

# Important scoring systems for assessing the severity of COVID-19 based on COVID-19-related deaths in Wuhan, China

Feihong Yang, Hao Zou, Jiaohong Gan, Zhongxiang Zhang, Yan Zhao, Cheng Jiang\*, Jian Xia\*

## Abstract

**Background:** This study aimed to investigate the clinical characteristics of 21 deaths and evaluate potential factors affecting disease severity and mortality risk in patients with coronavirus disease (COVID-19).

**Methods:** This retrospective analysis assessed clinical data of 21 patients who died owing to COVID-19. Disease severity and mortality risk were assessed using Acute Physiology and Chronic Health Evaluation II (APACHE II); Sepsis-related Organ Failure Assessment (SOFA); multilobular infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hypertension and age (MuLBSTA); and pneumonia severity index (PSI) scores.

**Results:** The mean age of the patients was  $66 \pm 14$  years and 15 (71.4%) patients were men. Sixteen (76.2%) patients had chronic medical illnesses. Twelve (57.1%) patients were overweight. Decreased lymphocyte proportions were observed in 17 (81.0%) patients on admission. Elevated D-dimer levels were observed in 11 (52.4%) patients, and the levels significantly increased when pneumonia deteriorated. The initial APACHE II and SOFA scores demonstrated that 18 (85.7%) and 13 (61.9%) patients, respectively, were in the middle-risk level. MuLBSTA and PSI scores after admission were associated with higher risks of mortality in 13 (61.9%) patients. Most patients developed organ failure and subsequently died.

**Conclusions:** Older, overweight, male patients with a history of chronic illnesses and continuously decreased lymphocyte proportions and increased D-dimer levels might have higher risks of death owing to COVID-19. The combination of general scoring (SOFA) and pneumonia-specific scoring (MuLBSTA and PSI) systems after admission might be sensitive in assessing the mortality risk of patients with COVID-19 who are in critical condition.

**Keywords:** Acute respiratory distress syndrome, COVID-19, Mortality risk, Severity

## Introduction

Coronavirus disease (COVID-19) is an infectious disease that emerged in early December 2019. On January 20, 2020, the National Health Commission (NHC) of China reported that COVID-19 could spread from person to person via the respiratory routes. As of March 24, 2020, more than 370,000 patients had contracted this disease worldwide. Severe acute respiratory syndrome coronavi-

rus 2 (SARS-CoV-2), the virus causing COVID-19, was also found to cause acute respiratory distress syndrome (ARDS), myocardial injury, kidney and liver damage, coagulation abnormality,<sup>[1,2]</sup> and central nervous system lesions (confirmed but unpublished by Beijing Ditan Hospital). These combined organ dysfunctions accelerate disease progression and can lead to death.<sup>[1,3]</sup> SARS-CoV-2 infection resulted in more than 18,000 deaths worldwide by March 24, 2020. The two homologous coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), have caused more than 1700 deaths in the past two decades, with mortality rates of more than 10% owing to SARS and 37% owing to MERS.<sup>[4]</sup> SARS-CoV-2 seems to have a stronger infectivity and relatively weaker lethality than SARS-CoV and MERS-CoV.

In a recent single-center study, SARS-CoV-2 infection resulted in a mortality rate of up to 61.5% in critically ill patients.<sup>[1]</sup> Another single-center study reported the potential relationship between older age, respiratory failure, and multiorgan dysfunction and SARS-CoV-2-related mortality.<sup>[5]</sup> One multicenter retrospective cohort study analyzed risk factors for death in adults with COVID-19 and identified that older age, elevated D-dimer levels, and higher Sepsis-related Organ Failure Assessment (SOFA) scores on admission were associated with higher risks of in-hospital mortality.<sup>[2]</sup> These studies helped clinicians understand the clinical features of death cases and probable risk factors of mortality in patients with

FY and HZ contributed equally to this work.

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Emergency Center, Zhongnan Hospital of Wuhan University, 169 Donghu Road, Wuhan, Hubei, China.

\*Corresponding author. Address: Emergency Center, Zhongnan Hospital of Wuhan University, 169 Donghu Road, Wuhan, Hubei 430071, China. E-mail address: jianjian\_1998@sina.com (J. Xia); chengjiang@whu.edu.cn (C. Jiang).

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COVID-19 to some extent. However, because of the COVID-19 pandemic and the relatively insufficient medical resources worldwide, we need to determine some useful methods or assessment tools to identify the severity and mortality risk in patients with COVID-19 as early as possible.

The present study intended to investigate the clinical characteristics of 21 deaths and evaluate potential factors affecting disease severity and mortality risk in patients with COVID-19. Clinical characteristics and several influential factors are herein presented. Disease severity and mortality risk were assessed using different scoring systems, which could suggest a more cautious assessment and identification in the early phase of the disease. Thus, more intensive care and beneficial treatment may be offered to certain individuals at high risks of progressing quickly to critical cases to reduce mortality and disability rates.

## Methods

### Study design and participants

In this retrospective, descriptive, single-center study, we enrolled 21 patients admitted to the emergency intensive care unit (EICU) of Zhongnan Hospital of Wuhan University from January 3, 2020 to February 15, 2020. Zhongnan Hospital of Wuhan University is one of the major COVID-19-designated hospitals. All patients included in this study were diagnosed as having COVID-19 based on laboratory tests according to the World Health Organization interim guidance.<sup>[6]</sup> The study was approved and written informed consent was waived by Zhongnan Hospital Ethics Committee (No. 2020005-1K), owing to the rapid emergence of this infectious disease. However, these cases have not been reported in any other publications.

### Procedures and data collection

We collected and scanned electronic medical records of the 21 patients who died. Demographic, epidemiological, clinical, laboratory, and radiological characteristic; treatment; and outcome data, as well as nursing records, were obtained and reorganized using a standardized data collection form (a modified form for severe acute respiratory infection clinical characterization shared by the International Severe Acute Respiratory and Emerging Infection Consortium). The key duration from the first symptom to death was recorded. Disease severity and organ dysfunction were assessed. Acute Physiology and Chronic Health Evaluation II (APACHE II); SOFA; multilobar infiltration, hypo-lymphocytosis, bacterial coinfection, smoking history, hypertension and age (MuLBSTA); and pneumonia severity index (PSI) scores were calculated according to accepted standards upon admission. Two advanced physicians or radiologists reviewed the data (including images) to ensure accuracy.

### Outcomes

The primary outcomes were early evaluations of disease severity and mortality risk using standard scoring systems. Various original and statistical data or images described in the abovementioned procedures were also summarized

and analyzed. All the data were objectively gathered and certified.

### Statistical analysis

Continuous variables are described as mean  $\pm$  standard deviation or median (25%–75% interquartile range) and categorical variables as numbers (percentages). All statistical analyses were performed using SPSS software (version 25.0, IBM Inc, New York, USA).

## Results

### Baseline characteristics and pre-hospital treatment

The study included 21 death cases with confirmed COVID-19, none of which had any exposure history to the Huanan Seafood Market. As shown in Table 1, the mean age of the patients was  $66 \pm 14$  years, and 10 (47.6%) patients were older than 70 years. Fifteen (71.4%) patients were men. Twelve (57.1%) patients were overweight based on their body mass index. Among the 21 patients, 16 (76.2%) had coexisting chronic medical illnesses, and 9 patients had more than one illness. Before admission, the most common symptoms were fever ( $n=18$ , 85.7%), shortness of breath ( $n=16$ , 76.2%), and dry cough ( $n=11$ , 52.4%). Among patients with fever, four (19.0%) had a highest temperature of under  $38.0^{\circ}\text{C}$ , six (28.6%) in the  $38.1$ – $39.0^{\circ}\text{C}$  range, and four (19.0%) above  $39.0^{\circ}\text{C}$  before admission. The temperatures of the other four (19.0%) patients with fever were vague and thus were not included in the analysis. Fourteen (66.7%) patients were normothermic on admission. Nineteen (90.5%) patients received treatment in the outpatient department because of a lack of beds, and one (4.8%) patient accepted residential treatment in another hospital before admission. Thirteen (61.9%) of those patients were treated with antibiotic drugs, 8 (38.1%) with antiviral drugs, 1 (4.8%) with systemic corticosteroids, and 1 (4.8%) with immunoglobulins. In this study, the duration from the first symptoms to admission was  $5 \pm 3$  days. Nineteen (90.5%) patients were classified as having severe status and 2 (9.5%) as critical status on admission according to the guidelines for the diagnosis and treatment of COVID-19 (7<sup>th</sup> edition) published by NHC. Most patients had tachypnea with a respiratory rate of  $24 \pm 6$  breaths/min, and two (9.5%) patients were aged over 30 years. We also analyzed images of patients within 24 h before or immediately after admission to ascertain if there were any pulmonary lesions before treatment initiation. All 21 patients showed multiple bilateral ground-glass opacities on computer tomography or X-ray. Bilateral injuries from the superior to inferior lobes were observed in 19 (90.5%) patients. The remaining two patients showed abnormalities in either the superior or the inferior fields. The affected area of 12 (57.1%) patients exceeded 50% of the total area, showing extensive effusion and consolidation.

### Vital laboratory parameters and imaging features

On admission, the leukocyte counts were below the normal range in 8 (38.1%) patients and above the normal range in 3 (14.3%) patients (Table 2). Procalcitonin,

**Table 1**  
**Baseline Clinical Characteristics on Admission of 21 Patients with Confirmed COVID-19**

Clinical Characteristics	Patients (n=21)
Age, years	66 ± 14
Sex	
Male	15 (71.4%)
Female	6 (28.6%)
History of smoking	
Positive	3 (14.3%)
Negative	18 (85.7%)
Body mass index, kg/m <sup>2</sup>	25.1 ± 4.5
<18.5	2 (9.5%)
18.5–23.9	7 (33.3%)
>23.9	12 (57.1%)
Chronic medical illness	
Cardiovascular diseases	9 (42.9%)
Urinary system diseases	5 (23.8%)
Cerebral vascular diseases	4 (19.0%)
Lung diseases	4 (19.0%)
Diabetes mellitus	3 (14.3%)
Major symptoms on admission	
Fever	18 (85.7%)
Shortness of breath	16 (76.2%)
Dry cough	11 (52.4%)
More than one sign and symptom	19 (90.5%)
Fever, dry cough, and shortness of breath	7 (33.3%)
Highest temperature before admission	38.6 ± 0.6
<37.3°C	3 (14.3%)
37.3–38°C	4 (19.0%)
38.1–39°C	6 (28.6%)
>39°C	4 (19.0%)
Missing	4 (19.0%)
Fever on admission	
Yes	7 (66.7%)
No	14 (33.3%)
Treatment before admission	
Outpatient service	19 (90.5%)
Hospitalization elsewhere	1 (4.8%)
Antibiotic therapy	13 (61.9%)
Antiviral therapy	8 (38.1%)
Systemic corticosteroid therapy	1 (4.8%)
Immunoglobulin therapy	1 (4.8%)
No treatment	1 (4.8%)
Days from first symptoms to admission	5 ± 3
Days from first symptoms to death	18 ± 8
Days from admission to death (hospital stay)	12 (8–17)
Days from admission to noninvasive ventilation	1 (0–5)
Days from admission to invasive ventilation	4 ± 3
Days from invasive ventilation to death	8 ± 5
Disease severity status	
Severe	19 (90.5%)
Critical	2 (9.5%)
Respiratory rate on admission (times/min)	24 ± 6
>30 times/min	2 (9.5%)
Imaging features on admission	
Bilateral involvement	21 (100.0%)
All fields	19 (90.5%)
Upper fields	1 (4.8%)
Lower fields	1 (4.8%)
Involved area > 50%	12 (57.1%)
Involved area < 50%	9 (42.9%)

interleukin-6 (IL-6), and C-reactive protein levels were generally higher than normal. The leukocyte and neutrophil counts increased in accordance with infectious indicators when co-infected with a bacterial outbreak. A

lymphocyte count of  $0.7 \pm 0.5 \times 10^9$  cells/L, which was below the normal range, was observed in 17 (81.0%) patients on admission. Platelet counts were below the normal range in 11 (52.4%) patients. The lymphocyte proportions and platelet counts decreased gradually with the progression of inflammation (Fig. 1), which is a feature of COVID-19 in this study. Decreased albumin levels were observed in most patients. Biomarkers reflecting organ function are shown in Table 2. The maximum high-sensitivity troponin I level exceeded 50,000 pg/mL in a patient with acute myocardial infarction. Prothrombin time (PT) increased to a relatively higher level as the condition worsened (Fig. 1). Eleven (52.4%) patients had elevated serum D-dimer levels on admission, and the proportion of patients increased to 100% when pneumonia deteriorated.

Chest computer tomography or radiography was conducted at approximately 3-day intervals. Representative radiologic findings of two patients are presented in Figure 2. On admission, multiple ground-glass opacities and exudations appeared in the bilateral subpleural areas. Lesions expanded rapidly within several days and manifested as ground-glass opacity and air bronchograms coexisting with extensive consolidation or fibrous stripes. A white lung appearance could be seen in each case during end-stage COVID-19.

### Severity of illness scores

In this study, we evaluated the severity, progression, and prognosis of patients' condition by dynamically determining APACHE II, SOFA, MuLBSTA, and PSI scores. In Table 3, we present different values of the four scores after admission, before ventilation, and the maximum value during the course. The initial APACHE II and SOFA scores were  $14 \pm 3$  and 7 (5–8), respectively. Furthermore, the initial APACHE II and SOFA scores demonstrated that 18 (85.7%) and 13 (61.9%) patients, respectively, were in the middle-risk level. Both APACHE II and SOFA scores increased before ventilation, and more patients reached high-risk levels with the deterioration of patients' condition and the urgent requirement for noninvasive or invasive ventilation. We found that 13 patients had MuLBSTA scores >12 on admission, which predicted a high risk of death. However, no significant fluctuation in the MuLBSTA score was observed from admission to ventilation. Similar changes in PSI scores were observed. The PSI score was 137 (102–146) after admission and 138 (125–157) before ventilation, with 13 (61.9%) patients having a PSI score over 130 in the high-risk level in both stages. All four scores were maximum just before death, including those in the same 19 (90.5%) patients at each high-risk level, with a median APACHE II score of 24 (22–32), SOFA score of 14 (12–16), MuLBSTA score of 15 (13–16), and PSI score of 163 (149–185) implying very high mortality.

### Main interventions and complications

Patients with COVID-19 were treated in isolation. According to the guidelines of NHC, all patients received antiviral treatments, including intravenous potassium sodium dehydroandroan drographolide succinate and

**Table 2**  
**Laboratory Results of 21 Patients Including the Baseline Values on Admission and the Maximum, Minimum Values During Hospitalization**

Laboratory Findings	Admission	Increase/Decrease (n=21)	Maximum	Minimum
WBC (×10 <sup>9</sup> /L, 3.5–9.5)	10.5±8.2	8 (38.1%) / 3 (14.3%)	20.8±8.4	7.7±5.1
Lymphocytes (×10 <sup>9</sup> /L, 1.1–3.2)	0.7±0.5	0 / 17 (81.0%)	1.3±0.9	0.3±0.3
Lymphocyte proportion (%),20.0–40.0)	9.9±7.8	0/19 (90.5%)	11.7±8.1	2.3±1.6
Neutrophils (×10 <sup>9</sup> /L, 1.8–6.3)	9.2±7.9	10 (47.6%) / 0	19.3±8.3	6.6±4.6
Hemoglobin (g/L, 115–150)	129.1±24.4	3 (14.3%) / 4 (19.0%)	134.4±24.5	108.0±26.1
Platelets (×10 <sup>9</sup> /L, 125–350)	140±66.2	0 / 11 (52.4%)	173.2±74.1	70.9±54.1
PCT (ng/mL, 0–0.05)	3.1±5.6	21 (100.0%) / 0	11.3±14.8	1.1±1.9
IL-6 (pg/mL, 0–7)	77.0±23.7	5/5 (100%) / 0	472.5±405.8	33.3±20.5
CRP (mg/L, 0–10)	125.4±74.0	20 (95.2%) / 0	230.9±107.0	88.9±85.6
ALT (U/L, 7–45)	38.8±20.1	7 (33.3%) / 0	125.1±237.7	22.6±10.8
AST (U/L, 13–35)	66.0±33.9	16 (76.2%) / 0	309.6±733.5	33.6±18.1
Total bilirubin (μmol/L, 5–21)	16.6±6.7	6 (28.6%) / 0	30.1±16.4	13.6±6.1
Direct bilirubin (μmol/L, 0–7)	8.4±5.0	9 (42.9%) / 0	16.4±11.4	4.9±3.1
Total protein (g/L, 65–85)	61.2±8.1	0 / 14 (66.7%)	65.8±7.8	53.6±7.1
Albumin (g/L, 40–55)	32.1±5.6	0 / 20 (95.2%)	34.9±3.4	25.2±4.6
Glucose (mmol/L, 3.9–6.1)	9.9±6.1	15 (71.4%) / 1 (4.8%)	15.7±7.1	7.9±2.9
Urea (mmol/L, 2.8–7.6)	10.1±7.2	10 (47.6%) / 0	22.6±11.8	8.7±6.8
Creatinine (μmol/L, 49–90)	168.5±251.1	9 (42.9%) / 0	333.9±350.3	113.6±157.9
K <sup>+</sup> (mmol/L, 3.5–5.3)	4.0±0.7	2 (9.5%) / 6 (28.6%)	5.1±0.9	3.7±0.7
Na <sup>+</sup> (mmol/L, 137–147)	137.8±9.5	3 (14.3%) / 10 (47.6%)	152.3±13.5	135.6±7.9
hs-TnI (pg/L, 0–26.2)	504.6±1623.63	7 (33.3%) / 0	1283.4±2110.4	86.7±221.8
CK-MB (ng/mL, 0–6.6)	3.3±3.2	2 (9.5%) / 0	15.8±22.1	1.8±2.0
BNP (pg/mL, 0–100)	166.6±188.2	6 (28.6%) / 0	504.8±567.4	157.5±162.1
PT (s, 9.4–12.5)	13.6±2.3	11 (52.4%) / 0	20.2±12.4	12.4±1.5
Fibrinogen (mg/dL, 238–498)	452.7±116	5 (23.8%) / 0	546.0±99.4	314.6±140.0
D-dimer (ng/mL, 0–500)	2726.4±4538.2	11 (52.4%) / 0	24311.9±36589.9	1654.2±3162.1

The column of 'Increase/decrease' shows the number of people whose admission laboratory results were out of the normal range.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; CK-MB, creatine kinase-MB; CRP, C-reactive protein; PCT, procalcitonin; PT, prothrombin time; WBC, white blood cell.

oral oseltamivir or lopinavir and ritonavir tablets and abidol hydrochloride tablets, after admission (Table 4). In addition, all patients were administered empirical antibiotic treatments for common pathogens and some atypical pathogens. In 18 (85.7%) patients with secondary bacterial infection or septic shock, higher level and combined antibiotics such as carbapenems and anti-gram-positive drugs were administered according to bacterial culture and drug sensitivity. Two (9.5%) patients were treated with antifungal drugs. Sixteen (76.2%) patients received systemic corticosteroids with an initial dose of 1–2 mg/kg per day based on the patient’s condition, and 3 (14.3%) patients received a large dose of immunoglobulins. Low-molecular-weight heparin was subcutaneously administered for prophylactic anticoagulation in patients with a hypercoagulable status. Fourteen (67%) patients received high-flow nasal cannula oxygen therapy. Eight (38.1%) patients were administered intermittent or continuous noninvasive ventilation for 1–11 days after a duration of 1 (0–5) days since admission. Invasive ventilation was required in 18 (85.7%) patients 4 ± 3 days after admission. Nineteen patients were administered norepinephrine to correct hypotension. Six (28.6%) patients received renal replacement therapy owing to renal failure, among whom two patients underwent long-term regular hemodialysis for chronic renal diseases. Another 3 (14.3%) patients had refractory hypoxemia and received extracorporeal membrane oxygenation as salvage therapy, including after successful cardiopulmonary resuscitation.

The total course from first symptoms to death was 18 ± 8 days, with a duration of 12 (8–17) days of hospitalization. The patients died within 8 ± 5 days after invasive ventilation. During disease progression, all patients were diagnosed with severe pneumonia followed by ARDS, and the majority of patients (n=19, 90.5%) developed multiple organ dysfunction. Acute renal, liver, and cardiac injuries developed in 17 (81.0%), 12 (57.1%), and 7 (33.3%) patients, respectively. Another two patients had fatal acute myocardial infarction or upper gastrointestinal tract and died in the convalescence stage of pneumonia. All patients developed coagulation abnormalities. Secondary infections were observed, and they progressed to septic shock in 18 (85.7%) patients. Hospital-acquired infections were noted in five (23.8%) patients. Multidrug-resistant *Cinetobacter baumannii* infection was identified in sputum samples of three (14.3%) patients, one of whom had a coinfection with *Escherichia coli*. *Corynebacterium striatum* was identified in the blood culture of one (4.8%) patient. Another patient was diagnosed with urinary tract infection with a urine culture of *Candida glabrata*.

**Discussion**

COVID-19 has spread to more than 100 countries as of late March 2020, making it much more infectious and invasive than SARS and MERS.<sup>[4]</sup> The severe cases reached a peak of 11977 (16.1%) on February 18, 2020 and gradually decreased later in China according to data

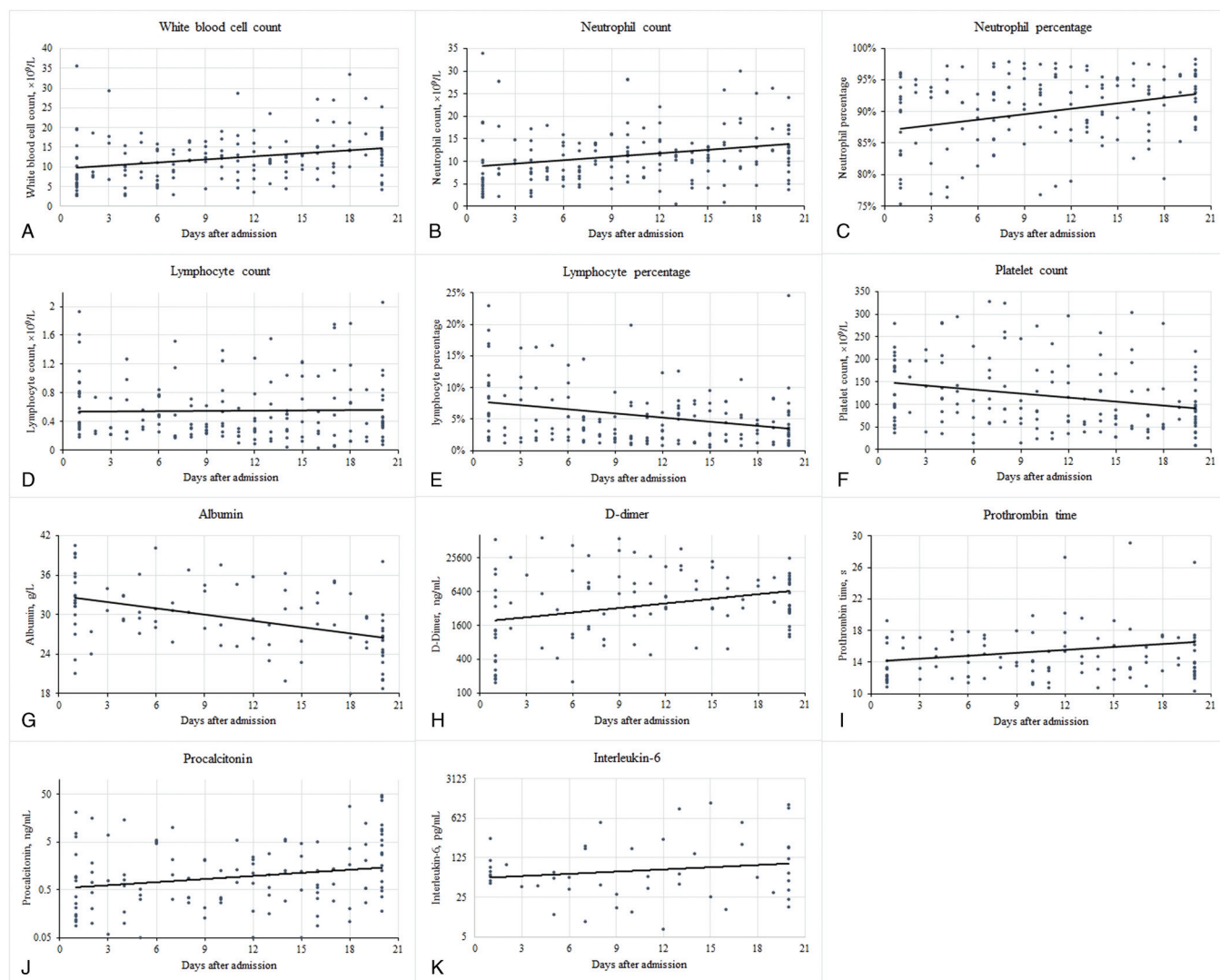


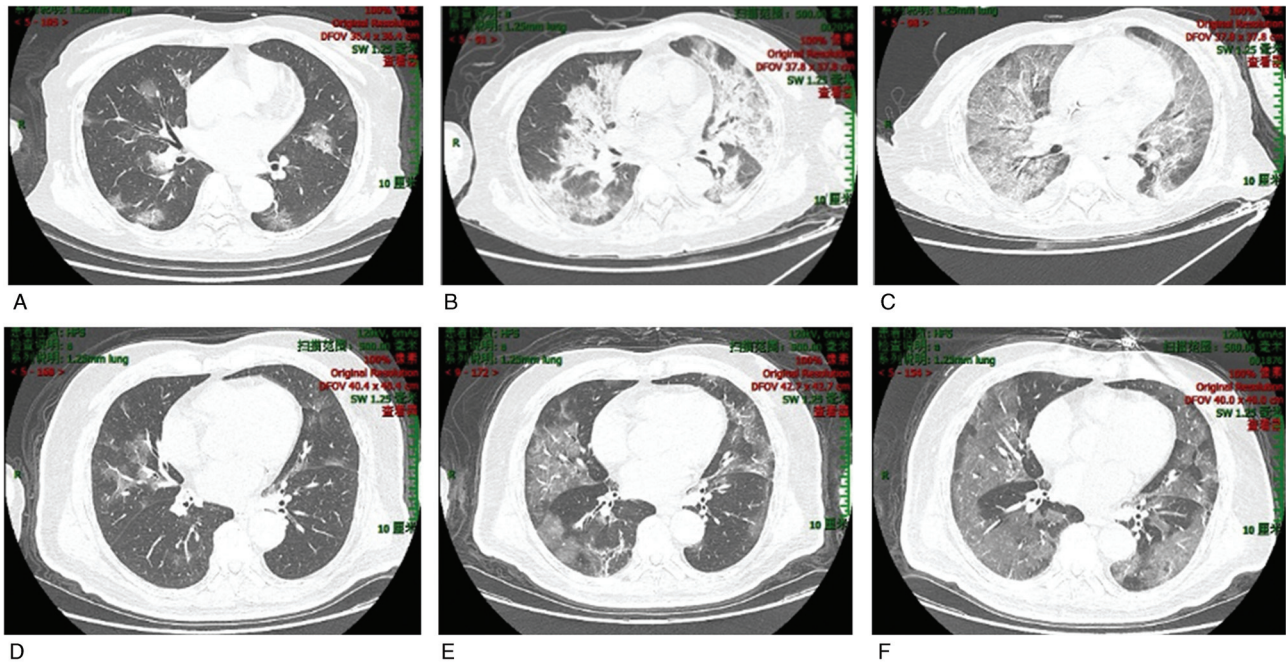
Figure 1. Results of laboratory tests during hospitalization.

published by NHC. The total mortality rate (4.0%; March 26, 2020) of COVID-19 was much lower than that of SARS in 2003 and MERS in 2015.<sup>[4]</sup> However, the rate mortality of severe patients exceeded 60% according to a previous report.<sup>[1]</sup> In this single-center retrospective study, we described and analyzed the demographic and clinical characteristics of 21 patients who died owing to confirmed COVID-19 in the EICU of Zhongnan Hospital of Wuhan University.

Male (71.4%) patients accounted for the majority of cases in this study, similar to that reported in other studies in different hospitals.<sup>[1,2,5]</sup> The mean age of the patients was 66 years, with almost half of the patients aged over 70 years. Combined with COVID-19 studies in other centers during the same period, older male individuals seem most susceptible to SARS-CoV-2 infection and are the primary members in the severe group with poor prognosis,<sup>[1,2,5]</sup> which is supported by our data. Similar findings were reported in previous SARS<sup>[7,8]</sup> and MERS studies.<sup>[9,10]</sup> We found that overweight adults accounted for more than half of the study population, which was previously ignored. We

should also pay attention to the fact that a few patients had self-healing diarrhea during the course. The mean time from illness onset to hospital admission was 5 days, which was less than the 11 days reported in research conducted in Jinyintan Hospital and Wuhan Pulmonary Hospital.<sup>[2]</sup> Twenty patients received oral or intravenous medications, including antibiotic and antiviral therapy, before admission. However, no drugs seemed effective in delaying the progression of COVID-19 in the early stage of the epidemic.

According to laboratory test results, reduced lymphocyte proportions, a characteristic index of SARS-CoV-2 infection, were observed in most patients in our study, which is also reported by many other studies.<sup>[3,11,12]</sup> We speculate that the continuous decrease in lymphocyte proportions may indicate excessive consumption by SARS-CoV-2, similar to the mechanism in SARS-CoV and MERS-CoV infections.<sup>[13,14]</sup> Lymphopenia seemed more common in severe patients<sup>[2,3]</sup> and could thus reflect the severity and higher mortality rate of patients with COVID-19. Lymphocyte subpopulations were assessed,



**Figure 2.** CT images of a woman aged over 75 years (A, B, C) and a man aged over 70 years (D, E, F); both had COVID-19. (A) Day 6 after symptoms onset: multifocal patchy ground-glass opacities in bilateral subpleural areas. (B) Day 9 after symptoms onset: expansion of bilateral pulmonary lesions and denser pulmonary consolidation. (C) Day 15 after symptoms onset: extensive ground-glass opacities in both sides showing a white lung appearance with air bronchograms. The woman died 7 days after the final scan. (D) Day 7 after symptoms onset: multifocal patchy ground-glass opacities in bilateral areas. (E) Day 11 after symptoms onset: enlarged crescent ground-glass opacities in both subpleural areas. (F) Day 14 after symptoms onset: extensive ground-glass opacities with obvious air bronchograms in bilateral areas. The man died of anteroseptal ST-segment elevation myocardial infarction 3 days after the final scan. CT, computer tomography; ST, segment.

and proportions of both cluster of differentiation (CD)4-positive and CD8-positive T lymphocytes decreased significantly. Damage of T lymphocytes and inhibition of the cellular immune system may contribute to deterioration. Serum IL-6 levels increased rapidly in a short period, which could be explained by an active inflammatory storm.<sup>[5,6]</sup> In this study, we detected reduced

platelet counts on admission and their progressive decline during hospitalization, which were previously demonstrated to be related to severe inflammation.<sup>[15,16]</sup> Urea and creatinine levels increased according to different

**Table 3**  
**Severity Assessment of APACHE II, SOFA, MuLBSTA, and PSI Scores on Admission, Before Ventilation, and the Maximum Value During Hospitalization in 21 Patients**

Scores	Admission	Before Ventilation	Maximum
APACHE II	14 ± 3	17 ± 4	26 (22–32)
<10	1 (4.8%)	0	0
10–19	18 (85.7%)	13 (61.9%)	2 (9.5%)
≥20	2 (9.5%)	8 (38.1%)	19 (90.5%)
SOFA	7 (5–8)	8 (7–12)	14 (12–16)
0–5	8 (38.1%)	2 (9.5%)	0
6–10	13 (61.9%)	11 (52.4%)	2 (9.5%)
> 11	0	8 (38.1%)	19 (90.5%)
MuLBSTA	13 ± 2	13 ± 2	15 (13–16)
>12 (High risk)	13 (61.9%)	14 (66.7%)	19 (90.5)
<12 (Low risk)	8 (38.1%)	7 (33.3%)	2 (9.5%)
PSI	137 (102–146)	138 (125–157)	163 (149–185)
71–90	3 (14.3%)	1 (4.8%)	0
91–130	5 (23.8%)	7 (33.3%)	2 (9.5%)
>130	13 (61.9%)	13 (61.9%)	19 (90.5%)

APACHE II, Acute Physiology and Chronic Health Evaluation II; MuLBSTA, multilobar infiltration, hypolymphocytosis, bacterial coinfection, smoking history, hypertension and age; PSI, pneumonia severity index. SOFA, Sepsis-related Organ Failure Assessment.

**Table 4**  
**Main Interventions and Complications of 21 Patients During Hospitalization**

Main intervention and complications	Patients (n=21)
Main interventions	
Antiviral therapy	21 (100%)
Antibiotic therapy	21 (100%)
Antifungal therapy	1 (4.8%)
Systemic corticosteroids therapy	16 (76.2%)
Immunoglobulin therapy	3 (14.3%)
Low molecular heparin therapy	9 (42.9%)
High-flow nasal cannula oxygen therapy	14 (66.7%)
Mechanical ventilation	
Noninvasive mechanical ventilation	8 (38.1%)
Invasive mechanical ventilation	18 (85.7%)
Continuous renal replacement therapy	6 (28.6%)
Extracorporeal membrane oxygenation	3 (14.3%)
Norepinephrine therapy	19 (90.0%)
Main complications	
Acute respiratory distress syndrome	21 (100%)
Multiple organ dysfunction syndrome	19 (90.5%)
Acute kidney injury	17 (81.0%)
Liver dysfunction	12 (57.1%)
Acute cardiac injury	7 (33.3%)
Coagulation abnormality	21 (100%)
Secondary infection	18 (85.7%)
Septic shock	18 (85.7%)
Hospital-acquired infection	5 (23.8%)

degrees, representing renal dysfunction owing to viral invasion, hypoxemia, hypoperfusion, or original kidney diseases. Coagulation dysfunction was observed in almost all cases with prolonged PTs and significantly increased serum D-dimer levels.

Despite many clinical assessments and prediction scores, there is no standard recommendation to predict the severity and risk of mortality in patients with viral pneumonia. Viral pneumonia, including that associated with COVID-19, might progress rapidly to critical illness and develop into ARDS and multiple organ failure and even result in death. The APACHE II scoring system has been widely used to assess patient severity and predict outcomes of critically ill patients.<sup>[17]</sup> The SOFA scoring system has also been used to predict prognosis and assist in the diagnosis of sepsis/septic shock in the intensive care unit (ICU). In our study, the APACHE II and SOFA scores on admission were  $14 \pm 3$  and 7 (5–8), respectively. The highest APACHE II and SOFA scores were 26 (22–32) and 14 (12–16), respectively. Both scores increased with disease progression. The SOFA score of survivors was similar to that of nonsurvivors on ICU admission in one study of critically ill COVID-19 patients<sup>[3,6]</sup>; however, the APACHE II score was similar in both survivors and nonsurvivors. Another study found that a higher SOFA score at admission was associated with higher odds of death in COVID-19 patients.<sup>[2]</sup> This study did not present the APACHE II score. SOFA scores, including the mean and highest SOFA scores, are good predictors of prognosis. Independent of the initial score, an increase in the SOFA score during the first 48 hours predicted a mortality rate of 50%.<sup>[18]</sup> In contrast, the SOFA score is a diagnostic marker for sepsis/septic shock.<sup>[19]</sup> In our study, 18 (85.7%) patients developed septic shock. The study demonstrated that more than 50% of patients with COVID-19 developed sepsis,<sup>[2]</sup> reminiscent of the possibility of virus-induced sepsis syndrome in addition to SARS-CoV-2 infection combined with bacterial infection. An APACHE II score of 10–20 suggests a mortality rate of approximately 50% and a score above 20 suggests a mortality rate of approximately 80%. Although there were differences among the aforementioned studies, we still considered that the APACHE II score had a general predictability of the outcome of patients with COVID-19, which might be less sensitive than the SOFA score.

In our study, we used two special scoring systems to predict the probability of mortality associated with pneumonia: MuLBSTA<sup>[20]</sup> and PSI.<sup>[21]</sup> Both score results in our study showed that 13 (61.9%) patients had a high risk of mortality on admission. The highest MuLBSTA and PSI scores increased to 15 (13–16) and 163 (149–185), respectively, in 19 (90.5%) patients. To date, few studies have analyzed pneumonia special severity scoring systems in patients with pneumonia owing to SARS-CoV-2 infection. One study on COVID-19 mortality analysis found that the CURB-65 score was significantly higher in the nonsurvival group than in the survival group.<sup>[2]</sup> Our study identified the usefulness of the MuLBSTA and PSI scoring systems in predicting mortality risk in patients with COVID-19. However, the accurate sensitivity and specificity of these pneumonia special severity scoring systems require further research and verification.

All death cases had complications, including ARDS (100%), septic shock (85.7%), acute kidney injury (81.0%), liver dysfunction (57.1%), and acute cardiac injury (33.3%), which have also been observed in similar studies.<sup>[2,5,6]</sup> The primary cause of the progressive effect of SARS-CoV-2 on multiorgans is that the binding receptor for SARS-CoV-2, i.e., angiotensin-converting enzyme 2 (ACE2), mainly exists in blood vessels and lung alveolar type II epithelial cells.<sup>[22]</sup> ACE2 also exists in the heart, kidney, liver, and other organs. Thus, viral infection may stimulate immune cells to release pro-inflammatory cytokines and damage target organs, which may even cause death.

The treatments for COVID-19 mainly include antipathogen therapy, different types of oxygen therapy, glucocorticoid therapy, immunoglobulin therapy, and advanced life support for organ function, which were similar to those reported in published studies.<sup>[2,5,6,11]</sup> Nine (42.9%) patients received low-molecular-weight heparin therapy in our study. During the treatment of patients with COVID-19, coagulation abnormalities can be observed based on laboratory findings, including D-dimer levels and PT; however, not all cases may develop to have some detectable relative clinical manifestations. In a large retrospective cohort study on COVID-19, researchers found that an elevated D-dimer level of  $>1 \mu\text{g/L}$  on admission was a risk factor for mortality in adult patients with COVID-19.<sup>[2]</sup> The final effect of coagulation abnormalities can be understood based on lung biopsy conducted by the Shenzhen Third People's Hospital.<sup>[23]</sup> The whole lung tissue displayed a diffuse congestive appearance with variable degrees of hemorrhagic pulmonary infarction and microthrombosis formation prominently present in the outer edge of the lung. The biopsy also indicated that hemorrhagic necrosis in the outer edge of the lung could be the origin of COVID-19-related manifestations and one of the main causes of death in severe patients. Coagulation abnormalities can be observed in patients with severe pneumonia and sepsis. In a study of community-acquired pneumonia, D-dimer levels were persistently elevated in 86.5% of patients, even among least severe cases.<sup>[24]</sup> Research on patients with infection or sepsis identified in the emergency department showed that high D-dimer levels were associated with 28-day mortality.<sup>[25]</sup> These findings highlight the complexity of the coagulation response to viral infection and the corresponding coagulation-based therapeutics.

### Limitations

This study had several limitations. First, this was a retrospective, descriptive, single-center study with a small sample size. Further large cohort studies or randomized controlled trials are needed to confirm our findings. Second, some cases had incomplete or missing data, including outpatient information, laboratory results in certain periods, and sequential images, which would influence the accuracy of the analysis in this study.

### Conclusions

Older, overweight, male patients with a history of chronic illnesses and continuously decreased lymphocyte propor-

tions and increased serum D-dimer levels may have higher risks of death. The combination of general scoring (SOFA score) and pneumonia-specific scoring (MuLBSTA score and PSI score) systems after admission might be sensitive in assessing the risk of mortality among critically ill patients with COVID-19. We suggest increased attention and further study of coagulation abnormalities and relevant definitive therapy in patients with COVID-19.

### Conflict of interest statement

Yan Zhao is an Associate Editor of *Emergency and Critical Care Medicine*. The article was subject to the Journal's standard procedures, with peer review handled independently of this Associate Editor and their research groups. The authors declare no conflict of interest.

### Author contributions

Feihong Yang participated in manuscript preparation, data collection, and literature search. Hao Zou participated in manuscript preparation, data collection, and literature search. Jiaohong Gan participated in manuscript preparation, analysis of data, and literature search. Zhongxiang Zhang participated in analysis of data. Yan Zhao participated in data collection and study design. Cheng Jiang participated in literature search, study design, analysis of data, and review of manuscript. Jian Xia participated in study design and review of manuscript. All authors have read and approved the final version of the manuscript. They have agreed to be personally accountable for each author's own contributions.

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### Ethical approval of studies and informed consent

The study was approved and written informed consent was waived by Zhongnan Hospital Ethics Committee (No. 2020005-1K), owing to the rapid emergence of this infectious disease.

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