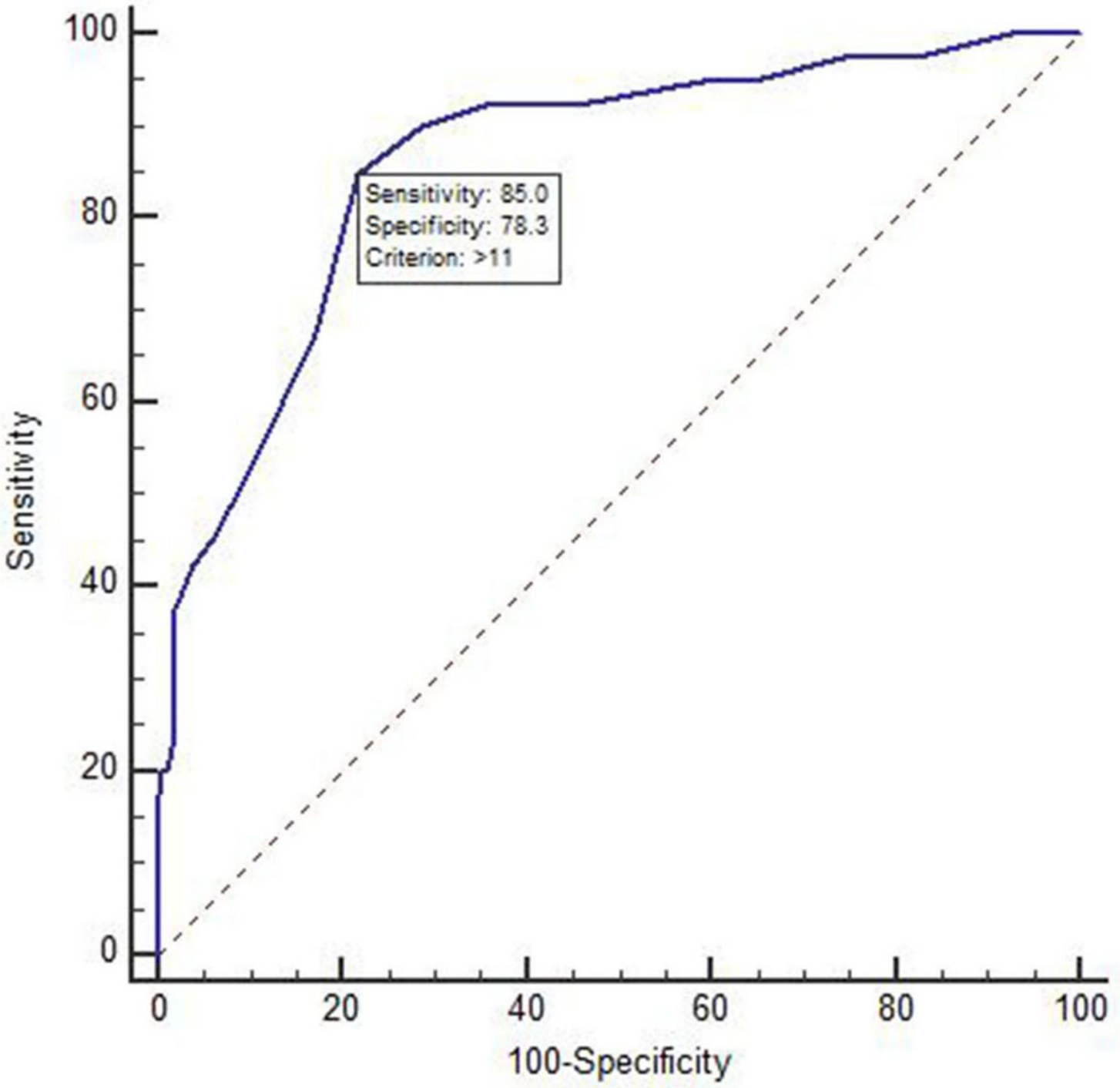

Figure 3

Receiver operating characteristic curves analyses of the highest CT score for prediction of disease deterioration.