Clinical analysis of severe COVID-19 patients

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Abstract.
BACKGROUND: Patients with unexplained pneumonia appeared in Wuhan, Hubei Province at the end of 2019.
OBJECTIVE: To analyze the clinical data of patients with severe COVID-19.
METHODS: Medical records of 28 severe patients admitted to the intensive care unit of Wuhan Xinzhou District People's Hospital were collected from January 31 to March 17.
RESULTS: The mortality rate of severe patients in our study was 39.3%. There were statistically significant differences in age, admission systolic blood pressure, lymphocyte count, albumin, total bilirubin, and lactate dehydrogenase between the death group and the survival group ($P < 0.05$). There were statistically significant differences in APACHE II, CURB-65, SOFA, respiratory frequency, systolic pressure, platelet, procalcitonin, albumin, creatinine, creatine kinase isoenzyme, lactate dehydrogenase, chloride ion, prothrombin time, international normalized ratio, arterial partial pressure of oxygen, and FiO2 at ICU between the death group and the survival group ($P < 0.05$).
CONCLUSIONS: Fever and cough are the main symptoms, which is useful for predicting the prognosis to dynamically measure the APACHE II, CURB-65, SOFA, respiratory frequency, lymphocyte count, platelet, lactate dehydrogenase, and coagulation tests. The drugs that protect the liver and heart may improve the survival rate of patients with severe COVID-19.

Keywords: Coronavirus disease 2019, critical illness, prognosis

1. Introduction

Patients with unexplained pneumonia appeared in Wuhan, Hubei Province at the end of 2019. The pneumonia spread rapidly in Wuhan, and most patients had a history of contact with the South China Seafood Market. Since then, more and more patients developed symptoms like fever and cough. In January 2020, the Chinese Center for Disease Control and Prevention (CDC) announced that the pathogen was a new type of coronavirus, which was subsequently named 2019-nCoV by the WHO [1]. As the situation worsened, the World Health Organization declared the outbreak a "Public Health Emergency of International Concern" (PHEIC). In February 2020, International Committee on Taxonomy of Viruses renamed the virus to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Later, the WHO announced that the epidemic disease caused by SARS-CoV-2 to be Coronavirus Disease 2019 (COVID-19). After the outbreak of COVID-19, the Chinese government activated First-Level Public Health Emergency Response on January 26, 2020. While preventing and controlling the spread of the

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disease, additional skilled medical personnel from other regions were recruited to Wuhan to assist in outbreak responses. On January 28, 2020, 5 medical staff from the Department of Intensive Care Medicine of our hospital accompanied Qinghai-to-Hubei medical team to help with the treatment of patients with coronavirus in Wuhan. In this report, we analyzed and summarized clinical features of 28 patients with COVID-19 treated by our team.

2. Methods

2.1. Study population

We collected the medical records of 28 severe and critically-ill COVID-19 patients admitted to the Department of Intensive Care Medicine at Xinzhou District People's Hospital in Wuhan from January 31 to March 17 of 2020. All patients were confirmed positive for COVID-19 by specific molecular testing and CT examination. The chest CT in the detection of COVID-19 showed bilateral ground-glass opacities and consolidations [2,3]. Inclusion criteria described: All patients admitted to the ICU meet the severe and critical diagnosis criteria in the "Notification on Issuing the New Coronavirus Pneumonia Diagnosis and Treatment Protocol (Seventh Trial Edition)" [4] issued by the General Office of the National Health Commission. Severe: Adults who meet any of the followings: a) Shortness of breath, RR $\geqslant$ 30 beats/min; b) in resting state SaO2 $\leqslant$ 93%; c) Arterial blood Partial Pressure of Oxygen (PaO2)/Fraction of Inspired Oxygen (FiO2) $\leqslant$ 300 mmHg, lung imaging shows within 24–48 hours, the lesions progressed significantly > 50% according to severe management. Critical: Those who meet one or more of the following conditions: a) Respiratory failure, and requirement of assisted ventilation; b) Shock; c) Combined with other organ failure, requirement of intensive care. Exclusion criteria: None.

2.2. Data collection

We collected each patient's general information, APACHE II score, SIRS score, SOFA score, and CURB-65 score upon entering the ICU. Vital signs, blood tests, biochemical tests, coagulation analysis, and blood gas analysis were performed. We also collected each patient's number of ICU hospitalization days and the prognosis when exiting the ICU. According to the different prognoses when leaving the ICU, we divided our cohort into the survival group and the mortality group. Blood routine testing was performed with a XN9000 analyzer (Sysmex Corporation, Japan). Biochemical analysis was performed with a Siemens ADVIA 2400 automatic biochemical analyzer. Brain natriuretic peptide (BNP) levels were measured with a DXi800 (Beckman Coulter, USA). Procalcitonin (PCT) was measured with a Cobas 8000 (Roche, Germany). C-reactive protein (CRP) levels were measured with an AU5800 (Beckman Coulter, USA). All detection reagents used the manufacturer's matching reagents.

2.3. Treatments

Intensive care, oxygen therapy (i.e., oxygen masks, non-invasive ventilators, invasive ventilators), acid-suppression agents to protect gastric mucosa (pantoprazole), anti-infection agents (sulbactam, cefoperazone, levofloxacin, azithromycin, imipenem), antiviral agents (oseltamivir, interferon, lopinavir/ritonavir tablets), hormones (methylprednisolone sodium succinate, dexamethasone), liver-protection agents (glutathione), nebulizer-inhalation agents (budesonide, terbutaline), phlegm/asthma-reduction agents (ambroxol, tanreqing, doxofylline), and other treatments (i.e., immunoglobulin, human albumin, Lianhua Qingwen capsules, Chinese herbal medicine) were administered to patients included in the present study.

2.4. Statistical analysis

SPSS 22.0 statistical software was used for data analysis. Non-normally distributed measurement data are represented by P50 (P25, P75), and Mann-Whitney U test is used for comparison between the two groups (Survival and Death). The enumeration data was analyzed by χ^2 test. Normally distributed measurement data were presented as mean $\pm$ standard deviation, and the independent sample t test was used for comparison between two groups. Significance level $a < 0.05$ indicates that the difference is statistically significant.

3. Results

The general symptoms of patients included the following: dyspnea (3 out of 28), wheezing (8 out of 28), chest pain (1 out of 28), chest tightness (10 out of 28), cough (23 out of 28), expectoration (8 out of 28), fatigue (4 out of 28), sore throat (1 out of 28), and fever (22 out of 28). The highest body temperature fluctuated between 38.5–40.0°C. Furthermore, the following additional ailments were found in our cohort: hypertension (5 out of 28), diabetes (3 out of 28), coronary heart disease (1 out of 28), chronic bronchitis (3 out of 28), hepatitis B (13 out of 28), syphilis (1 out of 28), adenovirus infection (3 out of 28), respiratory syncytial virus infection (1 out of 28), and coxsackie virus infection (1 out of 28).

The following hospital-admission measurements between the survival group and mortality group were significantly different ($P < 0.05$): age, systolic blood pressure upon admission, lymphocyte count (LY), albumin (ALB), total bilirubin (TBIL), and lactate dehydrogenase (LDH). There were no significant differences in any other hospital-admission indicators between the two groups ($P > 0.05$) (Table 1).

The following ICU-admission measurements between the survival group and mortality group were significantly different ($P < 0.05$): APACHE II, CURB-65, SOFA, respiratory rate, systolic blood pressure, platelet count (PLT), PCT, ALB, creatinine (CREA), creatine kinase isoenzyme (CK-MB), lactate dehydrogenase (LDH), chloride ions (Cl), prothrombin time (PT), international normalized ratio (INR), and PaO2/FiO2. There were no significant differences in any of the remaining ICU-admission indicators between the two groups ($P > 0.05$) (Table 2).

In terms of follow-ups, none of the deceased patients in the mortality group underwent an autopsy. The follow-ups were completed on May 8, 2020. Of the 17 surviving patients, two patients did not participate in the follow-ups. Among the 15 patients that participated in follow-ups, 12 patients were re-examined via computed tomography after discharge; and it was revealed that in 5 out of 12 of these patients, the exudate was not completely absorbed. Nucleic-acid re-examinations of all 15 patients that participated in follow-ups were negative.

4. Discussion

A total of 28 severe and critical patients were involved in this study, including 18 males and 10 females. The average age of the disease is 54.8 $\pm$ 15.1 years. The age distribution in this study is similar as that reported in other studies [5,6] but with higher male-female ratio. Among these patients, 15 out of 28 COVID-19 patients suffered from one or more underlying diseases, including hypertension, diabetes, coronary heart disease, and chronic bronchitis [7]. The median time from onset to doctor's visit was 7 days. Among them, the median time for patients in the death group was 9 days, but there was no statistical difference between the two medians. This is consistent with the average duration of 5.8 days

Table 1
Admission indicators between the survival group and the death group

Indicators		Total	Survival group	Death group	Statistics	P
Number gender	Case	28	17	11		
	Male: Female	18:10	9:8	9:2	$X^2 = 1.331$	0.249
Age	Year	54.8 ± 15.1	49.9 ± 14.0	62.4 ± 14.0	$t = -2.302$	0.030
Onset to admission	Day	7.0 (4.3, 12.0)	7.0 (4.0, 16.5)	9.0 (5.0,12.0)	$Z = -0.189$	0.850
Admission to the ICU	Day	5.0 (0.3, 7.0)	7.0 (4.5, 8.5)	2.0 (0.0,4.0)	$Z = -2.828$	0.005
Admission temperature	°C	36.8 (36.3, 37.4)	37.0 (36.5, 38.0)	36.6 (36.3, 37.0)	$Z = -1.818$	0.069
Admission heart rate	/min	87 (83, 104)	86 (81, 101)	98 (86, 108)	$Z = -1.650$	0.099
Admission respiratory rate	/min	20 (20, 24)	20 (20, 22)	23 (20, 31)	$Z = -1.826$	0.068
Admission systolic pressure	mmHg	129 ± 21	123 ± 18	139 ± 23	$t = -2.063$	0.049
Admission diastolic pressure	mmHg	80 ± 15	76 ± 14	85 ± 17	$t = -1.631$	0.115
Admission WBC	$\times 10^9$/L	7.7 ± 3.5	7.2 ± 4.0	8.4 ± 2.6	$t = -0.924$	0.364
Admission LY	$\times 10^9$/L	0.86 ± 0.36	0.98 ± 0.38	0.67 ± 0.23	$t = 2.462$	0.021
Admission HGB	g/L	141 ± 19	141 ± 19	142 ± 19	$t = -0.126$	0.901
Admission PLT	$\times 10^9$/L	183 ± 63	189 ± 74	173 ± 39	$t = 0.741$	0.466
Admission PCT	ng/ml	0.20 (0.13, 0.28) ($N = 24$)	0.2 (0.1, 0.2) ($N = 14$)	0.2 (0.2, 0.78) ($N = 10$)	$Z = -1.705$	0.088
Admission BNP	ng/L	741 (269, 917) ($N = 11$)	377 (50, 781) ($N = 5$)	829 (568, 2205) ($N = 6$)	$Z = -1.461$	0.144
Admission ALT	U/L	39 (31, 54)	36 (30, 49)	41 (31, 57)	$Z = -0.801$	0.423
Admission AST	U/L	31 (23, 42)	27 (23, 35)	41 (28, 59)	$Z = -1.600$	0.110
Admission ALB	g/L	34.7 ± 6.3 ($N = 27$)	37.5 ± 5.6 ($N = 16$)	30.7 ± 5.0	$t = 3.198$	0.004
Admission TBIL	umol/L	14.0 ± 6.7 ($N = 25$)	11.6 ± 4.6 ($N = 15$)	17.6 ± 8.0 ($N = 10$)	$t = -2.405$	0.025
Admission BUN	mmol/L	6.1 ± 2.7 ($N = 20$)	5.1 ± 2.1 ($N = 11$)	7.3 ± 3.0 ($N = 9$)	$t = -1.886$	0.076
Admission CREA	umol/L	74 (71, 85) ($N = 27$)	71 (66, 89) ($N = 16$)	74 (72, 85)	$Z = -1.115$	0.265
Admission GLU	mmol/L	5.9 (4.9, 6.9)	5.8 (4.6, 6.3)	6.6 (5.3, 9.4)	$Z = -1.671$	0.095
Admission CK	U/L	148 (62, 337)	188 (76, 401)	83 (50, 165)	$Z = -1.201$	0.230
Admission CK-MB	U/L	16 (10, 25)	11 (10, 26)	17 (11, 25)	$Z = -0.969$	0.333
Admission LDH	U/L	368 (301, 448)	315 (268, 407)	502 (386, 638)	$Z = -3.058$	0.002
Admission K	mmol/L	5.3 ± 0.9	4.5 ± 0.9	4.1 ± 0.9	$t = 1.056$	0.301
Admission Na	mmol/L	136 ± 5	136 ± 3	137 ± 6	$t = -0.666$	0.511
Admission Cl	mmol/L	101 ± 4	100 ± 2	102 ± 6	$t = -1.113$	0.288
Admission Ca	mmol/L	2.4 (2.2, 2.5)	2.4 (2.3, 2.5)	2.3 (2.1, 2.4)	$Z = -1.551$	0.121
Admission P	mmol/L	1.0 (0.8, 1.2)	1.1 (1.0, 1.2)	0.9 (0.6, 1.1)	$Z = -1.735$	0.083
Admission PT	sec.	12.2 ± 1.9	11.8 ± 2.0	12.8 ± 1.8	$t = -1.305$	0.203
Admission APTT	sec.	31.2 ± 6.1	30.3 ± 6.1	32.5 ± 6.1	$t = -0.922$	0.365
Admission INR		1.05 ± 0.17	1.02 ± 0.17	1.10 ± 0.16	$t = -1.247$	0.223
Admission FIB	g/L	3.67 ± 0.67	3.58 ± 0.53	3.81 ± 0.87	$t = -0.900$	0.377
Admission DD	mg/L	0.9 (0.4, 2.5)	1.0 (0.5, 2.1)	0.7 (0.3, 2.9)	$Z = -0.118$	0.906

from the onset of the disease to the first visit that some studies have shown (95% CI 4.3 to 7.5 days) similar to the previous studies [8–10]. In clinical manifestations, the symptoms of 22/28 patients are cough and fever, which are consistent with other reported studies [11–14]. 13/28 of the patients had viral hepatitis B but it is unclear whether viral hepatitis B renders people more susceptible to COVID-19. Though other studies have shown that some COVID-19 patients developed symptoms of intestinal involvement [15], this group of patients did not show any gastrointestinal symptoms. Overall, the median body temperature of all patients at admission was 36.8°C, and there was no manifestation of elevated body temperature, which may be related to the use of fever reducers after the patients found themselves with fever before admission. The death group had a higher heart rate than the survivors (98 vs 86 beats/min) upon admission, but

Table 2
Indicators between the survival group and the death group when admitted to ICU

Indicators		Total	Survival group	Death group	Statistics	P
Number	Case	28	17	11		
Admitted to ICU APACHE II		7.5 (5.0, 11.0)	6.0 (3.5, 9.0)	13.0 (9.0, 24.0)	$Z = -3.096$	0.002
Admitted to ICU CURB-65		1.0 (0.3, 2.0)	1.0 (0.0, 1.0)	3.0 (1.0, 3.0)	$Z = -3.607$	< 0.001
Admitted to ICU SIRS		2.0 (2.0, 3.0)	2.0 (1.0, 2.5)	2.0 (2.0, 3.0)	$Z = -1.565$	0.117
Admitted to ICU SOFA		3.0 (3.0, 5.0)	3.0 (2.0, 3.0)	6.0 (4.0, 7.0)	$Z = -3.666$	< 0.001
Admitted to ICU temperature	°C	37.0 ± 0.8	37.1 ± 0.9	36.9 ± 0.6	$t = 0.596$	0.556
Admitted to ICU heart rate	/min	92 ± 14	88 ± 16	97 ± 10	$t = -1.679$	0.105
Admitted to ICU respiratory rate	/min	26 (21, 35)	22 (20, 26)	33 (31, 43)	$Z = -3.421$	0.001
Admitted to ICU systolic pressure	mmHg	132 ± 16	126 ± 14	141 ± 15	$t = -2.691$	0.012
Admitted to ICU diastolic pressure	mmHg	77 ± 14	75 ± 13	79 ± 17	$t = -0.778$	0.443
Admitted to ICU WBC	$\times 10^9$/L	10.5 ± 5.2	9.2 ± 5.8	12.5 ± 3.5	$t = -1.695$	0.102
Admitted to ICU LY	$\times 10^9$/L	0.64 (0.53, 0.97)	0.69 (0.57, 1.00)	0.58 (0.49, 0.95)	$Z = -0.895$	0.371
Admitted to ICU HGB	g/L	130 ± 20	125 ± 19	136 ± 19	$t = -1.565$	0.130
Admitted to ICU PLT	$\times 10^9$/L	183 (134, 287)	250 (156, 377)	142 (112, 195)	$Z = -2.541$	0.011
Admitted to ICU PCT	ng/ml	0.2 (0.2, 0.4) ($N = 26$)	0.2 (0.1, 0.2) ($N = 15$)	0.3 (0.2, 1.2)	$Z = -2.440$	0.015
Admitted to ICU BNP	ng/L	952 (751, 3461) ($N = 12$)	886 (641, 9716) ($N = 6$)	1731 (723, 11575) ($N = 6$)	$Z = -0.401$	0.688
Admitted to ICU ALT	U/L	35 (25, 54)	31 (23, 45)	38 (32, 68)	$Z = -1.506$	0.132
Admitted to ICU AST	U/L	33 (24, 53)	32 (25, 46)	33 (24, 59)	$Z = -0.283$	0.777
Admitted to ICU ALB	g/L	29.4 (27.1, 33.2)	31 (29, 34)	27 (26, 29)	$Z = -2.872$	0.004
Admitted to ICU TBIL	umol/L	19.8 (13.1, 26.2)	18.7 (12.5, 20.9)	26.4 (17.4, 35.7)	$Z = -1.624$	0.104
Admitted to ICU BUN	mmol/L	6.8 (4.6, 9.7)	5.5 (4.3, 8.8)	9.2 (5.8, 13.7)	$Z = -1.741$	0.082
Admitted to ICU CREA	umol/L	72 (57, 80)	63 (56, 77)	77 (73, 123)	$Z = -2.001$	0.045
Admitted to ICU GLU	mmol/L	6.2 (4.8, 8.1)	6.1 (4.9, 7.8)	6.3 (4.6, 9.4)	$Z = -0.071$	0.944
Admitted to ICU CK	U/L	83 (42, 201)	81 (41, 197)	118 (42, 444)	$Z = -0.376$	0.707
Admitted to ICU CK-MB	U/L	15 (10, 21)	11 (6, 16)	17 (15, 29)	$Z = -2.518$	0.011
Admitted to ICU LDH	U/L	419 (347, 640)	372 (305, 441)	638 (474, 722)	$Z = -3.082$	0.002
Admitted to ICU K	mmol/L	3.9 ± 0.6	4.0 ± 0.6	3.6 ± 0.6	$t = 1.824$	0.080
Admitted to ICU Na	mmol/L	137 ± 5	136 ± 4	138 ± 6	$t = -1.516$	0.142
Admitted to ICU Cl	mmol/L	102 (100, 104)	102 (100, 103)	103 (103, 105)	$Z = -1.965$	0.049
Admitted to ICU Ca	mmol/L	2.2 (2.2, 2.3)	2.3 (2.2, 2.3)	2.2 (2.1, 2.2)	$Z = -1.712$	0.087
Admitted to ICU P	mmol/L	0.9 ± 0.2	0.9 ± 0.2	0.8 ± 0.2	$t = 1.769$	0.089
Admitted to ICU PT	sec.	12.4 (11.5, 14.2)	11.8 (10.9, 12.7)	14.3 (12.0, 15.0)	$Z = -2.542$	0.011
Admitted to ICU APTT	sec.	27.3 (23.7, 33.8)	26.5 (23.1, 30.3)	31.6 (23.9, 37.8)	$Z = -1.835$	0.067
Admitted to ICU INR		1.07 (0.99, 1.25)	1.01 (0.94, 1.09)	1.23 (1.03, 1.30)	$Z = -2.424$	0.015
Admitted to ICU FIB	g/L	3.47 (2.76, 4.07)	3.66 (3.16, 4.13)	2.87 (1.57, 3.65)	$Z = -1.576$	0.115
Admitted to ICU DD	mg/L	2.47 (0.61, 6.59)	2.77 (0.79, 6.13)	1.35 (0.28, 12.75)	$Z = -0.353$	0.724
Admitted to ICU PH		7.49 ± 0.07	7.49 ± 0.05	7.49 ± 0.09	$t = -0.177$	0.861
Admitted to ICU PCO$_2$	mmHg	31 ± 6	32 ± 6	29 ± 5	$t = 1.482$	0.150
Admitted to ICU PO$_2$	mmHg	69 (60, 89)	82 (64, 109)	62 (52, 67)	$Z = -2.660$	0.008
Admitted to ICU Lac	mmol/L	1.40 (1.03, 2.20)	1.4 (0.9, 1.9)	1.5 (1.1, 2.6)	$Z = -1.132$	0.258
Admitted to ICU FiO2		0.45 (0.41, 0.60)	0.45 (0.39, 0.55)	0.60 (0.45, 0.60)	$Z = -2.186$	0.029
PO$_2$/FiO2		172 ± 89	209 ± 97	115 ± 20	$t = 3.854$	0.001

the difference was not statistically significant. The median respiratory rate in the death group was 23 breaths/min, which was also higher than 20 breaths/min in the survival group, and the difference was also not statistically significant. The mean systolic blood pressure and diastolic blood pressure of the death group were higher than those of the survival group (139 vs 123 mmHg; 85 vs 76 mmHg). Three patients in the death group and 2 patients in the survival group were in combination with high blood pressure. We exclude the possibility of pre-existing hypertension-causing diseases. The possible reason is that hypoxia leads to an increase in the body's heart rate, an increase in myocardial contractility, and

ultimately an increase in cardiac output [16]. Laboratory examinations at admission showed that the lymphocyte count (LY) of patients in the survival group was significantly increased, but the lymphocyte counts of the two groups were significantly lower than the normal value, which is consistent with previous studies [17–19]. Lymphocytes play a central role in the immune response. Lymphocytes mainly include T lymphocytes and B lymphocytes. Unfortunately, due to limited conditions, we did not make further classification of lymphocyte subgroups. Lymphocyte reduction in the death group indicates the cells responsible for immune response were severely damaged. Related studies have also shown that a decrease in lymphocyte counts indicates a poor prognosis [20]. The albumin (ALB) level of the survival group was significantly higher than that of the death group. The decrease in albumin in the body is mainly due to the decrease in synthesis and the increase in consumption during the course of the disease. The decrease in synthesis may be due to insufficient intake of nutrients and impaired liver function, and consumption is directly manifested in the stress response caused by COVID-19, which directly causes albumin to be consumed as calories. The total bilirubin (TBIL) levels of the surviving group were significantly reduced compared to the death group. There was no significant difference in hemoglobin levels between the two groups, and the levels were largely within the normal range, so the increase in TBIL caused by the blood system can basically be ruled out. It is more likely that the rise of TBIL levels is the result of impaired liver functions. Correspondingly, the liver function tests revealed that liver enzymes of the death group were also higher than those of the survival group, but there was no statistical difference. There was no difference in renal function indexes between the two groups. The lactate dehydrogenase (LDH) levels of the survival group were significantly reduced compared to the death group. LDH is classified into 5 subtypes. LDH1 and LDH2 are mainly expressed when myocardial tissue is damaged, LDH3 is expressed when lung tissue is damaged, and LDH4 and LDH5 are expressed when liver tissue is damaged. The LDH levels of all patients in the present study were significantly increased compared to those of normal values, and those of the mortality group were even more increased. It may be caused by damage to lung tissue, heart tissue and liver tissue. Unfortunately, we did not do subtype testing, so we could not exclude that SARS-CoV-2 infection causes damage to target organs other than the lung when the disease is severe. Some studies [9,21,22] also show that the above indicators of patients are obviously abnormal. Through coagulation test we found that the coagulation indexes were not significantly higher than the normal value, and the difference between the survival group and the death group was not statistically significant. The possible reason is that at the initial stage of the disease, even if the liver function is damaged, the coagulation function is not affected. However, as the disease progresses, changes in coagulation function may occur.

The median time from admission to ICU for this group of patients is 5 days. The median time for the survival group is 7 days, and the median time for the death group is 2 days. The difference in age between the two groups indicates that the disease progresses more rapidly and provide a higher risk of death in older patients (average age of the death group is 62.4 years) [23]. Upon entering the ICU due to disease worsening, the APACHE II score, the CURB-65 score and the SOFA score of the survival group were lower than those of the death group. Higher scores indicate a poor prognosis, which is in consistency with our observations. When entering the ICU, the respiratory rates of patients in the death group were significantly higher than those of patients in the survival group (33 vs 22 breaths/min). Hence, as the disease worsens, the increase in respiratory rate is the major clinical manifestation of severe patients. The respiratory failure may be related to the nerve invasion of SARS-CoV2 [24]. The average systolic blood pressures of the death group rose further (139 vs 141 mmHg) after entering the ICU, and were significantly higher than that of the survivors (141 vs 126 mmHg). The increase of blood pressure without significant changes in heart rate, may be the result of activation of the receptors that cause contraction of

blood vessels as response to stress. As the disease progresses, the two groups have significant differences in platelet count (PLT). Platelets are key regulators of intravascular immunity and inflammation in the host. In addition to participating in the clotting process, platelets can also directly identify, isolate and kill pathogens, activate and guide neutrophils to the site of infection and inflammation, enhance their ability to engulf and kill pathogens, inducing unique effective functions [25]. Our study shows that the PLT counts of the death group are lower than those of the survival group. The reason may be that platelets are recruited and consumed in the body's inflammatory response and the damage of the body's organs caused by COVID-19, which has adverse reactions to bone marrow hematopoietic cells, resulting in decreased platelet synthesis [26], related studies have shown that the reduction of platelets can increase the risk of death in the hospital [27–29]. The PT and INR values of the survival group and the death group were statistically different, suggesting that coagulation disorders may be related to the disease severity. There is no statistical difference in the FDP and DDL values between the two groups, but if these indexes are significantly higher than the normal value in the ICU, it also indicates disorders of the fibrinolytic system. Related research [30–32] suggests that coagulation plays an important role in the progression of the disease. The increase in procalcitonin (PCT) in the dead group indicates secondary bacterial infection during SARS-CoV-2 infection. Multiple infections directly worsened the disease and aggravated the body's toxic reaction [33,34]. Albumin (ALB) levels in the two groups were lower after admission to the ICU than at admission (37 vs 31; 31 vs 27 g/L), but the death group decreased more significantly (27 vs 31 g/L). This can be explained by further damage of the liver functions, revealed by coagulation disorders that occurred in the later stages of the disease, demonstrated by prolonged prothrombin time (PT). Renal function did not change significantly on admission, but when admitted to the ICU, the creatinine (CREA) levels of the death group were significantly increased. As SARS-CoV-2 infection causes damage to multiple organs, the lactate dehydrogenase (LDH) index gradually increased compared with levels at admission (368 vs 419 U/L), suggesting that lung, liver, and heart tissue damage was further aggravated. In the meantime, creatine kinase isoenzyme (CK-MB) levels are significantly higher in the death group than in the survival group, also indicating that SARS-CoV-2 gradually increase its toxic effect on the myocardium as the disease progresses [35–38]. The blood chloride ion (Cl) levels in the death group were higher, but still within the normal range. The cause of the increase may be respiratory alkalosis. In the blood gas analysis, the differences in the arterial Partial Pressure of Oxygen (PaO2) and Fraction of Inspired Oxygen (FiO2) were statistically different between the two groups, which directly reflected the difference in the degree of lung injury between the two groups. The oxygenation index of the death group was significantly decreased (115 vs 209, $P < 0.05$). Many patients infected with SARS-CoV-2, especially critically ill patients, had complications, including ARDS, shock, acute kidney injury, acute myocardial injury and secondary infections [39].

The chloroquine or remdesivir may be effective in the treatment of COVID-19 [40,41]. Both Pfizer and Moderna have developed and are distributing COVID-19 vaccines. Treatments for the patients in the present study included intensive care, oxygen therapy (oxygen by mask, non-invasive ventilator, or invasive ventilator), acid-suppression agents to protect gastric mucosa, anti-infection agents, anti-virus agents, hormonal application, liver protection, immunoglobulin, human albumin, Chinese herbal medicines, and other treatments [42]. The treatments achieved moderate outcomes, resulting in a mortality rate of 39.3% (11/28) in our present study. However, the mortality rate reported in the literature varies between 1.36% and 15% [43,44]. The reason for the higher mortality rate among the patients in the present study may be due to all patients in this group being severely ill.

5. Conclusion

Fever and cough on admission were the main symptoms of COVID-19 patients in our present study, and these symptoms were often accompanied by chest pain, chest tightness, and difficulty breathing. At present, chloroquine and hydroxychloroquine may be effective in the treatment of COVID-19, and antibiotics can be used to control the infection when secondary bacterial infection occurs. Additionally, the use of Chinese traditional medicine may improve the overall condition of the immune system, thereby increasing the survival rate of COVID-19 patients. At present, the in-hospital mortality rate of COVID-19 is 28%–62%, and 81% of these patients require mechanical ventilation [20,45,46]. The drugs that protect the liver and heart may improve the survival rate of patients with severe COVID-19. Hence, further research needed in order to control COVID-19 and reduce the mortality rate of severely ill patients.

Acknowledgments

Conflict of interest

None to report.

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