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Retrospective study of risk factors for severe SARS-Cov-2 infections in hospitalized adult patients

Short title: Risk Factors for Severe COVID-19 in Hospitalized Adult Patients

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Conflict of Interest

The authors of this study declare that they each have no conflict of interest.
What’s new?
SARS-CoV-2 can cause disease ranging from the common cold to more severe and even fatal multi-organ dysfunction. Our study showed that the elderly people with underlying disease were at high risk of SARS-CoV-2 infection. In particularly, the higher Sequential Organ Failure Assessment (SOFA) score and lymphocytopenia on admission were associated with greater risk of developing severe COVID-19. Therefore, the patients with high risk should be paid more attention, monitored closely and timely treatment, which may help to improve the prognosis.
Abstract

**Introduction:** Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been spread worldwide.

**Objectives:** To identify the clinical characteristics and risk factors associated with the severe incidence of SARS-CoV-2 infection.

**Patients and methods:** All adult patients (≥18 years old) consecutively admitted in Dabieshan Medical Center from January 30, 2020 to February 11, 2020 were collected and reviewed. Only patients diagnosed with COVID-19 according to WHO interim guidance were included in this retrospective cohort study.

**Results:** A total of 108 patients with COVID-19 were retrospectively analyzed. Twenty-five patients (23.1%, 25/108) developed severe disease, and of those 12 (48%, 12/25) patients died. Advanced age, co-morbidities with hypertension, higher blood leukocyte count, neutrophil count, higher sensitive C-reactive protein level, D-dimer level, Acute Physiology and Chronic Health Evaluation II (APECHE II) score and Sequential Organ Failure Assessment (SOFA) score were associated with greater risk of development of severe COVID-19, and so were lower lymphocyte count and albumin level. Multivariable regression showed increasing odds of severe COVID-19 associated with higher SOFA score (OR 2.450, 1.302–4.608; $p = 0.005$), and lymphocyte count less than $0.8 \times 10^9$ per L (OR 9.017, 2.808–28.857; $p <0.001$) on admission. The higher SOFA score (OR 2.402, 1.313–4.395; $p = 0.004$) on admission was identified as risk factor for in-hospital death.
Conclusions: Lymphocytopenia and the higher SOFA score on admission could help clinicians to identify patients with high risk for developing severe COVID-19. More related studies are needed in the future.

Keywords: COVID-19, risk factors, SARS-CoV-2, Severe infection
Introduction

The current outbreak of the novel coronavirus termed severe acute respiratory syndrome coronavirus (SARS-CoV-2) has spread to more than 100 countries and regions around the world. The World Health Organisation (WHO) declared the coronavirus disease 2019 (COVID-19) outbreak a public health emergency of international concern on 31 Jan 2020. As of 18 March 2020, WHO has reported a total of 207,855 cases across 166 countries and areas with 8,648 death.

SARS-CoV-2 is a new strain of coronavirus not previously identified in humans or animals [1]. Coronavirus are a large family of viruses including four subfamilies, namely alpha-, beta-, gamma- and delta- coronavirus. SARS-CoV-2 belongs to the B lineage of the beta- coronavirus and is closely related to the SARS-CoV virus [2]. Currently, SARS-CoV-2 appears to have a lower case fatality rate (4.0%, 3250/81,263) in China than either SARS-CoV (9.6%, 774/8096) or MERS-CoV (34.4%, 858/2494)[3]. Despite the lower case fatality rate [4], COVID-19 has so far resulted in more deaths (3056) than SARS and MERS combined (1632).

In concert with recent studies, the epidemiological and clinical characteristics of COVID-19 have been reported [5-8]. Most people infected with SARS-CoV-2 have mild disease and recover. Fever and dry cough are the dominant symptoms. Severe and critical illness occurred in approximately 20% of the patients after admission to hospital. The current evidence suggested that elder age and coexisting medical condition was associated with greater risk of poor outcome [9-11]. The high Sequential Organ Failure Assessment (SOFA) score and increased D-dimer were also
identified as risk factors for COVID-19 mortality [12]. However, the patients from Wuhan in the early stage of the COVID-19 outbreak were mainly concerned in these studies. The proportion of severe patients was significantly higher than that in other areas in China, and the mortality was as high as 20%-30% [9-11]. Some studies have confirmed that the characteristics of patients with COVID-19 outside of Wuhan differed from patients in Wuhan [7, 8, 13]. Therefore, the clinical outcomes and risk factors associated with severe COVID-19 remains to be determined. In this study, a total of 108 cases of Huanggang city from January 24, 2020 to February 8, 2020 were retrospectively analyzed. We aimed to compare the clinical characteristics, laboratory findings, treatments, and outcomes of patients with non-severe or severe 2019-nCoV infection, to explore the risk factors associated with the severe incidence of SARS-CoV-2 infection.

Patients and methods

Study design and participants

All adult patients (≥18 years old) consecutively admitted in Dabieshan Medical Center from January 30, 2020 to February 11, 2020 were collected and reviewed. Only patients diagnosed with COVID-19 on admission according to WHO interim guidance before admission were included in this retrospective cohort study. Dabieshan Medical Center is the designated hospital for patients with COVID-19 in Huanggang city, Hubei Province, China. It was affiliated to Huanggang Central Hospital and has been entrusted by Shandong medical rescue team since February 2, 2020. As of March 3, all included patients were discharged or died.
The study was approved by the institutional review board of Shandong Provincial Hospital (SWYX: NO.2020-012) and Huanggang Central Hospital (HGYY-2020-009). The requirement for informed consent was waived by the Ethics Commission as the urgent need to collect data on this emerging pathogen.

Data collection

Demographic, clinical, laboratory, imaging examination, treatment, and outcome data were collected using a standardized case-report form. All data were checked by two physicians (QY and PW), and then a third researcher (YC) determined any differences in interpretation between the two primary reviewers. The Acute Physiology and Chronic Health Evaluation (APACHE II) score, SOFA score, National Early Warning Score (NEWS2) score and the quick Sequential Organ Failure Assessment (qSOFA) score were calculated separately using the worst value of physiological variables within 24 hours of presentation.

Laboratory procedures

Throat-swab or sputum specimens were collected from all patients before admission for SARS-CoV-2 detection, and the detection was repeated twice every 24 hours. RT-PCR assays were performed in accordance with the protocol described previously [6].

Laboratory and imaging examination (Chest radiographs or computerized tomography scan) were conducted for all patients with SARS-CoV-2 infection on admission. Routine blood examinations were complete blood count, coagulation profile, serum biochemical tests (including renal and liver function, creatine kinase,
lactate dehydrogenase, and electrolytes), myocardial enzymes, procalcitonin and arterial blood gas analysis. The identification of other respiratory pathogens was also needed, including influenza A virus (H1N1, H3N2, h7n9), influenza B virus, respiratory syncytial virus, parainfluenza virus and adenovirus. Frequency of examinations and treatment were all determined by the treating physician. Patients met the discharge criteria if they had no fever for at least 3 days, substantial improvement in both lungs in chest CT, clinical remission of respiratory symptoms, and two throat-swab samples negative for SARS-CoV-2 RNA obtained at least 24 hours apart.

Definitions

The degree of severity of COVID-19 (severe vs. non-severe) was defined according to the American Thoracic Society guidelines for community-acquired pneumonia [14]. Briefly, severe COVID-19 should reach the following either one major criterion or three or more minor criteria. Minor criteria included respiratory rate more than 30 breaths per minute, PaO2/FIO2 ratio lower than 250, multilobar infiltrates confusion or disorientation, blood urea nitrogen level more than 7.1mmol/L, white blood cell count less than 4.0×10^9 per L, platelet count less than 100×10^{12} per L, core temperature lower than 36℃, hypotension requiring aggressive fluid resuscitation. Major criteria included septic shock with need for vasopressors, or mechanical ventilation. Fever was defined as axillary temperature of at least 37·3℃. Sepsis and septic shock were defined according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock [15]. Acute kidney injury was diagnosed
according to the KDIGO clinical practice guidelines [16] and acute respiratory distress syndrome (ARDS) was diagnosed according to the Berlin Definition [17]. Acute cardiac injury was diagnosed if serum levels of cardiac biomarkers (eg, high-sensitive cardiac troponin I) were above the 99th percentile upper reference limit, or if new abnormalities were shown in electrocardiography and echocardiography [6].

**Statistical analysis**

Patients were divided into non-severe, severe-alive and severe-dead three groups according to the criteria mentioned above. All continuous variables are presented as mean±SD or medians (interquartile range), as appropriate. Categorical data were summarized as number and percentage. Patient characteristics across the degree of severity of COVID-19 were compared using analysis of variance or the Kruskal–Wallis test for continuous variables and χ² or Fisher’s exact test for categorical variables. To explore the risk factors associated with the risk of progression to severe disease or death, logistic regression analysis was conducted to estimate OR and 95%CI. Considering the total number of severe cases (n=25) and deaths (n=12) in this study and to avoid overfitting in the model, two variables were chosen for multivariable analysis on the basis of previous findings and clinical constraints [10, 12, 18, 19]. We excluded variables from the univariable analysis if their between-group differences were not significant, if the number of events was too small to calculate odds ratios, and if they had colinearity with the SOFA score. A two-sided α of less than 0.05 was considered statistically significant. Statistical analyses were done using SPSS software, version 22.0.
Results

A total of 109 adult patients with COVID-19 were hospitalized in Dabieshan Medical Center from January 30, 2020 to February 11, 2020. After excluding one pregnant patient without available key information in their medical records, we included 108 inpatients in the final analysis. The degree of severity of COVID-19 was categorized as non-severe in 83 (76.9%) patients, severe-alive in 13 (12.0%) patients and severe-dead in 12 (11.1%) patients. The median age of 108 patients with COVID-19 was 52.0 years (IQR 37.0-58.0). The severe-dead patients (65.0, 51.0-73.5) were older than those severe-alive (56.0, 50.5-63.5) or non-severe patients (50.0, 34.0-56.0). The proportion of patients over 70 years old was the highest in the severe-dead group. The median time from illness onset to admission of all patients was 6 days (IQR 4,8), and there was no significant difference among the three groups.

Comorbidities were present in twenty-five (23.1%) patients, with hypertension being the most common comorbidity (14.8%), followed by diabetes (4.6%). The presence of any coexisting illness was more common among patients with severe disease than among those with non-severe disease (14.5% vs. 52%) (Table 1). Additionally, the advanced age, co-morbidities with hypertension, higher blood leukocyte count, neutrophil count, higher sensitive C-reactive protein level, D-dimer level, APECHE II score and SOFA score were associated with the development of severe COVID-19, and so were lower lymphocyte count and albumin level (shown in supplementary material).

Laboratory findings on hospital admission are summarized in Table 2. With the
illness deterioration, the white blood cell (WBC) count and neutrophils increased gradually in severe-dead patients. Lymphocytopenia was present in 25% of the patients. The median lymphoid count was $1.41 \times 10^9$ per L (1.01-1.77) in non-severe patients, while it decreased to less than $0.8 \times 10^9$ per L in severe patients. Approximately 40% patients (40/108) had an elevated D-dimer on admission. Compared with non-severe patients, the levels of D-dimer, high sensitive-C reaction protein, and procalcitonin were significantly higher in patients developing severe disease. There was no difference in alanine aminotransferase (ALT), Bilirubin (BIL), serum creatinine, cystatin c, creatine kinase, and creatine kinase isoenzyme-MB among three groups of patients. A total of 98 (90.7%) patients had findings of bilateral infiltrates on radiographic imaging, while 10 (9.3%) patients had unilateral infiltrates.

The main laboratory markers were tracked from day 4 to day 19 after the onset of disease at 2-day intervals (Figure 1). Data from 65 patients (44 non-severe, 11 severe-alive and 10 severe-dead) with complete data were analyzed. The baseline lymphocyte count in non-severe patients was significantly higher than severe-alive and severe-dead patients, and the lymphocyte count increased gradually in non-severe patients and severe-alive patients during hospitalization. However, the lymphocyte count decreased gradually in severe-dead patients, which was significantly less than $0.8 \times 10^9$ per L from day 10 after illness onset and continued to decrease until death. The WBC count, neutrophils count, levels of D-dimer and serum creatinine showed a significant rising trend during hospitalization in severe-dead patients compared with non-severe or severe-alive patients. Whereas the level of cystatin c in patients of three
groups had no significant difference on admission, it showed a significant increase in severe-dead patients on 10 days and 19 days after the onset of COVID-19.

All 108 patients received antivirals which was single or combined used, including α-interferon (50 ug twice daily, atomize), abidol (0.2 g twice daily, orally), and lopinavir/ritonavir tablets (500 mg twice daily, orally). More patients received corticosteroids, immunoglobulins and antibiotics in severe group than non-severe group. The development of sepsis, septic shock and ARDS in severe patients was higher than in non-severe patients, and so were acute kidney injury and myocardial injury. The median time from illness onset to discharge or death was 18 (16, 21) days in non-severe patients, 32 (28, 33) days in severe-alive patients and 25 (22, 31) days in severe-dead patients, respectively (Table 3).

Multivariable logistic regression analysis revealed that higher SOFA score (OR 2.450, 1.302–4.608; \( p=0.005 \)) and lymphocyte count less than \( 0.8 \times 10^9 \) per L (OR 9.017, 2.808–28.857; \( p<0.001 \)) on admission were associated with increased odds of the development of severe COVID-19 (Table 4). Additionally, the higher SOFA (OR 2.402, 1.313–4.395; \( p=0.004 \)) on admission was the independent risk factor for death (Table 5).

**Discussion**

This is a retrospective cohort study focusing on the risk factors associated with severe COVID-19. A total of 108 adults hospitalized with COVID-19 during January 31, 2020 to March 10, 2020 were included in this retrospective cohort study. In particular, the advanced age, co-morbidities with hypertension, higher blood
leukocyte count, neutrophil count, higher sensitive C-reactive protein level, D-dimer level, APECHE II score and SOFA score were more commonly seen in severe COVID-19 illness, and so were lower lymphocyte count and albumin level.

In the current study, the higher SOFA score at admission was also identified as an independent predictor for developing severe SARS-CoV-2 infection. The SOFA score was a morbidity severity score and was originally designed to focus on organ dysfunction and morbidity. It was made of 6 variables, and each representing an organ system [20]. But now, many studies have found that SOFA score can well predict the severity and outcome of the disease [21, 22]. SOFA score is also used to be a good diagnostic marker for sepsis and septic shock [15]. Of the 108 patients, 32.4% (35/108) developed sepsis, and 5.6% (6/108) developed septic shock. Additionally, the incidence of sepsis shock was as high as 50% in the dead patients. The result suggested that early organ dysfunction may be related to poor prognosis. In Bin C’s study, higher SOFA score was reported to be associated with increased odds of death [12]. Therefore, the early organ dysfunction in patients with COVID-19 should be paid more attention and monitored closely. APACHE II score is also an illness severity score and mortality estimation tool used widely in ICU [23]. In our study, APACHE II score in severe group was higher than non-severe group, and the difference was statistically significant. As the result of the small number of cases, the score was not included in the final multivariate regression analysis. Compared with the SOFA and APACHE II scores, the evaluation of NEWS and qSOFA was more convenient and fast [24], and even did not need laboratory examination. However, in
our study, these two scores did not show their advantages, and there was no significant difference between the severe and non-severe groups with COVID-19 at the time of admission.

Lymphocytopenia on admission was another risk factor associated with severe COVID-19 infection in this study. In the dynamic profile of laboratory markers as shown in Figure 1, we found that whereas absolute lymphocyte counts decrease to similarly low levels in severe-alive and severe-dead patients at the onset of COVID-19, absolute lymphocyte counts in severe-dead patients remained persistently low while severe-alive patients experience lymphocyte recovery. Additionally, white blood cells and neutrophils counts were significantly higher in non-survival patients with COVID-19. The findings were consistent with the results of two recent COVID-19 related studies [12, 25]. Lymphocytopenia is a common feature in the patients with COVID-19. In recent N. Zhong’s study, lymphocytopenia was present in 96.1% (147/153) of severe patients with COVID-19 [5]. Lymphocytopenia might serve as a biomarker for infection-induced immunosuppression and was a critical factor associated with some disease severity and mortality. Studies have shown that persistent lymphocytopenia in sepsis predicts early and late mortality [26, 27]. The initial fall in circulating lymphocytes at the onset of SARS-COV-2 infection might be related to separate processes. Firstly, lymphocytes were recruited out of the peripheral circulation to areas of infection and inflammation. Autopsy report of patients with COVID-19 showed that lymphocyte - dominated interstitial inflammatory exudation in both lungs [28]. And secondly, SRAS-CoV-2, might similar to SARS and MERS,
induced a number of stimuli that trigger lymphocyte apoptosis [18, 29]. The exact mechanism of lymphocytopenia needs further study.

In our study, patients with severe disease were significantly older than non-severe patients, and had more comorbid conditions. This suggests that patients who were older and have underlying disease were at a higher risk of developing severe illness. This finding has been widely confirmed in several previous studies related COVID-19 [9-11]. In previous SARS and MERS studies, older age related to death may be due to less robust immune responses [30]. Some animal studies also confirmed that older animals developed more severe responses to virus infections because of the senescence changes to the immune system [31]. Further studies are needed to find out how the immune system responds to viral attacks in elderly patients.

In this study, more than 70% of patients had increased cystatin c on admission. Whereas the level of cystatin c in patients of three groups had no significant difference on admission, it showed a significant increase in severe-dead patients about 10 days after the onset of COVID-19. Additionally, the level of cystatin c levels did not return to normal in most of the cure cases at the time of discharge. The cystatin c was not affected by age, gender, muscle mass, inflammation and other factors. As a result of good specificity and sensitivity, cystatin c appeared to be a more reliable in predicting AKI than serum creatinine [32-34]. It suggested that the extensive renal damage may be existed in patients with COVID-19. Additionally, regular monitoring of renal function in discharged patients might be necessary. This would help us to fully evaluate the damage of the virus to the kidney.
Among our cohort of 108 patients with COVID-19, 14.8% of patients had AKI, 7.2% of patients had acute cardiac injury. The incidence of complications in patients with COVID-19 reported in several recently published clinical studies was different, ranging from 0.5% to 29% of AKI [5, 12, 25, 35], 1% to 17% of acute cardiac injury [12, 25], and the incidence was significantly higher in severe or dead patients than non-severe patients. The current evidence revealed that 2019-nCoV RBD has a stronger interaction with angiotensin converting enzyme 2 (ACE2) [36]. In addition to pulmonary AT2 cells and respiratory epithelial cells exhibit high ACE2 expression, AT2 cells, proximal tubule cells of kidney, myocytes, vascular endothelial cells and gastrointestinal system also have high ACE2 expression [37]. In addition to the direct attack on the target organ by SARS-CoV-2, immune mediated organ injury was also one of the main causes of multiple organ dysfunction, including ARDS, acute cardiac injury, acute kidney injury and gastrointestinal injury.

This study has some notable limitations. First, since the retrospective study design, not all patients could have been continuously tested. Since the whole course of illness could not be evaluated dynamically, we could not find the effect of dynamic changes of some important indexes on the prognosis of the COVID-19. Unfortunately, dynamic monitoring is more meaningful for disease assessment and prediction. Second, this is a single-center study with limited sample size. To avoid overfitting in the multivariable logistic regression models, only two variables were chosen to analysis. A global multi-center study of patients with COVID-19 would help to fully understand the new disease for human. At last but not least, there is no assessment of
the follow-up effect of the SARS-CoV-2 on discharged patients, although patients in this study were thought to have definite outcomes. As far, the duration of SARS-CoV-2 RNA detection has not been well characterized. Therefore, further follow-up study is needed.

In conclusion, the higher SOFA score and Lymphocyte count less than $0.8 \times 10^9$ per L on admission was associated with greater risk of developing severe COVID-19. Therefore, the patients with high risk should be paid more attention, monitored closely and timely treatment, which may help to improve the prognosis.

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Contribution statement

QY, PW, XW, WL and MD collected the epidemiological and clinical data. LK and XT processed statistical data. QY, PW, XB and GQ drafted the manuscript. YC and MM revised the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Figure 1. Dynamic Profile of Laboratory Markers in 65 Patients with COVID-19 (44 non-severe, 11 severe-alive and 10 severe-dead) from Illness Onset.

Figure shows temporal changes in white blood cell (A), neutrophils (B), lymphocytes (C), cystatin c (D), serum creatinine (E), and D-dimer (F).

Abbreviations: COVID-19, coronavirus disease 2019.

a $P < 0.05$ for non-severe vs severe-dead.
Table 1. Demographic and Clinical Characteristics of 108 Patients Infected with COVID-19 in Huanggang, China. Values are numbers (percentages) unless stated otherwise.

| Characteristics                          | All patients N=108 | Non-severe N=83 | Severe-alive N=13 | Severe-dead N=12 | P value |
|------------------------------------------|--------------------|-----------------|-------------------|-----------------|---------|
| Age                                      |                    |                 |                   |                 |         |
| Median(IQR),yr                           | 52.0 (37.0-58.0)   | 50.0 (34.0-56.0)| 56.0 (50.5,63.5)  | 65.0 (51.0,73.5)| <0.001  |
| ≤18                                      | 1(0.9)             | 1(1.2)          | 0                 | 0               | -       |
| 19-40                                    | 31(28.7)           | 30(36.1)        | 1(7.7)            | 0               | 0.006   |
| 41-65                                    | 59(54.6)           | 44(53.0)        | 9(69.2)           | 6(50.0)         | 0.520   |
| 66-70                                    | 7(6.5)             | 5(6.0)          | 1(7.7)            | 1(8.3)          | 0.941   |
| ≥70                                      | 10(9.3)            | 3(3.6)          | 2(15.4)           | 5(41.7)         | 0.001   |
| Sex                                      |                    |                 |                   |                 |         |
| Male                                     | 43(39.8)           | 30(36.1)        | 6(46.2)           | 7(58.3)         | 0.307   |
| Female                                   | 65(60.2)           | 53(63.9)        | 7(53.8)           | 5(41.7)         | -       |
| Comorbidity                              |                    |                 |                   |                 |         |
| Hypertension                             | 25(23.1)           | 12(14.5)        | 5(38.5)           | 8(66.7)         | <0.001  |
| Diabetes                                 | 5(4.6)             | 2(2.4)          | 2(15.4)           | 1(8.3)          | 0.166   |
| Pulmonary diseasea                        | 3(2.8)             | 3(3.6)          | 0                 | 0               | -       |
| Cardiovascular diseas                     | 4(3.7)             | 2(2.4)          | 0                 | 2(16.6)         | -       |
| Chronic liver disease                    | 2(1.9)             | 1(1.2)          | 0                 | 1(8.3)          | -       |
| Cancer                                   | 2(1.9)             | 0(0)            | 1(7.7)            | 1(1.9)          | -       |
| Current smoker                           |                    |                 |                   |                 |         |
| Yes                                      | 4(3.7)             | 1(1.2)          | 0                 | 3(25.0)         | -       |
| Time from symptom onset to admission, median (IQR)d | 6(4,8) | 5(4,8) | 6(4,8) | 7(6,9) | 0.581 |
| Fever                                    |                    |                 |                   |                 |         |
| Any                                      | 80(74.1)           | 61(73.5)        | 11(84.6)          | 8(66.7)         | 0.574   |
| 37.3-38.0°C                              | 34(31.5)           | 26(31.3)        | 6(46.2)           | 2(16.7)         | 0.274   |
| 38.1-39.0°C                              | 34(31.5)           | 27(32.5)        | 4(30.8)           | 3(25.0)         | 0.865   |
| >39.0°C                                  | 10(9.3)            | 6(7.2)          | 1(7.7)            | 3(25.0)         | 0.222   |
| Dry cough                                | 84(77.8)           | 65(78.3)        | 9(69.2)           | 10(83.3)        | 0.678   |
| Expectoration                            | 34(31.5)           | 26(31.3)        | 3(23.1)           | 5(41.7)         | 0.606   |
| Myalgia or fatigue                       | 28(25.9)           | 20(24.1)        | 4(30.8)           | 4(33.3)         | 0.732   |
| Symptom                  | COVID-19 | Control     | COVID-19   | Control     | p-value |
|--------------------------|----------|-------------|------------|-------------|---------|
| Dyspnea                  | 15(13.9) | 6(7.2)      | 3(23.1)    | 6(50.0)     | 0.001   |
| Headache                 | 1(0.9)   | 1(1.2)      | 0          | 0           | -       |
| Diarrhea                 | 8(7.5)   | 6(7.3)      | 1(7.7)     | 1(8.3)      | 0.992   |
| Heart rate, median (IQR), bpm | 86(79.94) | 86(80.97) | 86(80.87) | 78(75.90) | 0.136   |
| Respiratory rate, median (IQR) | 20(19.21) | 20(18.21) | 20(19.22) | 20(19.22) | 0.364   |
| Mean arterial pressure <65mmHg | 0          | 0           | 0          | 0           | -       |
| NEWS2, median (IQR)      | 1(0.3)   | 1(0.2)      | 2(1.3)     | 3(0.6)      | 0.197   |
| APECHEII score, median (IQR) | 4(3,7) | 4(2.6)      | 6(4,8)     | 10(6.19)    | <0.001  |
| qSOFA score, median (IQR) | 0(0,0)   | 0(0,0)      | 0(0,0.5)   | 0(0,1)      | 0.936   |
| SOFA Score, median (IQR) | 1(1,2)   | 1(1,1)      | 2(1,3)     | 3(2,8)      | <0.001  |

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; NEWS2, National Early Warning Score 2; APECHII, Acute Physiology and Chronic Health Evaluation II; SOFA, Sequential Organ Failure Assessment; qSOFA, quick SOFA.

a Any patient with bronchiectasis, chronic obstructive pulmonary disease, or asthma.

b Any patient with hyperlipemia, coronary heart disease, hemorrhagic stroke, or ischemic stroke.
Table 2. Laboratory and chest radiography findings of 108 patients with COVID-19 in Huanggang, China. Values are numbers (percentages) unless stated otherwise.

| Characteristics                  | All patients N=108 | Non-severe N=83 | Severe-alive N=13 | Severe-dead N=12 | P value  |
|----------------------------------|--------------------|-----------------|------------------|-----------------|----------|
| White blood cell count (×10^9/L) | 4.83 (3.76,6.65)   | 4.65 (3.72,5.68)| 5.57 (3.0,9.16)  | 10.53 (6.57,11.9)| <0.001   |
| <4                               | 32(29.6)           | 27(32.5)        | 4(30.8)          | 1(8.3)          | 0.236    |
| 4-10                             | 64(59.3)           | 55(66.3)        | 7(53.8)          | 2(16.7)         | 0.005    |
| >10                              | 12(11.1)           | 1(1.2)          | 2(15.4)          | 9(75.0)         | <0.001   |
| Neutrophil count (×10^9/L)       | 2.82 (1.93,4.47)   | 2.53 (1.89,3.78)| 3.33 (1.99,5.07) | 6.55 (3.39,9.66)| 0.002    |
| Lymphocyte count (×10^9/L)       | 1.26 (0.82,1.68)   | 1.41 (1.01,1.77)| 0.79 (0.64,0.95) | 0.76 (0.63,1.58)| <0.001   |
| <0.8                             | 23(21.7)           | 10(12.2)        | 8(61.5)          | 5(45.5)         | <0.001   |
| >0.8                             | 85(77.4)           | 72(87.8)        | 6(38.5)          | 7(54.5)         | <0.001   |
| Haemoglobin (g/L)                | 125(116,135)       | 127(116,136)    | 117(115,130)     | 124(122,133)    | 0.278    |
| Platelet count (×10^9/L)         | 187(139,239)       | 195(148,239)    | 145(111,193)     | 159(137,200)    | 0.225    |
| <100                             | 10(9.3)            | 6(7.3)          | 3(23.1)          | 1(8.3)          | 0.181    |
| Normal, 100-400                  | 97(90.7)           | 76(92.6)        | 10(76.9)         | 11(91.7)        | 0.181    |
| >400                             | 1(0.9)             | 0               | 0                | 1(8.3)          | -        |
| D-dimer (ug/ml)                  | 1.55 (0.71,2.88)   | 1.28 (0.61,2.69)| 2.16 (0.98,2.67) | 15.89 (2.75,81.59)| <0.001   |
| >1                               | 40(37.0)           | 26(31.3)        | 5(38.5)          | 9(75.0)         | 0.014    |
| <1                               | 68(63.0)           | 57(68.7)        | 8(61.5)          | 3(25.0)         | -        |
| ALT (U/L)                        | 20.0 (14.0,29.5)   | 20.0 (14.0,30.0)| 23.0 (17.8,27.5) | 21.5 (17.5,23)  | 0.660    |
| >50                              | 6(5.6)             | 4(4.8)          | 0(0)             | 2(16.7)         | -        |
| Normal, 0-50                     | 102(94.4)          | 79(95.2)        | 13(100)          | 10(83.3)        | -        |
| Albumin (g/L)                    | 38.6 (35.5,41.4)   | 39.5 (37.3,42.1)| 37.7 (34.5,39.3) | 31.6 (27.8,33.8)| <0.001   |
| Bilirubin (μmmol/L)              | 10.1(7.6,14.3)     | 9.7(8.0,13.3)   | 12.7(8.4,15.0)   | 9.9(7.4,21.5)   | 0.690    |
| >20                              | 13(12.0)           | 7(8.4)          | 2(15.4)          | 4(33.3)         | 0.028    |
| Normal, 0-20                     | 95(88.0)           | 76(91.6)        | 11(84.6)         | 8(66.7)         | -        |
| K+ (mmol/L)                      | 4.11(3.8,4.6)      | 4.2(3.9,4.6)    | 3.6(3.5,4.0)     | 4.3(3.6,4.8)    | 0.033    |
| >5.4                             | 9(8.3)             | 7(8.4)          | 0(0)             | 2(16.7)         | -        |
| Normal, 3.8-5.4                  | 78(72.2)           | 67(80.7)        | 5(38.5)          | 6(50.0)         | 0.001    |
| <3.8                             | 21(19.4)           | 9(10.8)         | 8(61.5)          | 4(33.3)         | <0.001   |
| Na+ (mmol/L)                     | 138(136,141)       | 138(137,141)    | 136(133,139)     | 138(137,139)    | 0.078    |
| 136-148                          | 93(86.1)           | 76(91.6)        | 7(53.8)          | 10(83.3)        | 0.002    |
| Condition | Value (Mean, Range) | Value (Mean, Range) | Value (Mean, Range) | Value (Mean, Range) | Value (Mean, Range) |
|-----------|--------------------|--------------------|--------------------|--------------------|--------------------|
| Cl (mmol/L) | 96.2 (95.3, 100.5) | 96.0 (95.3, 100.3) | 96.4 (95.0, 100.5) | 98.4 (96.5, 103.0) | 0.201 |
| Creatinine (μmol/L) | 79.6 (67.1, 95.1) | 78.8 (68.4, 94.3) | 60.0 (54.0, 84.6) | 90.5 (74.7, 110.6) | 0.243 |
| Cystatin c (mg/L) | 1.42 (1.19, 1.74) | 1.38 (1.19, 1.71) | 1.43 (1.28, 1.89) | 1.61 (1.25, 2.80) | 0.843 |
| Creatine kinase (U/L) | 64.0 (43.0, 105.0) | 60.0 (42.0, 94.0) | 107.0 (54.0, 157.5) | 103.9 (63.5, 125.7) | 0.126 |
| Procalcitonin (ng/mL) | 0.2 (0.09, 0.40) | 0.20 (0.06, 0.3) | 0.19 (0.13, 0.43) | 2.06 (0.27, 5.93) | 0.002 |
| Bilateral pneumonia | 98 (90.7) | 73 (67.6) | 13 (100.0) | 12 (100.0) | 0.293 |

Abbreviations: COVID-19, coronavirus disease 2019; ALT, alanine amino transferase; CK-MB, creatine kinase isoenzyme-MB; HS-CRP, high sensitive c reaction protein.

*a*Any patient with a chest radiograph or CT imaging of pulmonary infections manifested single lung shadowing.

*b*Any patient with a chest radiograph or CT imaging of pulmonary infections
manifested double lung shadowing.
Table 3. Treatments and Prognosis in Patients with COVID-19 in Huanggang, China.

Values are numbers (percentages) of patients.

| Treatments and prognosis                  | All patients N=108 | Non-severe N=83 | Severe-alive N=13 | Severe-dead N=12 | P Value   |
|------------------------------------------|--------------------|----------------|------------------|------------------|-----------|
| **Treatments**                           |                    |                |                  |                  |           |
| Antiviral treatment                      | 108(100)           | 83(100.0)      | 13(100.0)        | 12(100.0)        | -         |
| Corticosteroids                          | 30(27.8)           | 10(12.0)       | 10(76.9)         | 10(83.3)         | <0.001    |
| Intravenous immunoglobulin              | 12(11.1)           | 3(3.6)         | 6(46.2)          | 3(25.0)          | <0.001    |
| Antibiotics                              | 48(44.4)           | 26(31.3)       | 10(76.9)         | 12(100.0)        | <0.001    |
| **Respiratory therapy**                  |                    |                |                  |                  |           |
| Nasal or mask oxygen                     | 27(25.0)           | 20(24.1)       | 7(53.8)          | 0(0)             | 0.003     |
| High-flow nasal cannula oxygen therapy   | 4(3.7)             | 0(0)           | 4(30.8)          | 0(0)             | -         |
| NIV                                      | 4(3.7)             | 0(0)           | 2(15.4)          | 2(16.7)          | -         |
| MV                                       | 10(9.3)            | 0(0)           | 0(0)             | 10(83.3)         | -         |
| CRRT                                     | 1(0.9)             | 0(0)           | 0(0)             | 1(8.3)           | -         |
| ECMO                                     | 0                  | 0              | 0                | 0                | -         |
| **Prognosis**                            |                    |                |                  |                  |           |
| Sepsis                                   | 35(32.4)           | 17(20.5)       | 7(53.8)          | 11(91.7)         | <0.001    |
| Sepsis shock                             | 6(5.6)             | 0(0)           | 0(0)             | 6(50.0)          | -         |
| ARDS                                     | 45(41.7)           | 20(24.1)       | 13(100.0)        | 12(100.0)        | <0.001    |
| AKI                                      | 16(14.8)           | 7(8.4)         | 2(15.4)          | 7(58.3)          | <0.001    |
| Acute cardiac injury                     | 8(7.2)             | -              | 2(15.4)          | 6(50.0)          | -         |
| ICU admission                             | 17(15.7)           | 0(0)           | 5(38.5)          | 12(100.0)        | <0.001    |
| Time from symptom onset to sepsis shock, median (IQR),d | 20(17,24)         | -              | -                | 20(17,24)        | -         |
| Time from symptom onset to ARDS          | 7(5,9)             | 7(4,8)         | 8(6,11)          | 7(4,7)           | 0.176     |
| Time from symptom onset to MV, median (IQR),d | 15(11,18)         | -              | -                | 15(11,18)        | -         |
| Time from symptom onset to AKI, median (IQR),d | 7(6,8)            | 6(6,8)         | 7(7,8)           | 7(6,10)          | 0.443     |
| Time from symptom onset to acute cardiac injury, median (IQR), d | 12(11,14) | - | - | 12(11,14) | - |
| Time from symptom onset to ICU admission, median (IQR), d | 13(10,17) | - | 12(8,13) | 16(11,19) | 0.221 |
| Time from symptom onset to discharge or death, median (IQR), d | 19(16,25) | 18(16,21) | 32(28,33) | 25(22,31) | <0.001 |

Abbreviations: COVID-19, coronavirus disease 2019; NIV, Non-invasive mechanical ventilation; MV, invasive mechanical ventilation; CRRT, Renal replacement therapy; ECMO, extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; IQR, inter quartile range; NIV, invasive mechanical ventilation.
Table 4. Multivariable Logistic Regression Analysis of Risk Factors for the 25 Patients with Severe COVID-19.

| Risk factors                                    | Odds Ratio | 95% CI         | P Value |
|-------------------------------------------------|------------|----------------|---------|
| SOFA                                            | 2.450      | 1.302-4.608    | 0.005   |
| Lymphocyte count less than 0.8×10⁹ per L        | 9.017      | 2.808-28.957   | <0.001  |

Abbreviations: COVID-19, coronavirus disease 2019; SOFA, Sequential Organ Failure Assessment; CI, confidence interval.
Table 5. Multivariable Logistic Regression Analysis of Risk Factors for death in patients with COVID-19.

| Risk factors                               | Odds Ratio | 95% CI      | P Value |
|--------------------------------------------|------------|-------------|---------|
| SOFA                                       | 2.402      | 1.313-4.395 | 0.004   |
| Lymphocyte count less than 0.8×10⁹ per L   | 4.000      | 0.800-20.012| 0.091   |

Abbreviations: COVID-19, coronavirus disease 2019; SOFA, Sequential Organ Failure Assessment; CI, confidence interval.