Clinical Course and Features of Critical Patients with COVID-19: A Single- Center, Retrospective Study from Wuhan Huoshenshan Hospital

Huisi He

Eastern Hepatobiliary Surgery Hospital

Zhichao Jin

Second Military Medical University

Yibin Ren

Second Military Medical University

Junxue Wang

Second Military Medical University

Shuzhen Chen

Second Military Medical University

Wen Wen

Second Military Medical University

Yushan Miao

Second Military Medical University

Xuewei Qi

CAS: Chinese Academy of Sciences

Taiyu Shang

Fudan University

Chenxu Zhang

Second Military Medical University

Hongyang Wang

Second Military Medical University

Weiqin Li

Nanjing University

Xijing Zhang

Fourth Military Medical University

Hao Tang (✉ tanghao_0921@126.com)

Changzheng Hospital: Shanghai Changzheng Hospital

Research

Abstract

Background: Nationally, the indicators tracking the coronavirus pandemic has remained stable. However, it's still a public health concern and it's worth providing more front-line data on critical illness. We aim to investigate the clinical course and features of critical patients with Corona Virus Disease 2019 (COVID-19).

Methods: The data on 124 consecutive critical patients from 8th February through April 16th 2020, including demographic and clinical information, were obtained from the intensive care unit (ICU) of Wuhan Huoshenshan Hospital. A cross-sectional survey and comparisons of key biomarkers between survivors and nonsurvivors were performed.

Results: Over the study period, 57 nonsurvivors and 67 survivors were included. The overall case-fatality rate for critical patients with COVID-19 was approximately 46%. The overall average age was 69.89±11.03 years, and the majority had underlying health problems such as hypertension (63[51%]) and diabetes (27[22%]). Compared with survivors, nonsurvivors were more likely to develop sepsis (57[100%] vs. 34[51%]), acute respiratory distress syndrome (52[91%] vs. 21[38%]) and organ dysfunction. Besides, the dynamic changes in some biomarkers (i.e. WBC, TLC, CRP, PLT) were significantly different between the two groups. The trajectories of temperature revealed that the group with a high temperature on admission that steadily declined had the highest percentage of deaths (84.21%).

Conclusions: The elderly with many concomitant diseases were at the highest risk. Lymphocyte, platelet, C-reactive protein and temperature were revealed to have potential as prognostic factors, whereas some other biomarkers, such as hepatic enzymes, may not offer additional information. Moreover, patients with high temperatures on admission should receive extra care.

1. Introduction

A new outbreak of Corona Virus Disease 2019 (COVID-19) occurred in late December 2019 in Wuhan, China, and has spread to other countries with cases doubling within days through person-to-person transmission, which has been confirmed both in and outside of China.[1,2] As of 1st October or roughly ten months into the outbreak, the number of cases of COVID-19 worldwide has exceeded 34 million across 215 countries, and China has confirmed 91,069 cases.[3] Although the viral pandemic has been controlled in China now and indicators tracking its activity continue to be stable, largely due to aggressive public health measures, COVID-19 is still a critical global issue.

According to the World Health Organization (WHO) interim guidelines[4] and Chinese Clinical Guidance For COVID-19 Pneumonia Diagnosis and Treatment (7th edition)[5], the confirmed patients are divided into four categories ranging from mild to critical, based on their clinical manifestations. Most studies have investigated COVID-19 at the very beginning, providing well-rounded, detailed illustrations of the clinical characteristics of infected patients.[1,2,6–10] However, there are certain drawbacks associated with the

sample sizes and study of critically ill patients who require the greatest use of medical sources. These findings indicate an urgent need to understand the clinical features of COVID-19 that exist among patients in critical condition.

In this study, we sought to analyze data from the intensive care unit (ICU) in Wuhan Huoshenshan Hospital, an emergency specialty field hospital constructed in response to the COVID-19 outbreak and runs under the management of the People's Liberation Army, to help address these research gaps and provide one of the first comprehensive clinical descriptions of critical patients with COVID-19 from the first anti-pandemic frontline.

2. Materials And Methods

2.1. Data source

This was a cross-sectional study focused on critical patients with COVID-19. We included all critically ill patients with COVID-19 registered in the ICU of Wuhan Huoshenshan Hospital from February 8th, the day this emergency specialty field hospital was put into use, to April 16th, when the hospital announced its closure.

2.2. Participants & Ethical consideration

Patients were included if they met the following criteria: 1) primary diagnosis of COVID-19 confirmed by next-generation sequencing or real-time polymerase-chain-reaction methods; 2) defined as critical based on the need for supportive care with mechanical ventilation or treatment for organ failure. And among those patients who were admitted to ICU twice, the second one was taken.

Informed consent was not obtained from the patients for this study due to the ongoing viral epidemic in mainland China during that period. This study was approved by the Ethics Commission of Wuhan Huoshenshan Hospital. (No. IEC-AF-SC-05)

2.3. Data collection

Demographic and clinical data were retrieved from electronic medical records and nursing records, including gender, sex, onset symptoms, underlying health problems, vital signs on admission, baseline laboratory data before treatment (i.e., blood routine, liver function, kidney function, electrolyte levels, coagulation function, cardiac function, C reactive protein [CRP], procalcitonin [PCT]), dynamic changes in key laboratory indexes (i.e., temperature, white blood cell count [WBC], total lymphocyte count [TLC], platelet [PLT], C-reactive protein [CRP], alanine transaminase [ALT], aspartate transaminase [AST], PCT, total bilirubin [TBIL], creatinine [CRE], creatine kinase-MB [CK-MB]), comorbidities and complications, and treatments. Data collection was completed by three independent authors.

2.4. Outcomes

The primary endpoint of interest was fatality after ICU admission. Those diagnosed as recovered patients were evaluated according to the Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (provisional, version 7.0).[5] Additionally, the follow-up was defined as the period from admission into the ICU until meeting the primary endpoint.

The secondary endpoints were diverse laboratory indexes and the incidence of complications. Acute respiratory disease syndrome (ARDS) was recognized based on the Berlin ARDS definition.[11] Acute kidney injury was diagnosed if CRE increased by 26.5 mmol/L or more in 48 h or rose by at least 1.5-fold from baseline within 7 days.[11] The diagnosis of gastrointestinal hemorrhage was based on complaints from the patients or aspiration of gastric contents. The term myocardial injury was used when troponin values were elevated above the 99% upper reference limit. Secondary bacterial infection was detected by symptoms, signs and blood tests (i.e., blood routine, CRP and PCT). The Sequential Organ Failure Assessment (SOFA) score was used to assess the patient's condition to diagnose sepsis (SOFA $\geq$ 2).[12] Coagulopathy was defined as a 3-second extension of the prothrombin time or a 5-second extension of the activated partial thromboplastin time. COVID-19-associated abnormal liver function was diagnosed if ALT or AST increased to 3-fold over the upper limit or if TBIL was more than twice the upper limit without another cause.[13]

2.5. Statistical analysis

Descriptive statistics were used to tabulate these patients' clinical features; means and standard deviation or median and interquartile ranges (IQR) are reported for continuous variables, and number is reported for categorical variables. Differences between the survivors and nonsurvivors groups were compared by the $\chi 2$ test, Wilcoxon rank-sum tests and Fisher's exact tests were applied for categorical variables, and t-tests, Wilcoxon rank-sum tests were applied for continuous variables. The distributions were considered significantly different with an α risk of 5% if the P-value was less than 0.05.

In addition, we adopted a group-based trajectory modeling approach to identify different patterns of temperature from admission to day 28 (temperature was recorded 6 times each day at 2 a.m., 6 a.m., 10 a.m., 2 p.m., 6 p.m. and 10 p.m.). The shapes and the optimal number of groups were determined by the following criteria: 1) Bayesian information criterion was highest; 2) the number of patients in each group was not less than 10% of the total; 3) high average posterior probability of assignment (> 0.7).

Data management and analysis were performed using SAS software (version 9.4) for Windows.

3. Results

3.1. Epidemiological data

Between 8th February and 16th April, 126 patients were admitted to the ICU of Wuhan Huoshenshan Hospital according to the records. Among them, two patients had two records, of which the second one was retained as the basis for endpoint. Ultimately, 124 critical patients met our inclusion criteria and were

included in this study. (Fig. 1) All 124 patients reached the endpoint with full medical records. Overall, 57 (46%) of them eventually died, another 67 (54%) patients survived.

An overview of the baseline characteristics of nonsurvivors (n = 57) and survivors (n = 67) in terms of demographic and underlying health problems is provided in Table 1. There were 81 (65%) males and 43 (35%) females, and the average age was 69.89 ± 11.03 years. We found that the average age was significantly higher in nonsurvivors than in survivors (71.12 ± 9.24 vs. 68.85 ± 12.33), which can also be observed visually in Table 1. Closer inspection of this table showed that more than half of the patients had underlying health problems, of which the first few were hypertension (63 [51%]), diabetes mellitus (27 [22%]) and cardiovascular diseases (23 [19%]). Moreover, the most frequently observed symptom was fever (83 [67%]), followed by dry cough (69 [56%]) and fatigue (60 [48%]). Interestingly, few patients developed infrequent conditions, such as headache (4 [3%]), diarrhea (4 [3%]) and vomiting (2 [2%]).

Table 1
Baseline characteristics for critical patients with COVID-19

	Overall (n = 124)	Non-survivors (n = 57)	Survivor (n = 67)
Gender, n (%)			
Male	81 (65)	40 (70)	41 (61)
Female	43 (35)	17 (30)	26 (39)
Age, years			
Mean ± SD	69.89 ± 11.03	71.12 ± 9.24	68.85 ± 12.33
Underlying health problems, n (%)			
Hypertension	63 (51)	25 (44)	38 (57)
Diabetes mellitus	27 (22)	14 (25)	13 (20)
Cardiovascular disease	23 (19)	14 (25)	9 (13)
Urinary system diseases	16 (13)	7 (12)	9 (13)
Chronic lung disease	13 (10)	6 (11)	7 (11)
Digestive system diseases	13 (10)	5 (9)	8 (12)
Malignancy	8 (6)	2 (4)	6 (9)
Symptoms, n (%)			
Fever	83 (67)	39 (68)	44 (66)
Dry cough	69 (56)	32 (56)	37 (55)
Fatigue	60 (48)	31 (54)	29 (43)
Breathlessness	45 (36)	22 (39)	23 (34)
Myalgia	26 (21)	13 (23)	13 (19)
Chest tightness	19 (15)	6 (11)	13 (19)
Headache	4 (3)	2 (4)	2 (4)
Diarrhea	4 (3)	2 (4)	2 (3)
Vomiting	2 (2)	1 (2)	1 (1)
Data presented as Mean ± SD or n (Percentage)			

3.2. Clinical features before treatment

The clinical features before treatment were summarized in Table 2. Interestingly, many features were significantly different between the two groups, including SaO$_2$, Neutrophil ratio, Lymphocyte ratio, PLT, AST, TBIL, CRE, CK-MB, LDH, PCT, etc. Higher WBC (11.49 ± 8.51 vs. 8.52 ± 3.45) and lower TLC (0.74 ± 0.43 vs. 0.90 ± 0.51) were presented in nonsurvivors while there was no statistical significance. Although the PLT in each group were in the normal range, a lower PLT was observed in nonsurvivors (185.47 ± 127.79 vs. 224.34 ± 99.64). The CRP level, cardiac function and PCT level and coagulation function in nonsurvivors were more severely impaired than those in survivors as well, while most liver function and kidney function remained normal or mildly abnormal.

Table 2
Basic data of vital signs on admission and laboratory tests before treatments

	Non-survivors (n = 57)	Survivor (n = 67)	P-value
Vital signs			
T, °C	36.94 ± 0.74	36.66 ± 0.53	0.0137*
SBP, mmHg	131.35 ± 19.98	133.24 ± 19.37	0.5950
DBP, mmHg	76.88 ± 15.08	79.78 ± 13.41	0.2595
RR, n	22 (20, 24)	21 (19, 24)	0.3585
P, n	89 (81, 98)	87 (78, 98)	0.5222
SaO2, %	92.28 (7.09)	96.42(3.31)	< 0.0001*
Laboratory Tests			
Complete Blood Cell			
WBC, *10^9/L	11.49 ± 8.51	8.52 ± 3.45	0.1189
Neutrophil ratio, %	85.65 ± 10.19	80.62 ± 10.30	0.0025*
Lymphocyte ratio, %	9.05 ± 7.71	12.24 ± 8.01	0.0063*
TLC, *10^9/L	0.74 ± 0.43	0.90 ± 0.51	0.0749
RBC, *10^12/L	3.84 ± 0.65	3.82 ± 0.73	0.7906
HGB, g/L	119.11 ± 19.70	116.14 ± 22.86	0.4816
PLT, *10^12/L	185.47 ± 127.79	224.34 ± 99.64	0.0120*
Liver Function			
ALT, IU/L	40.61 ± 37.55	35.49 ± 32.01	0.2805

Data presented as Mean ± SD or Median (Q1, Q3)

Abbreviation: T, Temperature; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; RR, Respiratory rate; P, Pulse; SaO2, Oxygen Saturation; WBC, White blood cell count; TLC, Total lymphocyte count; RBC, Red blood cell count; HBG, Hemoglobin; PLT, Platelet; CRP, C-reactive protein; ALT, Alanine transaminase; AST, Aspartate transaminase; TBIL, Total bilirubin; TA, Total bile acid; ALP, Alkaline phosphatase; GGT, Gamma-glutamyl transferase; CRE, Creatinine; CK-MB, Creatine kinase-MB; LDH, Lactate dehydrogenase; BNP, B-type natriuretic peptide; hsTNI, hypersensitive troponin I; PT, Prothrombin; INR, International Normalized Ratio; APTT, Activated partial thromboplastin time; PCT, Procalcitonin

*P < 0.05 for comparison with survivor and non-survivor

	Non-survivors (n = 57)	Survivor (n = 67)	P-value
AST, IU/L	48.11 ± 45.20	32.61 ± 28.63	0.0456*
Albumin, g/L	31.69 ± 4.56	32.62 ± 4.18	0.4488
TBIL, μmol/L	19.08 ± 20.16	10.35 ± 4.95	0.0003*
TBA, μmol/L	6.74 ± 8.19	3.57 ± 4.01	0.0205*
ALP, IU/L	97.74 ± 40.46	89.50 ± 48.57	0.1092
GGT, IU/L	67.11 ± 51.73	62.65 ± 59.07	0.8906
Kidney Function			
UREA, mmol/L	9.32 ± 6.06	8.61 ± 6.73	0.3995
CRE, mmol/L	96.84 ± 71.44	123.91 ± 223.03	0.0461*
Electrolytes			
K^+, mmol/L	4.28 ± 0.58	4.22 ± 0.72	0.3491
Na^+, mmol/L	141.68 ± 8.62	139.96 ± 4.96	0.8202
Cardiac function			
CK-MB, IU/L	20.77 ± 19.61	14.42 ± 10.99	0.0211*
LDH, IU/L	438.04 ± 162.74	296.48 ± 122.92	< 0.0001*
BNP, pg/ml	309.40 ± 403.34	182.48 ± 326.95	0.0601
Coagulation function			
PT, s	16.38 ± 3.41	14.10 ± 2.22	0.0006*
INR, n	1.37 ± 0.28	1.17 ± 0.19	0.0005*

Data presented as Mean ± SD or Median (Q1, Q3)

Abbreviation: T, Temperature; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; RR, Respiratory rate; P, Pulse; SaO2, Oxygen Saturation; WBC, White blood cell count; TLC, Total lymphocyte count; RBC, Red blood cell count; HBG, Hemoglobin; PLT, Platelet; CRP, C-reactive protein; ALT, Alanine transaminase; AST, Aspartate transaminase; TBIL, Total bilirubin; TA, Total bile acid; ALP, Alkaline phosphatase; GGT, Gamma-glutamyl transferase; CRE, Creatinine; CK-MB, Creatine kinase-MB; LDH, Lactate dehydrogenase; BNP, B-type natriuretic peptide; hsTNI, hypersensitive troponin I; PT, Prothrombin; INR, International Normalized Ratio; APTT, Activated partial thromboplastin time; PCT, Procalcitonin

*P < 0.05 for comparison with survivor and non-survivor

	Non-survivors (n = 57)	Survivor (n = 67)	P-value
APTT, s	31.60 ± 9.06	29.70 ± 5.28	0.6988
D-dimer mg/L	4.24 ± 4.41	3.61 ± 4.71	0.3788
CRP, mg/L	40.98 ± 48.75	30.69 ± 41.99	0.3217
PCT, ng/ml	0.96 ± 2.31	0.30 ± 0.78	0.0018*

Data presented as Mean ± SD or Median (Q1, Q3)

Abbreviation: T, Temperature; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; RR, Respiratory rate; P, Pulse; SaO2, Oxygen Saturation; WBC, White blood cell count; TLC, Total lymphocyte count; RBC, Red blood cell count; HBG, Hemoglobin; PLT, Platelet; CRP, C-reactive protein; ALT, Alanine transaminase; AST, Aspartate transaminase; TBIL, Total bilirubin; TA, Total bile acid; ALP, Alkaline phosphatase; GGT, Gamma-glutamyl transferase; CRE, Creatinine; CK-MB, Creatine kinase-MB; LDH, Lactate dehydrogenase; BNP, B-type natriuretic peptide; hsTNI, hypersensitive troponin I; PT, Prothrombin; INR, International Normalized Ratio; APTT, Activated partial thromboplastin time; PCT, Procalcitonin

*P < 0.05 for comparison with survivor and non-survivor

Table 3
Clinical manifestation, including symptoms, complications and treatments of these patients

	Overall (n = 124)	Non-survivors (n = 57)	Survivor (n = 67)	P-value
The first apartment, n (%)				
ICU	81 (65)	40 (70)	41 (61)	0.0251*
Non-ICU	43 (35)	17 (30)	26 (39)	
Treatments				
Non-invasive ventilation	65 (52)	47 (82)	18 (27)	< 0.0001*
Invasive ventilation	55 (44)	50 (88)	5 (7)	< 0.0001*
ECMO	5 (4)	5 (9)	0	0.0437
Glucocorticoids	84 (68)	46 (81)	38 (57)	0.0044*
Antiviral drugs				
Arbidol hydrochloride	76 (61)	40 (70)	36(54)	0.0610
Lianhua Qingwen	71 (57)	30 (53)	41 (61)	0.3368
Interferon	16 (13)	5 (9)	11(16)	0.2056
Ribavirin	13 (10)	4 (7)	9 (13)	0.2452
Hydroxychloroquine	8 (10)	1 (2)	7 (10)	0.1102
CBPT	18 (15)	15 (26)	3 (4)	0.0006*
Convalescent plasma	17 (14)	5 (9)	12 (18)	0.1403
Complication, n (%)				
Sepsis	96 (73)	57 (100)	34 (51)	< 0.0001*
ARDS	73 (59)	52 (91)	21 (38)	< 0.0001*
Secondary bacterial infection	59 (48)	42 (74)	17 (25)	< 0.0001*
Myocardial injury	40 (32)	29 (51)	11 (17)	< 0.0001*
AKI	46 (37)	37 (65)	9 (13)	< 0.0001*

Abbreviation: ARDS, acute respiratory distress syndrome AKI, acute kidney injury ECMO, Extracorporeal membrane oxygenation; CBPT, Continuous blood purification therapy

*P < 0.05 for comparison with survivor and non-survivor

	Overall (n = 124)	Non-survivors (n = 57)	Survivor (n = 67)	P-value
Coagulopathy	39 (31)	35 (55)	4 (6)	< 0.0001*
Abnormal liver function	37 (30)	29 (51)	8 (12)	< 0.0001*
Gastrointestinal hemorrhage	14 (11)	9 (7)	5 (8)	0.1442
Abbreviation: ARDS, acute respiratory distress syndrome AKI, acute kidney injury ECMO, Extracorporeal membrane oxygenation; CBPT, Continuous blood purification therapy				
*P < 0.05 for comparison with survivor and non-survivor				

3.3 Findings during clinical course

As a whole, patients who were transferred to ICU had a higher fatality rate than those received treatments in ICU at the very start (49% [40/81] vs. 40% [17/43], P < 0.05). Most patients required supplemental oxygen with noninvasive mechanical ventilation (52%) and invasive mechanical ventilation (44%) were also used in patients, among whom nonsurvivors accounted for a higher proportion and had worse illness. Extracorporeal membrane oxygenation was used in 5 patients; unfortunately, none of them survived. Regarding medications, glucocorticoids and antiviral drugs were widely used; interestingly, the use of glucocorticoids was statistically significant between the two groups (P < 0.05) and all kinds of antivirals showed no statistical difference. Not surprisingly, sepsis (100% [57/57]) and acute respiratory distress syndrome (ARDS) (91% [52/57]) were the two most common complications in nonsurvivors. Compared to survivors, nonsurvivors also showed a significantly higher proportion of secondary bacterial infection (74% [42/57] vs. 25% [17/67]), myocardial injury (51% [29/57] vs. 17% [11/67]), acute kidney injury (65% [37/57] vs. 13% [9/67]), coagulopathy (55% [35/57] vs. 6% [4/67]) and abnormal liver function(51% [29/57] vs. 12% [8/67]).

As shown in Fig. 2, the dynamic changes in several key laboratory indexes were compared. It was apparent that TLC and PLT were generally lower in nonsurvivors than in survivors, whereas WBC and CRP levels were higher. WBC level fluctuated among nonsurvivors during the clinical course while it was under baseline condition among survivor. TLC levels were both at low standard throughout but the level of TLC gradually increased. As for CRP, the inflammatory indicator, overall level among nonsurvivors was remarkably higher than that in survivors. Moreover, biochemical indices of liver function, CK-MB, CRE and D-dimer did not differ significantly between two groups and the variations were small as a whole. (see Figure E1 in the online data supplement).

The distinct trajectories of temperature during the follow-up, which could provide valuable insight to monitoring the recovery of patients, are demonstrated in Fig. 3. The patients were classified into 3 groups based on the temperature trajectory after admission as follows: group 1 (stabilized group; n = 69, 55.65%),

maintained a stable temperature below 37°C; group 2 (down-and-up group; n = 36, 29.03%), had a mean temperature that fell a little at the beginning and finally climbed up; and group 3 (steady-declining group; n = 19, 15.32%), the temperature of these patients was initially higher than normal and dropped gradually to approximately 36.6°C from the above normal body temperature. Patients with these 3 temperature trajectories had distinct fatalities. Group 1 had the lowest fatality rate at 21.74%, with a mean temperature of 36.60 °C. Patients in group 2 had a mean temperature of 36.81 °C and a fatality rate of 69.44%. In particular, the steady-declining group was characterized by the highest fatality rate of 84.21% (mean temperature, 37.44 °C). The characteristics at baseline and laboratory tests on admission stratified by temperature trajectory groups were presented in Table E1. Among group 3, the WBC, TLC, PLT and CRP levels were found to be significantly severer than the rest two. (see Table E1 in the online data supplement)

4. Discussion

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is genetically similar to the severe acute respiratory syndrome (SARS) coronavirus that resulted in the SARS outbreak in 2002, is responsible for a global pandemic of COVID-19.[14] The outbreak began in China but has since spread around the world.[15–17] The hospitals and clinics were initially overwhelmed, and both patients and healthcare providers became severely ill and died soon after. However, as the healthcare system response ramped up from the very beginning, more designated and newly built hospitals, like Wuhan Huoshenshan Hospital, and better equipment became available, the situation was under control within a short period in China.[18]

In our study, there were 124 confirmed cases of COVID-19 in the ICU of Wuhan Huoshenshan Hospital, and the 47 deaths resulted in a fatality rate of 46%, which is close to the data reported by the Chinese Centers for Disease Control and Prevention.[19] As mentioned in the previous literature[19], approximately 80% of patients with COVID-19 have mild symptoms, and few people do not develop any symptoms or signs at all. For the remaining 20%, as our study shows, these patients can range from mild symptoms, such as fever and dry cough, all the way to severe conditions, such as ARDS and even sepsis. Based on our data, the rate of critically ill patients is overwhelmingly male, overwhelmingly older. Similarly, both the rates of critical illness and the fatality rate are higher for patients with underlying health problems than for those without any of these conditions. In addition, many elderly patients typically have one or more of these conditions, so it is not surprising that these factors go hand in hand. Unlike seasonal flu, vaccines for SARS-CoV-2 have not yet been well established, although both are respiratory viruses.[20] Therefore, elderly patients with underlying health problems are truly the ones at the highest risk.

The inflammation caused by SARS-CoV-2 builds up much fluid within and around the lung and results in ARDS and even subsequent multiple organ dysfunction syndrome, which means that the whole body starts shutting down.[21] ARDS is a common complication during the clinical course and is the main cause of death. Among the nonsurvivors, all patients were diagnosed with ARDS and sepsis, which is often caused by severe infection. Our experience revealed that ARDS always had a sudden onset and rapid

development, so few patients died soon. So far, not many treatment options exist for coronavirus, so the only option is offering supportive treatment, such as maintaining respiratory function with oxygen and ventilatory support, while the patient's immune system fights off the virus. Besides, multiple antiviral drugs have been tested, including arbidol hydrochloride, Lianhua Qingwen capsules and broad-spectrum antiviral agents. Unfortunately, none of them provide significant benefits. However, there are still debates about when and how to use glucocorticoids and whether patients should be incubated, though the results were statistically significant. In addition, it can be seen from Table 2 that the greatest need is a risk prediction model based on basic data at admission if the sample size is sufficient since many laboratory indexes are significantly different between survivors and nonsurvivors.

The dynamic changes in these biomarkers raise intriguing questions regarding the nature and extent of targeting of SARS-CoV-2. For example, obviously increased ALT/AST and TBIL occurred among patients with acute liver injury (37[30%]), while those hepatic function indexes did not seem to change significantly overall and we supposed that the influence of underlying health problems cannot be ruled out.[22] Nonetheless, we have reasons to believe that COVID-19-associated liver injury may be affected by various elements, such as hepatotoxic agents and a body-wide inflammatory reaction, and it may not be a common complication.[13] Moreover, other statistically significant biomarkers, like WBC, TLC, PLT and CRP, are a compelling reminder for a poor prognosis. Numerically, TLC levels, which was expected based on the biological characteristics of the virus, dropped significantly among two groups in particular and nonsurvivors remained at a lower level.

Temperature trajectories reflect the potential dynamic changing patterns of temperature during the clinical course. We suppose that temperature is a consequence of infection and response of the body to it and patients in group 3 may be not able to fight against the virus in the later time of treatment. This observation provides new insights into COVID-19-associated temperature changes and indicates that critical patients with a high temperature should be particularly paid attention to by health care providers, especially those with high temperature on admission.

5. Limitations

On the other hand, our study has several limitations. First, the results of the arterial blood gas analysis, which we believe are quite valuable for prognosis, were incomplete due to strict controls involving blood samples; hence, we did not perform a thorough analysis. Another potential limitation is that we did not conduct further exploration based on findings (e.g. the difference between subgroups based on transfers) in this article because of the limited space of this thesis. Further studies that take these flaws and unanswered questions into account will need to be undertaken.[23]

6. Conclusions

The strengths of this study include that it is a large retrospective cohort study of critical patients in the ICU with information on COVID-19 and its associated outcomes from the first anti-pandemic frontline. It is

worth mentioning that early in the disease, high temperature should receive extra care.

Abbreviations

COVID-19: Corona Virus Disease 2019

ICU: Intensive care unit

WHO: World Health Organization

PCT: Procalcitonin

WBC: White Blood Cell

TLC: Total lymphocyte count

PLT: Platelet

CRP: C-reactive protein

ALT: Alanine transaminase

AST: Aspartate transaminase

TBIL: Total bilirubin

hsTNI: hypersensitive troponin I

CRE: Creatinine

ARDS: Acute respiratory distress syndrome

SOFA: Sequential Organ Failure Assessment

IQR: Interquartile ranges

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

SARS: Severe acute respiratory syndrome

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Commission of Wuhan Huoshenshan Hospital. (No. IEC-AF-SC-05)

Consent for publication

Informed consent was not obtained from the patients for this study due to the ongoing viral epidemic in mainland China at that time.

Availability of data and materials

Not applicable

Competing interests

There is no competing interest need to be declared.

Funding/Support

Author's contributions

WQL, XJZ and HT contributed to the study concept and design. YBR, JXW, WW and HT collected the original data. HSH, YSM, XWQ and TYS compiled the data. HSH, ZCJ, WW, HYW, WQL, XJZ and HT analyzed and interpreted the data. HSH wrote the draft manuscript. ZCJ and CXZ offered the statistical analyses. SZC, WW, JXW and HT revised the manuscript for important intellectual content. SZC, WW, HT and HYW obtained the funding. YBR, WW, XJZ, WQL, HT and HYW provided administrative support. XJZ, WQL, HT and HYW supervised the project and gave final approval.

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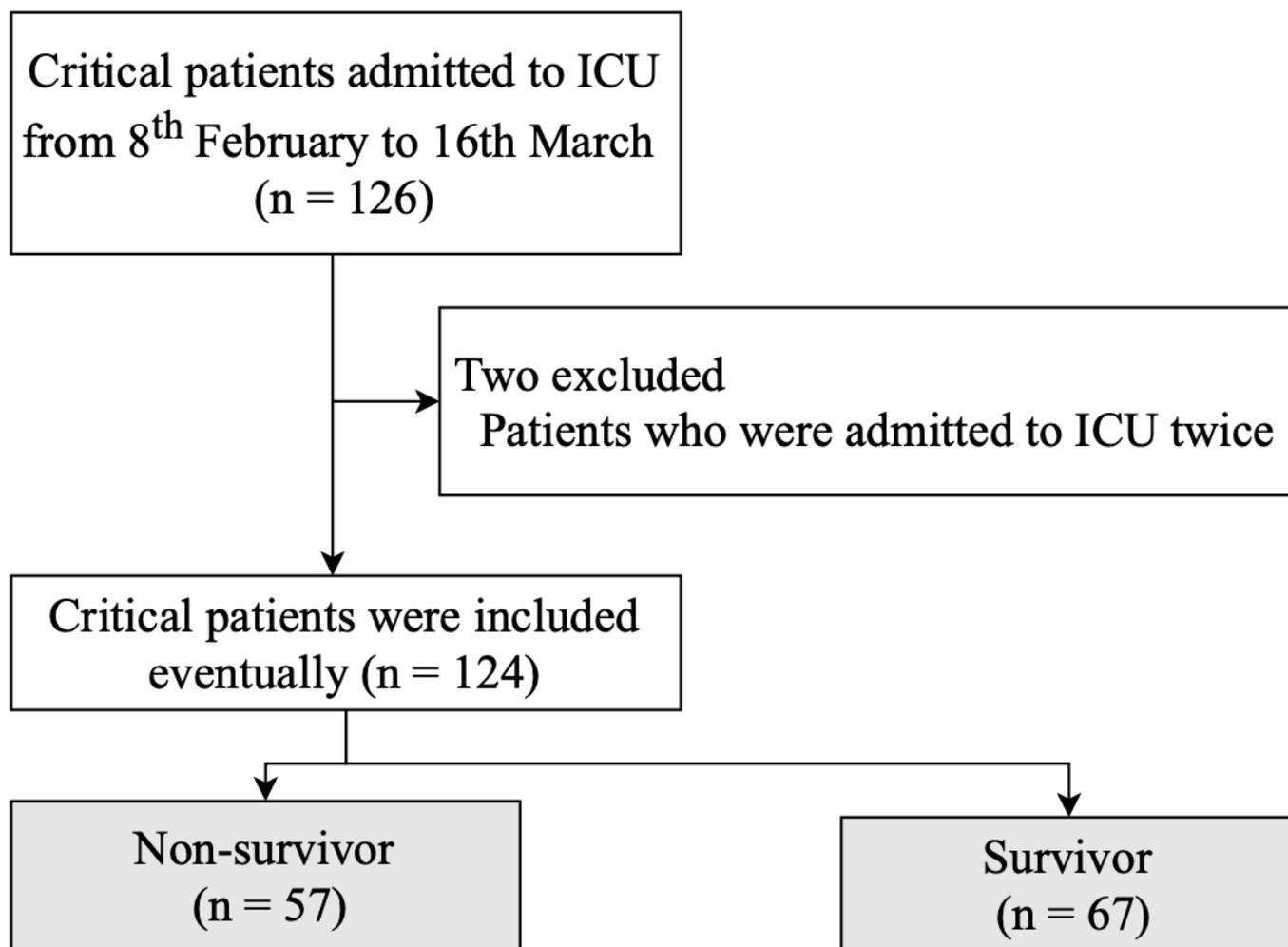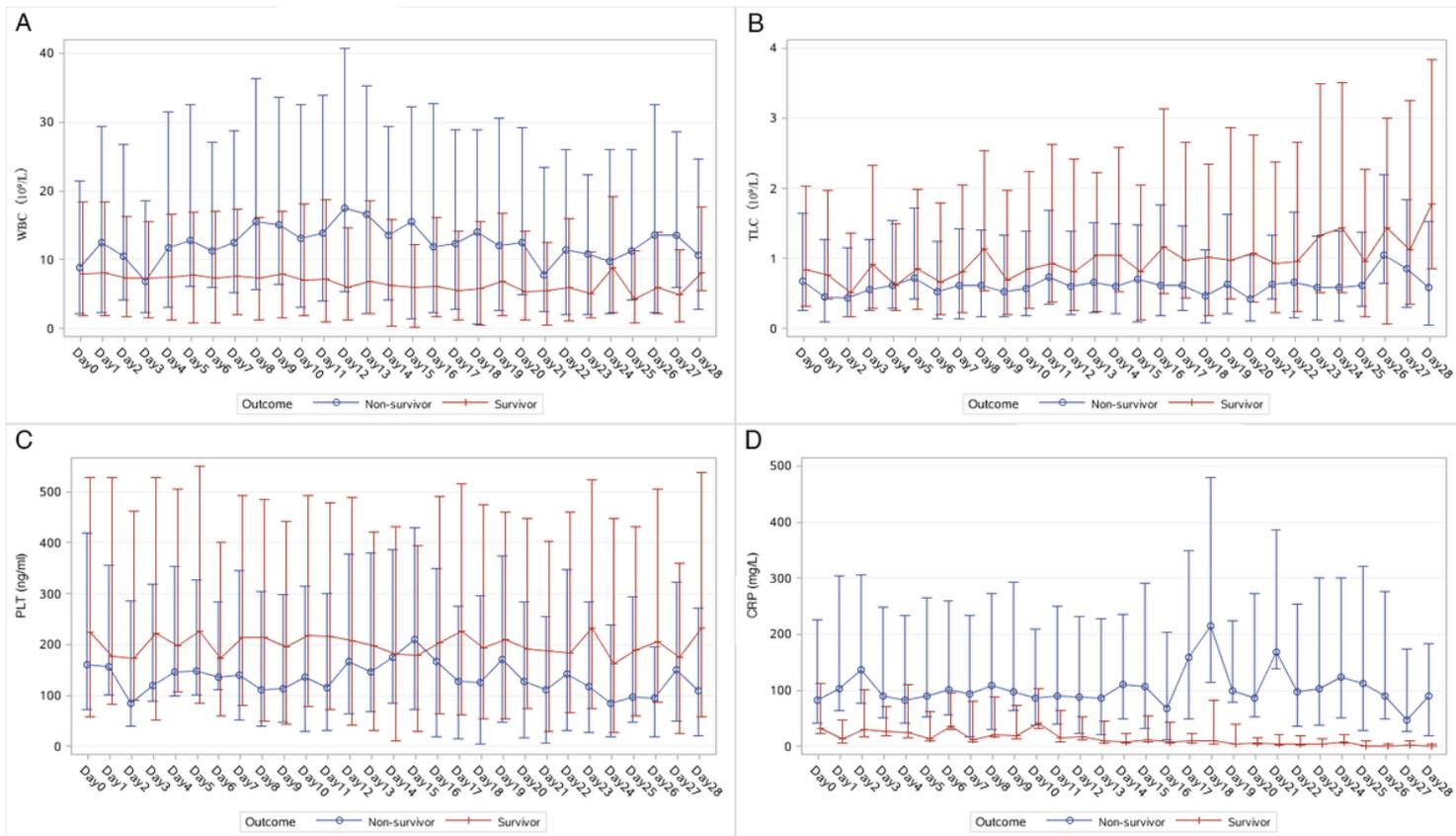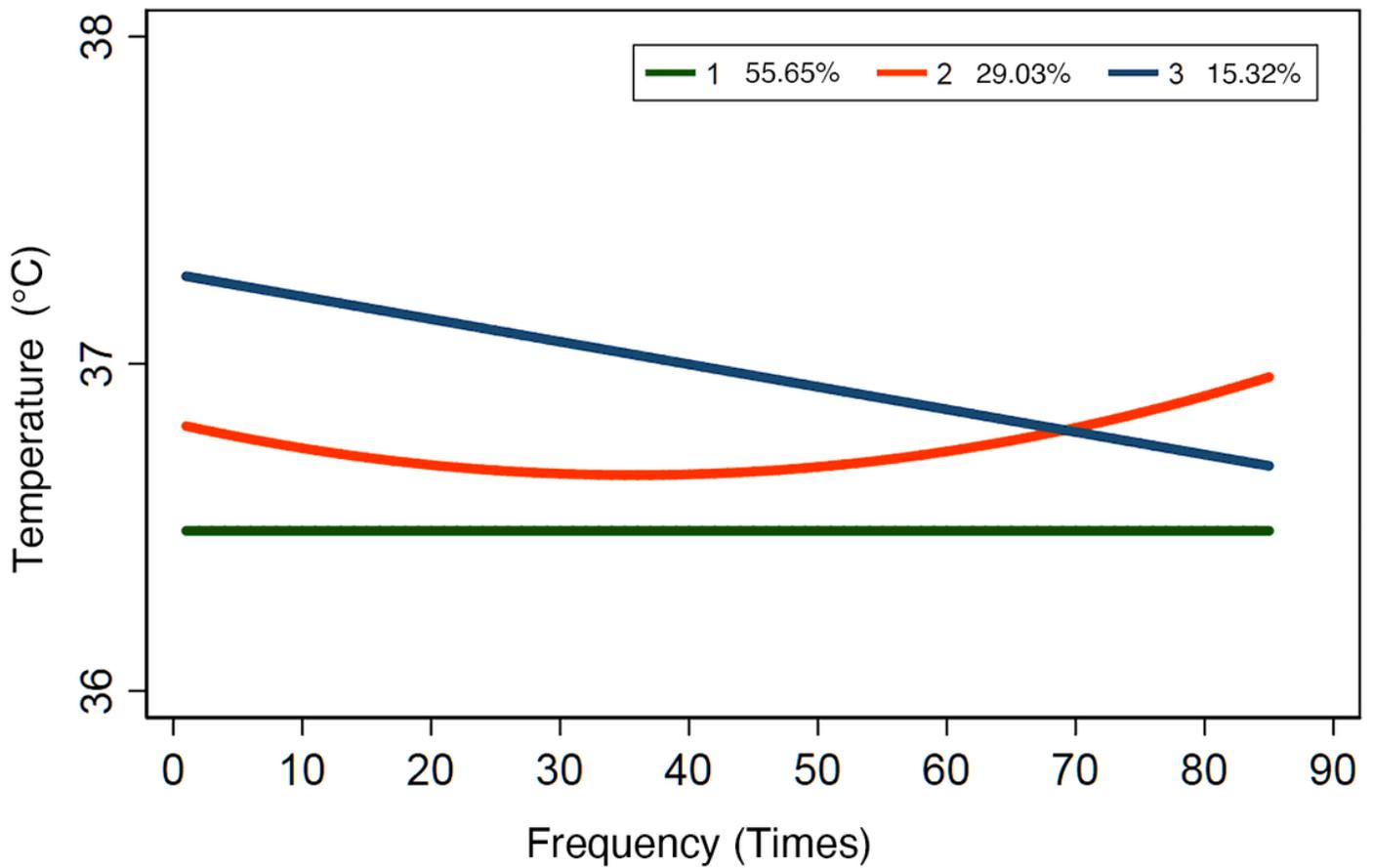
Figures

Figure 1

Flow chart of patient inclusion

Figure 2

Dynamic changes of several important laboratory indexes during the follow-up period. (A) White blood cell (WBC) counts; (B) Total Lymphocyte Count (TLC); (C) Platelet (PLT); (D) C-reactive protein (CRP);

Figure 3

Trajectories of temperature for patients from admission to 16th April. Group 1 (a stabilized group; n=69, 55.65%); Group 2 (a down-and-up group; n=36, 29.03%); Group 3 (a steady-declining group; n=19, 15.32%)

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