Death Risk Analysis for Patients With Severe COVID-19 Pneumonia

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Abstract

**Background:** Coronavirus Disease 2019 (COVID-19) is currently a global pandemic. Information about the death predicting of severe COVID-19 is not clear.

**Methods:** 151 in-patients from January 23th to March 8th 2020 were divided into severe and critically severe group, as well as survival and death group. The analysis of differences of clinical and imaging data were performed between groups. The logistic regression analysis of factors associated with death in COVID-19 were conducted, and the prediction model of death risk was developed.

**Results:** Many clinical and imaging indices were significantly different between groups, including the age, the epidemic history, the past medical history, the duration of symptoms prior to admission, blood routine, inflammatory related factors, Na⁺, myocardial zymogram, liver and renal function, coagulation function, fraction of inspired oxygen and complications. The proportion of patients in imaging stage III and comprehensive CT scores was increased significantly in death group. The area under receiver operating characteristic curve of the prediction model was 0.9593.

**Conclusions:** The clinical and imaging data reflect the severity of COVID-19 pneumonia. The prediction model of death risk might be a promising method to help clinicians to quickly identify and screen potential individuals who had a high-risk of death.

Introduction

Coronavirus disease 2019 (COVID-19), pathogenic agent of which is severe acute respiratory syndrome corona virus 2 (SARS-COV-2), is currently a global pandemic. SARS-COV-2 is a novel betacoronavirus belonging to the sarbecovirus subgenus of Coronaviridae family, which is closely related to severe acute respiratory syndrome coronavirus (SARS-CoV) and middle east respiratory syndrome coronavirus (MERS-CoV). It can lead to respiratory symptoms or severe pneumonia symptoms [1]. According to the estimation of the World Health Organization, 14% patients with SARS-COV-2 infection are severe type, requiring hospitalization and 5% are critical severe, requiring intensive care [2, 3]. The mortality rate of SARS-COV-2 infected patients could be as high as 4% [2], which is much greater than that of seasonal influenza.

A study on the epidemiological characteristics of 72314 cases in China pointed out that SARS-COV-2 was highly infectious, but most patients were with mild clinical performances [4]. The death cases were often more than 60 years old and suffering from some basic diseases such as hypertension, cardiovascular disease and diabetes. Furthermore, a few severe patients rapidly developed to acute respiratory distress syndrome (ARDS) and died from multiple organs failure [5]. The latest biopsy samples from autopsy of a patient with severe illness demonstrated diffuse alveolar damage [6]. Additionally, the inconsistence existed in clinical and imaging performances of patients with COVID pneumonia and diversity imaging features might exist in a certain clinical stage of the disease [7–9]. A few studies[10–14] summarized the comprehensive clinical, laboratory and / or imaging findings of severe and critically severe patients,
which is of great importance for clinicians to adjust the treatment plan and afford clues to predict the death. Therefore, clinical and imaging evidence of severe and clinical severe COVID-19 patients need to be further explored. And it is also urgent to explore the risk factor of death for the severe and critically severe patients, in the international environment of many countries still in, or entering, the pandemic.

The purpose of this study was to conclude the clinical and imaging characteristics and to develop a model for predicting the risk of death in patients with severe or critically severe COVID-19 pneumonia.

**Methods**

**Patients enrollment**

This was a multicenter, retrospective clinical study that was performed at 6 hospitals in Jiangsu and 1 hospital in Wuhan, China. 151 in-patients (104 severe and 47 critical severe) with COVID-19 pneumonia were included from January 23th to March 8th 2020. All the cases were confirmed by reverse transcription-polymerase chain reaction (RT-PCR), and conformed with following diagnosis criteria: Severe type, fulfill any one of the following conditions 1) respiratory distress, respiratory rate (RR) \( \geq 30 \) times per minute, 2) resting state oxygen saturation (SaO2) \( \leq 93\% \), or 3) oxygenation index (calculated by partial pressure of oxygen /fraction of inspired oxygen (FiO2)) \( \leq 300\text{mmHg} \) (1mmHg = 0.133kPa); Critically severe type, fulfill any one of the following conditions 1) respiratory failure and mechanical ventilation needed, 2) shock, 3) concomitant failure of other organs. There were respectively 104 patients diagnosed as severe type and 47 as critical severe type COVID-19 pneumonia. In addition, 114 patients were divided into survival group and 37 into death group according to their clinical outcome. This multicenter research was approved by the institutional review board at each study center, and informed consent was obtained from the patients or their surrogates.

**Clinical Data**

Epidemic history, past medical history, symptoms and signs, as well as age and gender, were recorded. The detailed outcomes of initial laboratory examinations during the severe course were also recorded, containing blood routine, infection related factors, serum ion concentration, myocardial zymogram, liver and kidney function test, coagulation function test, RR, blood gas analysis and complications. Diagnostic criteria of cardiac injury: the serum troponin is the most important index, and its confidence interval greater than 95% of the normal value indicates myocardial damage, and the increase of other indexes can also indicate myocardial damage, in the order of importance: creatine kinase isoenzyme, creatine kinase, lactic dehydrogenase (LDH) [15]. Diagnostic criteria for renal injury: estimated glomerular filtration rate (eGFR) was calculated based on serum creatinine, and it was defined as impaired renal function when eGFR/60 ml/min [16]. The score of the past medical history was determined by additions of these items if any (3 for malignant tumor, 2 for benign tumor, renal or liver malfunction, 1 for Chronic obstructive pulmonary disease, hypertension, diabetes or others).

**Imaging Data**
At the beginning of severe course, the initial imaging (138 patients underwent chest CT and 13 underwent chest radiograph) was analyzed, among which 76 patients were with follow-up CT examination and 31 patients were with follow-up chest radiograph examination. The scanning parameters for CT were as following: tube voltage 120kV, tube current 110mA, pitch 1.0, rotation time ranging from 0.5s to 0.75s, slice thickness 5mm, with 1mm or 1.5mm section thickness for axial, coronal and sagittal reconstructions. The parameters for chest radiograph were as following: the flat panel detector was attached to the patients’ chest, and the voltage and current were 120kV and 200mA, respectively. The chest imaging of 151 patients were analyzed by two experienced attending radiologists, who were blinded to the clinical information, and separately evaluated the imaging and recorded the severity. The chest CT imaging and chest radiograph were classified into mild (stage I), progressed (stage II) and severe stage (stage III), according to the scope of lung field involved, with mild stage less than 25%, progressed stage 26–50% and severe stage more than 50%. The CT score of ground-glass opacity (GGO), consolidation, and the comprehensive score of inflammatory pulmonary infiltration were analyzed quantitatively using a radiologic scoring system ranging from 0–25 points, which was an adaptation of the method previously used to describe idiopathic pulmonary fibrosis and SARS [17]. Each lung lobe was evaluated by 0–5 points, on the basis of the area involved, with score 0 for normal performance, 1 for less than 5% of lung lobe areas involved, 2 for 6–25%, 3 for 26–50%, 4 for 51–75%, and 5 for more than 75%. A total score was eventually calculated via the addition of the score of each lobe.

**Statistical analysis**

Mann-Whitney U test and two-sample T test were used respectively for non-normal distributed and normal distributed data to compare the continuous variables and Pearson Chi-square test was used to compare the categorical variables, between severe and critically severe group, and between survival and death group, by statistical analysis system software (SAS ver. 9.4, SAS Institute Inc., Cary, NC). Then, univariate and multivariable logistic regression analysis were conducted, and the prediction model for mortality in patients with severe COVID-19 pneumonia was developed. Finally, the model was tested by the receiver operating characteristic (ROC) curve. A *P* value less than 0.05 was considered statistically significant. The mean value of the continuous variables in normal distribution was recorded as Mean (SD) and the mean value of non-normal distributed data was recorded as Median (IQR). The categorical variables were recorded as count and percentage.

**Results**

**Clinical Features**

The clinical data of 151 patients with severe COVID-19 pneumonia and results of group comparison were shown in Table 1. There were 91 (60.26%) men and 60 (39.74%) women included, with mean age 62.47 (13.39) years old (range 26–92 years). The average age of patients in survival group 58.52 (13.99) years was significantly lower than that of patients in death group 68.54 (10.83) years (*P*< 0.001). The epidemic
history, past medical history, score of past medical history and the duration of symptoms prior to admission were different between survival and death group.
| Items                              | Mean (SD) | Median (IQR) | Severe vs. critically severe group | Survival vs. death group |
|-----------------------------------|-----------|--------------|------------------------------------|--------------------------|
|                                   | n (%)     |              | P value               | T/Z/x² value | P value | T/Z/x² value |
| Sex                               |           |              | 0.120                  | 2.413        | 0.374   | 0.789        |
| Male                              | 91 (60.3%)|              |                       |              |         |              |
| Female                            | 60 (39.7%)|              |                       |              |         |              |
| Age (years)                       | 60.97 (13.94) | 0.130              | -1.523                      | < 0.001       | -3.984   |              |
| Epidemic history                  | 125 (82.8%)| 0.418          | 1.744                      | 0.007         | 9.823    |              |
| Past medical history              | 85 (56.3%)| 0.368          | 0.812                      | 0.049         | 3.892    |              |
| Score of past medical history     | 1.00 (0, 2.00) | 0.561           | 0.581                      | 0.014         | 2.457    |              |
| Time interval a (days)            | 10.00 (5.00, 15.00) | 0.185           | 1.324                      | 0.026         | 2.223    |              |
| Time interval b (days)            | 10.00 (7.00, 15.00) | 0.400           | 0.841                      | 0.105         | 1.621    |              |
| Time interval c (days)            | 3.00 (0, 9.00) | 0.697           | 0.389                      | 0.136         | -1.492   |              |
| Symptoms                          |           |              | 0.495                  | 1.408        | 0.036   | 6.644        |
| Fever                             |           |              |                       |              |         |              |
| < 37                              | 51 (33.8%)|              |                       |              |         |              |
| 37.0–38.0                         | 48 (31.8%)|              |                       |              |         |              |
| > 38.0                            | 52 (34.4%)|              |                       |              |         |              |
| Cough                             | 112 (74.2%)|              |                       |              |         |              |

a: The duration of symptoms prior to admission; b: The duration of symptoms prior to severe phase; c: The duration of severe illness prior to initial CT scan; WBC: white blood cell; RBC, red blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IL-6: interleukin-6; IL-8: interleukin-8; IL-10: interleukin-10; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; eGFR: estimated glomerular filtration rate; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; PaO₂: partial pressure of oxygen; PCO₂: partial pressure of carbon dioxide; SaO₂: oxygen saturation; FiO₂: fraction of inspiration O₂; ARDS, acute respiratory distress syndrome; DIC: disseminated intravascular coagulation; AKI: acute kidney injury. T/Z/x² value corresponding to Mean (SD), Median (IQR) and n (%) were respectively from two-sample T test, Mann-Whitney U test and Pearson Chi-square test. “None” means that the P value cannot be calculated due to too many missing values of the variate.
| Items                        | Mean (SD)          | Median (IQR)       | Severe vs. critically severe group | Survival vs. death group |
|-----------------------------|--------------------|--------------------|------------------------------------|--------------------------|
|                             | n (%)              |                    | *P value*                          | *T/Z/x² value*           | *P value*                          | *T/Z/x² value*           |
|                             |                    |                    |                                    |                          |                                    |                          |
| Dyspnea                     | 76 (50.3%)         | 0.026              | 4.974                              | 0.098                    | 2.744                              |
| Fatigue                     | 70 (46.4%)         | 0.436              | 0.608                              | 0.066                    | 3.383                              |
| Throat irritation            | 19 (12.6%)         | 0.964              | 0.002                              | 0.929                    | 0.008                              |
| Diarrhea                    | 37 (24.5%)         | 0.304              | 1.058                              | 0.977                    | 0.001                              |
| Headache                    | 13 (8.6%)          | 0.732              | 0.117                              | 0.644                    | 0.214                              |
| Muscle soreness             | 19 (12.6%)         | 0.102              | 2.675                              | 1.000                    | < 0.001                            |
| Nausea and vomiting         | 11 (7.3%)          | 0.959              | 0.003                              | 0.887                    | 0.020                              |
| Blood routine               |                    |                    |                                    |                          |                                    |                          |
| WBC (×10⁹ /L)               | 6.40 (4.38, 9.26)  | < 0.001            | 3.888                              | 0.001                    | 3.250                              |
| Neutrophil (×10⁹ /L)        | 4.86 (3.12, 8.84)  | < 0.001            | 3.658                              | 0.003                    | 3.007                              |
| Neutrophil ratio (%)        | 76.45 (11.64)      | 0.361              | 0.923                              | None                     | None                                |
| Lymphocyte (×10⁹ /L)        | 0.86 (0.56, 1.12)  | < 0.001            | -4.327                             | < 0.001                  | -4.299                             |
| Lymphocyte ratio (%)        | 16.34 (9.84)       | 0.358              | -0.928                             | None                     | None                                |
| RBC (×10¹²/L)               | 4.21 (3.98, 4.77)  | 0.532              | -0.629                             | 0.904                    | 0.891                              |
| Platelet (×10³ /L)          | 198.50 (133.00, 246.50) | 0.091          | -1.690                             | 0.071                    | -1.802                             |
| Infection related factors   |                    |                    |                                    |                          |                                    |                          |
| CRP (mg/L)                  | 61.50 (22.35, 104.15) | < 0.001        | 4.230                              | 0.001                    | 3.398                              |

a: The duration of symptoms prior to admission; b: The duration of symptoms prior to severe phase; c: The duration of severe illness prior to initial CT scan; WBC: white blood cell; RBC, red blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IL-6: interleukin-6; IL-8: interleukin-8; IL-10: interleukin-10; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alamine aminotransferase; eGFR: estimated glomerular filtration rate; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; PaO₂: partial pressure of oxygen; PCO₂: partial pressure of carbon-dioxide; SaO₂: oxygen saturation; FiO₂: fraction of inspiration O₂; ARDS, acute respiratory distress syndrome; DIC: disseminated intravascular coagulation; AKI: acute kidney injury. *T/Z/x² value corresponding to Mean (SD), Median (IQR) and n (%) were respectively from two-sample T test, Mann-Whitney U test and Pearson Chi-square test. “None” means that the *P* value cannot be calculated due to too many missing values of the variate.*
| Items                | Mean (SD)                        | Median (IQR)       | Severe vs. critically severe group | Survival vs. death group |
|----------------------|----------------------------------|-------------------|-----------------------------------|-------------------------|
|                      | n (%)                            |                   | P value | T/Z/\chi^2 value | P value | T/Z/\chi^2 value |
| ESR (mm/H)           | 28.0 (10.00, 53.00)              |                   | 0.022   | 2.288           | 0.013    | 2.485           |
| Procalcitonin (ng/ml)| 0.10 (0.08, 0.32)                |                   | < 0.001 | 3.635           | 0.008    | 2.648           |
| IL-6 (pg/ml)         | 25.43 (6.83, 52.55)              |                   | 0.009   | 2.620           | 0.003    | 2.949           |
| IL-8 (pg/ml)         | 19.75 (10.58, 30.63)             |                   | 0.016   | 2.411           | 0.029    | 2.186           |
| IL-10 (pg/ml)        | 5.75 (4.00, 10.98)               |                   | 0.001   | 3.358           | < 0.001  | 3.816           |
| Serum ion concentration |                               |                   |         |                 |         |                 |
| Na\(^+\) (mmol/L)    | 138.20 (134.60, 141.30)          |                   | 0.009   | 2.630           | 0.021    | 2.311           |
| K\(^+\) (mmol/L)     | 4.26 (3.68, 4.56)                |                   | 0.580   | -0.554          | 0.282    | 1.075           |
| Cl\(^-\) (mmol/L)    | 100.25 (96.95, 103.63)           |                   | 0.055   | 1.919           | 0.059    | 1.891           |
| Ca\(^{2+}\) (mmol/L) | 2.06 (0.15)                      |                   | 0.481   | 0.711           | 0.626    | -0.492          |
| Myocardial zymogram  |                                  |                   |         |                 |         |                 |
| CK (U/L)             | 108.00 (65.25, 147.75)           |                   | 0.266   | -1.111          | 0.647    | 0.458           |
| CK-MB (ng/ml)        | 3.00 (1.05, 12.00)               |                   | 0.379   | -0.880          | 0.483    | -0.702          |
| Myoglobin (ng/ml)    | 50.00 (45.00, 125.90)            |                   | 0.003   | 3.020           | < 0.001  | 5.758           |
| Troponin (ng/ml)     | 4.45 (0.05, 23.25)               |                   | < 0.001 | 4.305           | < 0.001  | 7.119           |

a: The duration of symptoms prior to admission; b: The duration of symptoms prior to severe phase; c: The duration of severe illness prior to initial CT scan; WBC: white blood cell; RBC, red blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; IL-6: interleukin-6; IL-8: interleukin-8; IL-10: interleukin-10; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; LDH: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; eGFR: estimated glomerular filtration rate; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; PaO\(_2\): partial pressure of oxygen; PCO\(_2\): partial pressure of carbon-dioxide; SaO\(_2\): oxygen saturation; FiO\(_2\): fraction of inspiration O\(_2\); ARDS, acute respiratory distress syndrome; DIC: disseminated intravascular coagulation; AKI: acute kidney injury. T/Z/\chi^2 value corresponding to Mean (SD), Median (IQR) and n (%) were respectively from two-sample T test, Mann-Whitney U test and Pearson Chi-square test. “None” means that the P value cannot be calculated due to too many missing values of the variate.
| Items                      | Mean (SD)            | Median (IQR)          | Severe vs. critically severe group | Survival vs. death group |
|----------------------------|----------------------|-----------------------|------------------------------------|-------------------------|
|                            | n (%)                |                       | P value | T/Z/X² value | P value | T/Z/X² value |
| LDH (U/L)                  | 307.00 (195.00, 509.00) | < 0.001               | 4.204 |              | < 0.001 | 5.020        |
| Liver function             |                      |                       |         |              |         |
| Total bilirubin (umol/L)   | 11.10 (7.80, 14.70)  | 0.003                 | 2.985  | 0.055       | 1.917   |
| Albumin (g/L)              | 33.90 (30.80, 36.80) | < 0.001               | -4.752 | < 0.001     | -3.787  |
| AST (U/L)                  | 31.50 (22.00, 45.93) | 0.035                 | 2.105  | 0.009       | 2.613   |
| ALT (U/L)                  | 27.00 (18.00, 46.00) | 0.766                 | 0.298  | 0.209       | 1.257   |
| Renal function             |                      |                       |         |              |         |
| eGFR (ml/min)              | 84.23 (27.83)        | 0.640                 | 0.470  | 0.008       | 2.722   |
| Serum creatinine (umol/L)  | 73.50 (57.00, 89.23) | 0.233                 | 1.192  | 0.006       | 2.725   |
| Serum urea nitrogen (mmol/L)| 5.40 (3.90, 9.05)   | 0.006                 | 2.724  | < 0.001     | 4.839   |
| Coagulation function       |                      |                       |         |              |         |
| PT (sec.)                  | 14.00 (12.75, 15.00) | < 0.001               | 4.523  | < 0.001     | 5.117   |
| APTT (sec)                 | 38.75 (34.48, 43.78) | 0.034                 | 2.122  | 0.001       | 3.362   |
| Fibrinogen (g/L)           | 4.63 (3.00, 6.04)    | 0.015                 | 2.434  | 0.356       | 0.922   |
| D-dimer (ng/mL)            | 2.50 (0.87, 25.00)   | 0.081                 | 1.744  | 0.309       | 1.018   |

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| Items                                      | Mean (SD)      | Median (IQR)  | Severe vs. critically severe group | Survival vs. death group |
|-------------------------------------------|----------------|---------------|-----------------------------------|-------------------------|
|                                           | n (%)          |               | P value | T/Z/x² value | P value | T/Z/x² value |
| INR                                       | 1.11 (1.05, 1.20) | < 0.001       |          | 3.900 | 0.003   | 3.019 |
| Respiratory rate (times/min)              | 21.00 (20.00, 26.00) | 0.017         | 2.391   |          | 0.065   | 1.848 |
| Blood gas analysis                        |                |               |         |          |         |        |
| PaO₂ (mmHg)                               | 76.85 (62.85, 95.63) | 0.199         | 1.309   |          | 0.104   | -1.673 |
| PCO₂ (mmHg)                               | 37.94 (6.70)   | 0.493         | -0.698  | None    | None    |
| SaO₂ (%)                                  | 96.00 (91.00, 98.00) | 0.023         | -2.280  |          | 0.099   | -1.651 |
| Oxygenation index (mmHg)                  | 286.38 (71.41) | 1.000         | < 0.001 | None    | None    |
| FiO₂                                       | 0.41 (0.30, 0.81) | < 0.001       | 4.246   | < 0.001 | 4.321 |
| Complications                             |                |               |         |          |         |        |
| Cardiac injury                            | 55 (36.4%)     | 0.293         | 1.107   | < 0.001 | 24.245 |
| Liver injury                              | 20 (13.2%)     | 0.050         | 3.831   | 0.010   | 6.590 |
| Kidney injury                             | 26 (17.2%)     | 0.375         | 0.788   | 0.188   | 1.736 |
| ARDS                                      | 43 (28.5%)     | < 0.001       | 31.976  | < 0.001 | 62.369 |
| Septic shock                              | 31 (20.5%)     | < 0.001       | 33.751  | < 0.001 | 66.463 |

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| Items | Mean (SD) | Median (IQR) | Severe vs. critically severe group | Survival vs. death group |
|-------|-----------|--------------|-----------------------------------|-------------------------|
|       | n (%)     |              | P value | T/Z/x² value | P value | T/Z/x² value |
| DIC   | 21 (13.9%) |              | < 0.001 | 23.107       | < 0.001 | 57.389       |
| AKI   | 31 (20.5%) |              | < 0.001 | 13.205       | < 0.001 | 33.760       |

**DIC:** disseminated intravascular coagulation; **AKI:** acute kidney injury. T/Z/x² value corresponding to Mean (SD), Median (IQR) and n (%) were respectively from two-sample T test, Mann-Whitney U test and Pearson Chi-square test. “None” means that the P value cannot be calculated due to too many missing values of the variate.

The count of white blood cell and neutrophil, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitoni, interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), Na⁺, myoglobin, troponin, LDH, aspartate aminotransferase, serum urea nitrogen, prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), FiO₂, the occurrence rate of ARDS, septic shock, disseminated intravascular coagulation (DIC) and acute kidney injury (AKI) were lower, while the count of lymphocytes and albumin were higher in severe and survival group than those in critically severe and death group (P < 0.05). The percentage of patients with dyspnea, total bilirubin, fibrinogen and RR were lower, while the SaO₂ was higher in the severe group than those in critically severe group (P < 0.05). The serum creatinine, the occurrence rate of cardiac injury and liver injury were lower, while the proportion of patients with moderate and high fever and estimated glomerular filtration rate were higher in survival group than those in the death group (P < 0.05).

**Imaging findings**

As showed in Table 2, among the 151 severe and critically severe patients, 6 (3.97%) patients were diagnosed as stage I (Fig. 1), 68 (45.03%) were stage II (Fig. 2), and 77 (50.99%) were stage III (Fig. 3) on chest CT or chest radiograph images. On CT images, 116 (84.06%) patients were with the whole lung involved. The lesions of 83 (60.14%) patients on chest CT were mainly peripherally distributed. The proportion of patients with stage III in the death group was significantly higher than that in the survival group (73.0% vs. 43.9%, P < 0.05). There was significant difference in comprehensive score not only between severe and critically ill group, but also between survival and death group (P < 0.05).
| Items                              | Median (IQR) n (%) | Severe vs. critically severe group | Survival vs. death group |
|-----------------------------------|--------------------|------------------------------------|--------------------------|
|                                   |                    | P value | Z/\chi^2 value | P value | Z/\chi^2 value |
| Imaging stage                     |                    | 0.185   | 3.379          | 0.007   | 9.828          |
| I                                 | 6 (4.0%)           |         |                |         |                |
| II                                | 68 (45.0%)         |         |                |         |                |
| III                               | 77 (51.0%)         |         |                |         |                |
| Number of lung lobes involved     |                    | 0.162   | 6.538          | 0.701   | 2.190          |
| One lobe                          | 2 (1.4%)           |         |                |         |                |
| Two lobes                         | 5 (3.6%)           |         |                |         |                |
| Three lobes                       | 7 (5.1%)           |         |                |         |                |
| Four lobes                        | 8 (5.8%)           |         |                |         |                |
| Five lobes                        | 116 (84.1%)        |         |                |         |                |
| Distribution of pulmonary lesions |                    | 0.202   | 1.631          | 0.777   | 0.080          |
| Peripheral                        | 83 (60.1%)         |         |                |         |                |
| Non-peripheral                    | 55 (39.9%)         |         |                |         |                |
| Comprehensive score              | 17.00 (11.00, 20.00)| 0.035   | 2.103          | 0.021   | 2.303          |
| GGO score                         | 14.00 (8.75, 17.25)| 0.054   | 1.930          | 0.054   | 1.924          |
| Consolidation score              | 5.00 (3.00, 9.00)  | 0.680   | 0.412          | 0.851   | 0.188          |
| Follow-up                         |                    | 0.309   | 2.347          | 0.735   | 0.615          |
| No obvious change                 | 8 (8.5%)           |         |                |         |                |
| Absorption                        | 66 (70.2%)         |         |                |         |                |
| Progress                          | 20 (21.3%)         |         |                |         |                |

GGO: ground-glass opacity. Z/\chi^2 value corresponding to Median (IQR) and n (%) were respectively from Mann-Whitney U test and Pearson Chi-square test.
94 patients had chest CT and/or chest radiograph follow-up, of which 8 patients showed no obvious change, 66 patients showed absorption and 20 patients showed progress of pulmonary lesions. The proportion of patients with absorption during imaging follow-up was higher (71.8% vs. 63.6%), while the proportion of patients with progress was lower (19.7% vs. 27.3%) in the survival group than that in the death group. However, there were no significant differences between the two groups ($P > 0.05$).

**Logistic regression analysis and prediction model**

The univariate logistic regression analysis of factors associated with death in COVID-19 was shown in Table 3. The value of odds ratio estimates in patients with DIC was the highest (59.105), followed by septic shock (37.500) and myocardial injury (34.500). Multivariate logistic regression analysis of factors associated with death in COVID-19 were shown in Table 3. The death prediction model of risk factors for a severe patient was written as:

\[
\ln \frac{p}{1-p} = -10.6756 + 0.0898 \text{age} + 2.5089 \text{cardiac_injury} + 1.4740 \text{AKI} + 3.8355 \text{ARDS}
\]

or

\[
p = \frac{e^{-10.6756 + 0.0898 \text{age} + 2.5089 \text{cardiac_injury} + 1.4740 \text{AKI} + 3.8355 \text{ARDS}}}{1 + e^{-10.6756 + 0.0898 \text{age} + 2.5089 \text{cardiac_injury} + 1.4740 \text{AKI} + 3.8355 \text{ARDS}}}
\]
Table 3
Logistic regression analysis of risk factors for death prediction

| Items                                      | Odds Ratio Estimates | 95% Wald Confidence Limits | P     |
|--------------------------------------------|----------------------|----------------------------|-------|
| Univariate analysis                        |                      |                            |       |
| Sex (Male/ Female)                         | 1.404                | 0.663–2.969                | 0.375 |
| Age (years)                                | 1.061                | 1.028–1.095                | <0.001|
| Past medical history                       | 2.203                | 0.995–4.879                | 0.051 |
| Score of past medical history              | 1.363                | 1.040–1.788                | 0.025 |
| Duration of symptoms prior to admission (days) | 1.052                | 1.001–1.106                | 0.044 |
| Duration of symptoms prior to severe illness (days) | 2.132                | 0.945–4.807                | 0.768 |
| Fever                                      | 0.328                | 0.369–0.833                | 0.005 |
| Cough                                      | 0.922                | 0.577–1.474                | 0.735 |
| Dyspnea                                    | 1.336                | 0.885–2.015                | 0.168 |
| Diarrhoea                                  | 0.942                | 0.398–2.229                | 0.892 |
| Headache                                   | 0.535                | 0.113–2.533                | 0.431 |
| Fatigue                                    | 2.091                | 0.983–4.448                | 0.056 |
| Muscle soreness                            | 1.116                | 0.373–3.339                | 0.844 |
| WBC (×10⁹ /L)                              | 3.728                | 1.595–8.714                | 0.002 |
| Neutrophil (×10⁹ /L)                       | 3.927                | 1.809–8.525                | <0.001|
| Lymphocyte (×10⁹ /L)                       | 0.152                | 0.051–0.450                | <0.001|
| Cardiac injury                             | 34.500               | 11.065-107.568             | <0.001|
| Live injury                                | 2.103                | 0.983–4.498                | 0.055 |
| Kidney injury                              | 4.208                | 1.731–10.230               | 0.002 |
| PT (sec.)                                  | 5.893                | 1.702–20.411               | 0.005 |
| APTT (sec.)                                | 3.040                | 1.280–7.222                | 0.012 |
| Fibrinogen (g/L)                           | 2.407                | 0.972–5.964                | 0.058 |

WBC: white blood cell; PT: prothrombin time; APTT: activated partial thromboplastin time; CRP: C-reactive protein; ARDS: acute respiratory distress syndrome; DIC: disseminated intravascular coagulation; AKI: acute kidney injury.
| Items                        | Odds Ratio Estimates | 95% Wald Confidence Limits | P    |
|-----------------------------|----------------------|----------------------------|------|
| CRP (mg/L)                  | 4.617                | 1.326–16.082               | 0.016|
| ARDS                        | 29.592               | 10.919–80.199              | <0.001|
| Septic shock                | 37.500               | 12.835-109.566             | <0.001|
| DIC                         | 59.105               | 12.676-275.596             | <0.001|
| AKI                         | 11.013               | 4.491–27.006               | <0.001|
| Comprehensive CT score      | 1.079                | 1.007–1.156                | 0.031|
| Consolidation score         | 1.030                | 0.933–1.138                | 0.558|
| Imaging stage               | 2.912                | 1.366–6.206                | 0.006|
| Number of lung lobes involved | 1.772               | 0.755–4.157                | 0.189|
| Multivariate analysis       |                      |                            |      |
| Age (years)                 | 1.094                | 1.024–1.168                | 0.008|
| Cardiac injury              | 12.291               | 2.872–52.607               | <0.001|
| AKI                         | 4.367                | 1.055–18.081               | 0.042|
| ARDS                        | 46.319               | 8.959–239.471              | <0.001|

**Discussion**

COVID-19 is a novel infectious disease, characterized by high transmissibility and serious harmfulness. A few patients with severe course of disease tend to have severe clinical symptoms, who may rapidly progress into ARDS and need the aids of intensive care unit [18]. Hence, it is essential to closely monitor the condition of patients, by dynamically monitoring the alteration of symptoms and laboratory examinations, the change of the chest imaging performances, which are helpful for the evaluation of the disease severity and to adjust treatment plan timely.

There were some characteristic clinical features pertaining to the severe disease course of SARS-COV-2 infected. The past medical history had an effect on disease mortality, which confirmed by the reports from Sohrabi et al [19], Guan et al [20] and Jordan et al [3]. In present study, the mean age of death cases was approximately 10 years older than that of survivors, which was similar to the previous study [21].
gender prevailing of patients with severe COVID-19 was obvious, almost 3: 2 for male-female ratio in present study. This was in consistence with Chen's study, suggested that older men were more likely to be infected with SARS-COV-2, resulting in severe and even fatal respiratory diseases such as ARDS [5]. In the death group, the duration of symptoms prior to admission was longer than that of survival group, reflecting that the prolonged duration of symptom onset to hospitalization tended to poorer outcomes, which was in consistence with Liang's study [22].

In present study, the main initial symptoms of the severe patients were fever and/or cough. The dyspnea was frequently seen in the severe course of the patients with COVID-19 pneumonia, especially in critically severe patients, due to the severe lung lesions of the pneumonia. The incidence of ARDS in critically severe and death group was significantly higher than that in severe and survival group, respectively. The RR in critically severe patients was significantly higher than that in severe patients, as well as the SaO2 and FiO2, which may be due to mechanical ventilation. As to the blood routine, increased leukocyte and neutrophil counts, decreased lymphocytes count and ratio were remarkable features, especially for critically severe group and death group. Wang et al firstly uncovered the continuous increase of neutrophil counts in dead cases [23]. It may be related to cytokine storm induced by virus invasion. And lymphopenia suggested SARS-COV-2 might mainly target at lymphocytes and lead to the progression of the disease [5].

The infection related factors, including CRP, ESR, procalcitonin, IL-6, IL-8 and IL-10, were increased in the severe patients, especially in critically severe patients and death cases. The study from Ulhaq et al suggested that continuous measurement of circulating IL-6 levels may be of great significance in identifying disease progression in patients infected with COVID-19 [24]. A retrospective study suggested that elevated levels of IL-6 was related to the high mortality of COVID-19 infection [25]. A significantly higher incidence of septic shock and DIC was seen in critically severe and death group. This may be due to the imbalance of thrombin production caused by the activation of vascular endothelium, platelets and white blood cells, which occurred locally and systematically in the lung system of patients with severe pneumonia, resulting in fibrin deposition, tissue damage and microangiopathy [26]. It could be aggravated by the occurrence of septic shock [27, 28]. It was reported that most of death cases and very few survivors have evidence of DIC, which occurred frequently in the deterioration of COVID-19 pneumonia and was often associated with mortality [29]. It also suggested that clinicians needed to be vigilant to identify the presence of DIC, especially in patients who had already experienced septic shock.

There was some significant relationship between multiple organs injury and mortality. In critically severe and death patients, myoglobin, troponin, LDH and the incidence of cardiac injury were more higher than those in non-death patients, which was similar to the results of some previous studies on the relationship between the severity of illness and myocardial injury in patients with COVID-19, and was consistent with the correlation study between heart injury and death after SARS-CoV-2 infection [30, 31]. Recent studies on COVID-19 had shown that the incidence of liver injury ranges from 14.8–53%, with the decreased albumin level in critically ill patients, and the incidence of liver injury might reach as high as 78.0% in the death cases of COVID-19 [32]. In this study, the incidence of liver injury in critically severe and death
The coagulation function and the serum Na$^+$ concentration changed in the severe course of COVID-19 pneumonia. Recently, the coagulation function was concerned and some related indices were studied between severe and non-severe patients [18, 35]. In this study, these indices were further compared between severe and critically severe patients, and between survival and death patients. PT, APTT, INR and fibrinogen level were related to the severity of the disease, and the former three might be related to the mortality. According to previous study [36], hyponatremia was a common electrolyte disorder, which was related to long-term hospitalization and death, and was more common in critically ill patients. Abnormal changes in the central nervous system and mental state may be the causes of hyponatremia, while the digestive tract or urinary system disorder cannot be ruled out [32]. In addition, it may also be related to a large number of intravenous supplements of sodium-containing fluids.

As to the imaging performances, multiple lung lobes were involved in 98.6% patients, and whole lung lobes were involved in 84.06% patients. The proportion of patients in stage III increased significantly in death group, as well as comprehensive CT imaging scores in critically severe and death group. Our results showed that the severity of CT findings was consistent with the severity of clinical course of the disease, as suggested by previous study [37]. Li et al [38] found that the development pattern of COVID-19 on CT images was similar to that of SARS or MERS. There were some common imaging features, so the final diagnosis had to be combined with the clinical manifestation, epidemic history and laboratory examination. However, the advantage of convenient and rapid CT examination was irreplaceable. A study about critically ill patients with SARS-CoV-2 pneumonia demonstrated that early or repeated radiological examination is helpful to screen patients with SARS-CoV-2 pneumonia [39].

The previous studies referred to the mortality risk, calculated overall probability based on the infection and confirmed population [40, 41]. However, the individual rough risk of death was important, especially in severe and critically severe patients, which might influence the treatment plan and the response of clinicians or medical institutions. In the univariate logistic regression analysis, DIC showed as the best predictor (nearly 59 times of the death risk for the patients without DIC), followed by septic shock and cardiac injury. The prediction model included evidence of patient’s age, cardiac injury, AKI and ARDS, among which the evidence of ARDS was the most powerful predictor. In the current COVID-19 epidemic, this prediction model might be a promising method to help clinicians to quickly identify and screen potential individuals who had a high-risk of death.
There were several limitations of this study. First, the clinical and imaging data of patients were from multiple centers, hence the data were heterogeneous which might affect the statistical results. Additionally, some indices were missing too many values, which lead to that the $P$ value could not be calculated in the test of group differences. Second, the initial imaging and follow-up imaging of the patients were lack of uniform standard. Some patients were only with chest X-ray because of the disease severity, and the follow-up interval was not identical. Finally, although both of the percent concordant and the area under curve of the prediction model were in a high level, a larger cohort study might be warranted to validate the accuracy and application value of the prediction model.

**Conclusion**

The clinical and imaging data reflect the severity of COVID-19 pneumonia and part of them were related to mortality. The prediction model of death risk might be a promising method to help clinicians to quickly identify and screen potential individuals who had a high-risk of death.

**Abbreviations**

AKI
Acute kidney injury; APTT:Activated partial thromboplastin time; ARDS:Acute respiratory distress syndrome; COVID-19:Coronavirus disease 2019; CRP:C-reactive protein; CT:Computed tomography; DIC:Disseminated intravascular coagulation; ESR:Erythrocyte sedimentation rate; FiO$_2$:Fraction of inspired oxygen; GGO:Ground-glass opacity; HRCT:High-resolution CT; INR:International normalized ratio; MERS-CoV Middle East respiratory syndrome coronavirus; PT:Prothrombin time; ROC:Receiver operating characteristic; RR:Respiratory rate; RT-PCR:Reverse transcription-polymerase chain reaction; SaO$_2$:Oxygen saturation; SARS-CoV:Severe acute respiratory syndrome coronavirus; SARS-CoV-2:Severe acute respiratory syndrome coronavirus 2

**Declarations**

*Ethics approval and consent to participate*

This study was conducted in accordance with the amended Declaration of Helsinki. Independent ethics committees approved this retrospective study [see Additional file 1], and written informed consent was obtained from all patients or their surrogates.

*Consent for publication*

The consent for publication of chest CT and radiograph images in this study had been obtained from relevant patients.

*Availability of data and materials*
The datasets used during the current study are available from Yonggang Li on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors' contributions**

YL is the chief investigator of the study. HD and RH made substantial contributions to the study design, data collection and analysis, interpretation of the data, and drafting of the manuscript. MM, YS, JH and NS made substantial contributions to the data collection and analysis, interpretation of the data. DZ and HL made substantial contributions to the conception, study designs, data collection and analysis. All authors read and approved the final manuscript.

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**Figures**

**Figure 1**

A 25-year-old woman diagnosed with severe COVID-19 on January 30th with diarrhea for 2 days. a-b. Axial chest CT on January 30th showed mild changes (stage I) with irregular high-density lesion in the
left upper lung lobe surrounded by ground-glass opacity (a, b, arrows), and patchy ground-glass opacity in the right upper lung lobe (a, arrow).

Figure 2

A 64-year-old woman diagnosed with severe COVID-19 on January 31th with vomiting and anorexia. a, c. Axial chest CT on February 1st showed progressed performances (stage II) with multiple lesions, including ground-glass opacity, consolidation and fibrosis, mainly distributed in the lower lung lobes. b, d. Axial chest CT on February 4th showed mild absorption of ground-glass opacity and consolidation.
Figure 3

A 58-year-old man diagnosed with severe COVID-19 on January 30th with asthma. Imaging showed severe performances (stage III). a. Chest radiograph (a) on January 31th showed multiple high-density lesions with peripheral distribution and blurred boundary. b-d. Axial chest CT on February 4th showed diffusely distributed ground-glass opacity in bilateral lungs involving the whole lung lobes, with mild consolidation.
Figure 4

Receiver operating characteristic curve of death prediction model. With the area under curve of 0.9593, the multivariate logistic regression model is reliable.

Supplementary Files

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