Clinical Characteristics and Risk Factors of Fatal Patients with COVID-19: a Retrospective Cohort Study in Wuhan, China

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Abstract

Background

The coronavirus disease 2019 (COVID-19) has caused global pandemic, resulting in considerable mortality. The risk factors, clinical treatments and especially comprehensive risk models for COVID-19 death are urgently warranted.

Methods

In this retrospective study, 281 non-survivors and 712 survivors with propensity score matching by age, sex and comorbidities were enrolled from January 13, 2020 to March 31, 2020.

Results

Higher SOFA, qSOFA, APACHE II and SIRS scores, hypoxia, elevated inflammatory cytokines, multi-organ dysfunction, decreased immune cells subsets and complications were significantly associated with the higher COVID-19 death risk. In addition to traditional predictors for death risk, including APACHE II (AUC = 0.83), SIRS (AUC = 0.75), SOFA (AUC = 0.70) and qSOFA scores (AUC = 0.61), another four prediction models that included immune cells subsets (AUC = 0.90), multiple organ damage biomarkers (AUC = 0.89), complications (AUC = 0.88) and inflammatory-related indexes (AUC = 0.75) were established. Additionally, the predictive accuracy of combining these risk factors (AUC = 0.950) was also significantly higher than that of each risk group alone, outperforming previous risk models, which was significant for early clinical management for COVID-19.

Conclusions

The potential risk factors could help to predict the clinical prognosis of COVID-19 patients at an early stage. The combined model might be more suitable for the death risk evaluation of COVID-19.

Background

The global spread of coronavirus disease 2019 (COVID-19) has become a major global public health issue. The COVID-19 pandemic was sweeping across borders, sickening and killing people in nearly every country. Until July 25, 2020, 3,634,172 cases were confirmed and [1][1]the death numbers of COVID-19 attained 251,446[1][1][1] currently. Considering the adverse effects of COVID-19 and its high mortality rate, it is urgent for us to understand the risk factors influence the incidence of death and develop a comprehensive risk model evaluating the death risk of COVID-19.

Recent evidence has showed that the infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) induces clusters of severe and even fatal pneumonia which had a high mortality [2]. There are several scores have been considered as good evaluation indexes for sepsis, septic shock, multi-organ dysfunction and even death in patients suffering from bacterial or viral pathogen infection, such as the sequential organ failure assessment (SOFA), quick SOFA (qSOFA), acute physiology and chronic health evaluation II (APACHE II) and systemic inflammatory response syndrome (SIRS) scores[3–8]. In addition, it has been reported that the pro-inflammatory cytokine IL-6 and organ damage biomarkers, such as D-dimer and NT-proBNP were risk factors for death of adults with COVID-19 [6, 9,
Some case series have reported the clinical characteristics or potential risk factors for fatal patients with COVID-19 [6, 9, 11]. However, the sample sizes in most of these reports were limited and detailed information about biochemical biomarkers dynamics, immune cells subsets or pertained treatments of fatal COVID-19 patients have not yet been well described. Most importantly, currently no researches have been done to develop a comprehensive prediction model integrating these scores, inflammatory indices, immune cells subsets and organ damage risk factors for death risk of COVID-19, which is of great value for better risk stratification, death-related biomarkers identification and clinical treatments strategies-making.

Here we performed a retrospective, observational study in fatal COVID-19 patients and presented the details of patients with definite clinical outcome (death or discharge) from Tongji Hospital, Huazhong University of Science and Technology (HUST), which is the biggest designated hospital treating severely or critically ill COVID-19 patients in Wuhan, an epicenter of COVID-19 outbreak. The objective of this study was to explore potential risk factors of death for COVID-19 and establish a comprehensive risk model evaluating the death risk of COVID-19, which is of utmost importance for early clinical management and successful establishment of standardized treatment protocols, ultimately curbing the rising fatality rate of COVID-19.

**Methods**

**Study Design and Participants**

This retrospective cohort study was performed in patients with confirmed COVID-19 from Tongji Hospital, Tongji Medical College, HUST, a designated hospital for severely or critically ill COVID-19 patients. All fatal patients with COVID-19 (N=281) were enrolled from January 13 to March 31, 2020. Subsequently, 712 survivors that were statistically matched by propensity score matching [12] at an approximate ratio of 3:1 based on age, sex and comorbidities. This study was approved by the Ethics Committee of Tongji Hospital, Tongji Medical College, HUST and granted a waiver of informed consent from study participants.

**Data Collection**

Epidemiological, clinical, radiological, laboratory, clinical treatments, and clinical outcomes data of all patients with laboratory-confirmed SARS-CoV-2 were obtained with data collection forms from electronic medical records of Tongji Hospital. The researches on other topics [9, 13] may obtain some information of deceased patients in Tongji hospital, however, our study collected more information about cases and detailed data. The admission and in-hospital data of these patients were collected, reviewed and verified by a trained team of physicians. Any missing or uncertain records were collected and clarified through communication with involved health-care providers and their families. The detailed and standardized information of demographic data, underlying comorbidities, initial symptoms, vital signs, and chest computed tomographic (CT) were recorded or diagnosed at hospital admission. The complications, treatments, clinical outcomes (survivors and non-survivors) and hospital length of stay were monitored to March 31, 2020, the final data of follow-up. Laboratory examinations including blood routine, immune cells subsets, inflammatory cytokines and biomarkers, blood gas assay, cardiac function test, renal function test, liver function test, pancreatic function test, coagulation test, and metabolism test were detected on the first diagnosed date. The time of follow-up was defined as the duration from admission to outcomes (survivor/non-survivor) of patients. There were no cases lost to follow-up in this study attributed to standardized government managements and close tracking for COVID-19 pandemic.

**Definitions**
The detailed definitions of complications including acute respiratory distress syndrome (ARDS), acute pancreatic injury, acute liver damage, acute cardiac injury, disseminated intravascular coagulation (DIC), SOFA, qSOFA, APACHE II and SIRS scores were listed in the supplementary methods.

**Statistical analysis**

Continuous variables were presented as median and interquartile range (IQR) or mean and standard deviation (SD). Categorical variables were expressed as number (%). For continuous variables, Student's \( t \)-test was used for normal distributed data, and Mann-Whitney U non-parameter test was used for non-normal distributed data. The Pearson's \( \chi^2 \) test or Fisher's exact test were applied for categorical variables. Time to events (recovered or death) were defined as the time from hospital admission to events. The univariate Cox regression models were used to determine hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between individual factors and death risk of COVID-19. The multivariate Cox model analysis were used to establish death risk prediction models. The significant variables from univariable analysis of the death risk were considered as the candidates. Time-dependent receiver operating characteristic (ROC) curves and areas under the curves (AUCs) were used to assess prognostic accuracy of each model [14]. A two-sided \( P \) value < 0.05 was considered statistically significant. All statistical analyses were performed using SAS (9.4).

**Results**

**Clinical characteristics and laboratory findings of non-survivors and survivors with COVID-19**

281 (28.30%) non-survivors and 712 (71.70%) survivors with COVID-19 were enrolled in this study. Considering that the age, sex and comorbidities had been reported as the common death risk factors of COVID-19, enrolled survivors and non-survivors were statistically matched based on these risk factors. As summarized in Table 1 and supplementary table 1, the most common symptoms of all patients were fever and cough, non-survivors were more likely to have dyspnea (50.39% vs 42.23%, \( P=0.026 \)) than survivors. Besides, non-survivors tended to have more abnormal vital signs on admission, such as higher temperature, heart rate and respiratory rate.

The abnormalities in chest CT images among these patients were also observed (Table 1 and Figure 1). The patchy shadows presence was the most typical manifestation of both groups, while pleural thickening (41.38% vs 26.90%; \( P=0.018 \)) was more frequently observed in non-survivors, compared with survivors. Consistently, blood gas analysis revealed the degree of hypoxia was more evident in non-survivors, which presented lower concentration of PaO\(_2\), SaO\(_2\), PaCO\(_2\), CaCO\(_2\) and bicarbonate than survivors. These findings suggest more serious impairment of lung function in non-survivors.

Previous studies reported that cytokine storm and lymphopenia were common features in severe COVID-19 patients [2, 15]. We observed that the serum levels of inflammatory cytokines including IL6 (61.35 vs 6.85 pg/mL; \( P<0.0001 \)), IL10 (10.30 vs 5.00 pg/mL; \( P<0.0001 \)), IL8 (28.40 vs 11.60 pg/mL; \( P<0.0001 \)), TNF-\( \alpha \) (11.45 vs 8.10 pg/mL; \( P<0.0001 \)), IL-1\( \beta \) (8.15 vs 6.49 pg/mL; \( P<0.0001 \)) and IL2R (1148.00 vs 599.50 U/mL; \( P<0.0001 \)) were significantly elevated in non-survivors compared with survivors. Moreover, the infection-related biomarkers including ferritin, CRP and procalcitonin also exhibited higher levels in non-survivors. Conversely, the baseline counts of lymphocytes (0.63 vs 1.09×10\(^9\)/L; \( P<0.0001 \)), CD3\(^+\)CD19\(^-\) T cells (276.50 vs 905.00/\( \mu \)L, \( P<0.0001 \)), CD3\(^+\)CD8\(^+\) T cells (62.00 vs 280.00/\( \mu \)L; \( P<0.0001 \)), B cells (73.50 vs 156.00/\( \mu \)L, \( P<0.0001 \)), NK cells (36.50 vs 209.00/\( \mu \)L, \( P<0.0001 \)) as well as the total number of T cells, B cells and NK cells (406.00 vs 1337.00/\( \mu \)L; \( P<0.0001 \)) were drastically decreased in non-survivors,
compared with survivors. Collectively, these findings demonstrate that aggravated inflammatory responses and severe lymphopenia might be correlated with the poor clinical outcome of COVID-19 patients.

Multiple-organ damage was more pronounced in non-survivors. We observed higher levels of ALT, TBIL, LDH, homocysteine, NT-proBNP, hs-cTnI, CK-MB and lower level of ALB/GLO in non-survivors. Besides, non-survivors had a falling count of eosinophils while elevated leukocytes and neutrophils, compared with survivors. Of note, in non-survivors, coagulation-related biomarkers of platelets counts were also substantially decreased, followed by the increased D-dimer and prolonged PT and APTT.

Additionally, in term of several scores evaluating disease severity, the fatal cases had more serious SOFA (4.00 vs 2.00, \( P < 0.0001 \)), qSOFA (1.00 vs 0.00, \( P < 0.0001 \)), APACHE II (17.00 vs 10.00, \( P < 0.0001 \)) and SIRS scores (2.00 vs 1.00, \( P < 0.0001 \)), compared to recovered patients (Table 1).

**Complications and clinical treatments of non-survivors and survivors with COVID-19**

SARS-COV-2 infection can cause both pulmonary and multi-system inflammation, leading critical complications (Table 2). The frequency of acute cardiac injury (79.72% vs 11.80%, \( P < 0.0001 \)), heart failure (71.53% vs 6.32%, \( P < 0.0001 \)), acute kidney injury (48.40% vs 4.35%, \( P < 0.0001 \)), acute liver injury (24.20% vs 2.39%, \( P < 0.0001 \)), acute pancreatic injury (4.27% vs 1.54%, \( P = 0.010 \)) especially acute respiratory distress syndrome (ARDS, 96.80% vs 53.79%, \( P < 0.0001 \)) and disseminated intravascular coagulation (DIC, 19.22% vs 0.56%, \( P < 0.0001 \)) were more higher in non-survivors than survivors. These critical complications could be the main cause of death, and the underlying mechanisms warrant further investigations.

Almost all deceased patients received antibiotic treatment (93.95% vs 88.48%, \( P = 0.0094 \), more than the number of recovered patients (Table 2). Fatal patients received more glucocorticoid therapy, intravenous immunoglobulin therapy or transfusion than recovered cases, since the cytokine storm and DIC were more often observed in non-survivors. Similarly, due to the higher proportions of patients developed acute kidney injury or ARDS in non-survivors, decreased patients received more mechanical ventilation, continuous renal replacement therapy, high flow nasal cannula and extracorporeal membrane oxygenation than recovered patients. These factors might result in more frequent ICU admission (52.69% vs 0.56%, \( P < 0.0001 \)) and shorter time of hospital stay (22[IQR 15-28] vs 8 [IQR 4-14], \( P < 0.0001 \)) in non-survivors than survivors. The clinical interventions were more intensive in non-survivors due to the more severe illness in fatal cases. Of note, recovered patients were undergoing more, antiviral therapy (91.15% vs 80.07%, \( P < 0.0001 \)) as compared to deceased cases.

**Risk factors associated with the death of COVID-19 patients**

Furthermore, we performed Cox analysis to identify the potential death risk factors of COVID-19 with adjustment of age, sex, comorbidities. As shown in Table 3 and supplementary table 2, the higher temperature, faster heart rate and respiratory rate and lower mean arterial pressure were associated with increased risk of death. In terms of laboratory parameters, elevated inflammatory cytokines and infection-related factors, such as TNF-\( \alpha \), IL-6, IL-10, IL-1\( \beta \), IL-2R, ferritin, hs-CRP and procalcitonin were significantly associated with higher death risk of COVID-19. Conversely, the immune cells subsets, such as lymphocytes (HR=0.220, 95%CI=0.161-0.302, \( P < 0.0001 \)), B cells (HR=0.994, 95%CI=0.990-0.998, \( P = 0.002 \)), NK cells (HR=0.985, 95%CI=0.981-0.990, \( P < 0.0001 \)), CD3\(^+\)CD19\(^-\) T cells (HR=0.996, 95%CI=0.995-0.997, \( P < 0.0001 \)) and CD3\(^+\)CD8\(^+\) T cells (HR=0.989, 95%CI=0.985-0.992, \( P < 0.0001 \)) were significantly associated with the lower death risk of COVID-19.
Indicators that represented organ damages, such as elevated ALT, AST, LDH, creatinine, amylase, hs-cTnl, NT-proBNP, CK-MB, and decreased ALB/GLO aggrandized the risk for COVID-19 death. Furthermore, coagulation-related biomarkers, including declined platelet counts (HR=0.994, 95%CI=0.992-0.995, P<0.0001), and increased PT, APTT, D-Dimer (HR=1.025~1.359, P<0.0001), might be strong indicators for death risk of COVID-19. Moreover, apart from abnormal biochemical dynamics, metabolism indices and blood gas analysis such as decreased serum level of PaO₂, SaO₂, PaCO₂, and CtCO₂ that could result in the degree of electrolyte disturbance or hypoxia, increasing the risk death of COVID-19.

We also analyzed the risk of death for patients with complications, patients with ARDS (HR=16.216, 95%CI=8.341-31.527, P<0.0001) had highest risk of death, followed by acute cardiac injury (HR=13.023, 95%CI=9.678-17.524, P<0.0001), heart failure (HR=10.722, 95%CI=8.227-13.974, P<0.0001), acute kidney injury (HR=6.063, 95%CI=4.759-7.724, P<0.0001) and DIC (HR=5.819, 95%CI=4.281-7.910, P<0.0001). Besides, the higher levels of SOFA, qSOFA, APACHE II and SIRS scores were significantly associated with increased death risk (HR=1.195~3.471, P<0.0001). These findings provided evidence supporting that dynamic of inflammatory cytokines, immune cells subsets, blood gas, organ damage biomarkers, and especially complications should be closely monitored, in case of poor outcomes.

### Comprehensive prediction models for death risk of COVID-19 patients

In light of the SOFA, qSOFA, APACHE II and SIRS scores have been reported as good diagnostic indicators for sepsis, septic shock and multi-organ failure [3, 4, 6-8, 16], we then calculated the prediction accuracy of these four scores in assessing death risk of COVID-19. As presented in Figure 2, these four scores had prominent prediction capacities evaluating COVID-19 death risk. The AUCs of SOFA, qSOFA, APACHE II and SIRS scores attained 0.697(95%CI=0.546-0.849), 0.610(95%CI=0.474-0.747), 0.826(95%CI=0.671-0.981) and 0.749(95%CI=0.629-0.869). Of note, discrimination of death risk models were better using APACHE II (AUC=0.826, P=0.022) and SIRS scores (AUC=0.749, P=0.013) than SOFA or qSOFA scores, which might partly be attributed to aggravated pro-inflammatory responses in non-survivors.

Besides, we also established another four prediction models based on inflammatory-related indices, immune cells subsets, organ damage biomarkers and complications, all of which were significantly associated with the COVID-19 death risk. Among death risk prediction models of each group alone, the predictive accuracy of the immune cells subsets group was the highest (AUC=0.901, 95%CI=0.801-1.000). Similarly, multiple-organ damage biomarkers (AUC=0.894, 95%CI=0.829-0.959), inflammatory-related indices (AUC=0.757, 95%CI=0.665-0.850) and complications (AUC=0.878, 95%CI=0.817-0.938) had better predictive effects in the discrimination of mortality, outperforming abovementioned SOFA, qSOFA scores (P<0.05) (Figure 2).

Finally, we integrated four score predictive systems, inflammatory-related indices, immune cells subsets, organ damage biomarkers and complications to construct a combine group. The combine score (AUC=0.950, 95%CI=0.853-1.000) was significantly higher than that of each risk group alone (Figure 2), suggesting the combined score system can comprehensively reflect the death risk of COVID-19.

### Discussion

This retrospective large cohort study identified several risk factors and established comprehensive risk models for death in COVID-19 patients. In particular, patients with higher SOFA, qSOFA, APACHE II and SIRS scores, decreased immune cells subsets, elevated inflammatory-related indices, dysregulated multi-organ damage biomarkers and deleterious complications had higher risk of in-hospital death of COVID-19. Notably, the predictive accuracy of the
immune cells subsets group was the highest (AUC = 0.901) among groups alone. Additionally, the predictive accuracy of combining these risk factors (AUC = 0.950) was also significantly higher than that of each risk group alone, outperforming previous risk models.

Our enrolled survivor and non-survivor patients with COVID-19 were statistically matched and excluded the effects of common risk factors, such as age, sex, and underlying comorbidities, on the COVID-19 death, which had been reported to affect COVID-19 mortality [6, 9, 17]. The current study is designed to identify additionally potential risk factors and establish a comprehensive evaluation system for death risk of COVID-19. The SOFA, qSOFA, APACHE II and SIRS scores have been considered as good evaluation predictors for sepsis, septic shock and multi-organ failure [3, 4, 6–8, 16]. Here, we confirmed that those with increased SOFA, qSOFA, APACHE II or SIRS score had higher death risk of COVID-19. Additionally, the AUC values predicting death risk of COVID-19 using SOFA, qSOFA, APACHE II or SIRS score attained 0.697, 0.610, 0.826 and 0.749, respectively, consistent with previous reports revealing that these scores are useful predictors of ICU mortality [18–20]. Strikingly, it was reported that SOFA and qSOFA scores had greater capacities predicting death in ICU cohort, compared to APACHE II or SIRS score [20, 21]. However, in the current study, compared to SOFA and qSOFA, APACHE II and SIRS scores are better predictors for COVID-19 death risk. It is possible that the validation of the scores might been affected by aggravated pro-inflammatory responses in fatal patients.

We found that the serum levels of multiple pro-inflammatory cytokines or biomarkers, including IL-6, IL-10, IL-8, TNF-α, IL-1β, IL-2R, ferritin, hs-CRP and procalcitonin, were substantially elevated in non-survivors with COVID-19. Moreover, significant increasing of leukocytes and neutrophils were also observed in deceased COVID-19 patients. Aggravated pro-inflammatory responses that could lead to increased vascular permeability, extensive pulmonary pathology, ultimately mediating respiratory failure and death[22], was also found to be a useful predictor evaluating COVID-19 mortality (AUC = 0.757).

Defeating SARS-CoV-2 infection requires well-coordinated innate and adaptive immune responses. Impaired adaptive immune responses may cause uncontrolled inflammatory responses, deleterious tissue damage and even death. Recent evidence has demonstrated that in severe COVID-19 patients, lymphopenia is a common feature, with drastically reduced numbers of CD4+ T cells, CD8+ T cells, B cells and NK cells [15, 23, 24]. These findings were confirmed in our study, revealing that immune cells subsets, such as CD8+ T cells, B cells and NK cells, were drastically reduced in non-survivors, compared to survivors, which is associated with enhanced death risk of COVID-19. Additionally, the AUC value of immune cells subsets that attained 0.901 was highest among risk groups alone. These findings indicated that in death patients with COVID-19, dysregulated immune responses are closely correlated to poor clinical outcome of COVID-19 and warranted to intensively monitor in the clinical treatments.

High levels of pro-inflammatory cytokines and dysregulated immune responses may lead to shock and tissue damage in the heart, liver, kidney and coagulation dysfunction, as well as respiratory failure or multiple organ failure [23]. In the current study, multiple-organ damage biomarkers, such as substantially elevated AST, LDH, hs-cTnl, CK-MB, PT-INR, NT-proBNP, PT, APTT, PTA, D-dimer and K+ concentration, and decreased Ca2+, ALB/GLB, eosinophils and platelet counts, were found to be abnormally dysregulated in non-survivors and were significantly associated with increased death risk of COVID-19. Additionally, the patients with increased levels of organ damage biomarkers were more likely to develop complications such as the heart failure, hypoxia, acidosis, acute cardiac, kidney and liver injury, especially ARDS and DIC. Of note, the COVID-19 patients with complications had a higher risk of developing death, consistent with recent reports which reveals that multiple-organ dysfunction and deleterious complications were more pronounced in severe and fatal COVID-19 cases [5, 9]. Similarly, cardiac or multiple-organ complications
have also been found to closely associated with poor outcomes in influenza and other respiratory viral infections [25–27]. The organ damage biomarkers (AUC = 0.894) and complications (AUC = 0.878) also presented prominent prediction effects of assessing death risk for COVID-19.

Considering that the indices related to inflammatory responses, adaptive immune responses and multiple organ damage showed great predictive effects of death risk (AUC = 0.950), the allocation of medical resources might be based on these indices. For these areas with more medical resources, inflammatory responses and immune dysfunction control, aggressive supportive medical care or earlier admission to the ICU might be the treatment emphasis for patients with high death risk. To date, no vaccine or specific antiviral treatment for COVID-19 has been widely applied, thus supportive therapy that eases the symptoms and protects against important organs damage may be more beneficial for decreasing fatality rate of COVID-19.

This study has several limitations. First, Given that age, sex, and comorbidities, such as diabetes, hypertension, and coronary heart disease (CHD) have been reported as the universal risk factors of COVID-19 death, these factors were statistically matched between survivors and non-survivors and were not included in this study. Our current study was the largest and the laboratory indices were the most comprehensive in fatal COVID-19 patients worldwide. However, due to the nature of the retrospective study, not all laboratory tests were done in all patients, such as lymphocytes subtypes and arterial blood gas tests. Furthermore, this is a single-center observational study, which needs be further confirmed in additional validation sets.

In summary, in this large retrospective cohort study with adequate, standardized and unified data, we identified that higher SOFA, qSOFA, APACHE II and SIRS scores, decreased immune cells subsets, elevated inflammation cytokines, dysregulated multi-organ damage biomarkers and deleterious complications were significantly associated with increased death risk of COVID-19. Finally, we established a combined model, comprehensively integrating immune and inflammatory-related factors and other risk factors, might be more suitable for death risk evaluation of COVID-19 than previous risk models, such as SOFA and qSOFA scores. Our data may provide critical information for the successful clinical management and health decision-making of COVID-19, especially for severe cases.

Declarations

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Authors’ contributions

JT, JX, and ZW were the overall principal investigators in this study who conceived the study and obtained financial support, were responsible for the study design, and supervised the entire study. JW, QZ, XR, CY, XZ, HL, BL, XC, Hx L recruited participants. ZL, JX, YW, KT, and JW drafted the paper. LW, YL, SZ, TD, and XY completed the statistical analyses. HC, JQ, HF, X-PY, ZH and SW completed data analysis, interpreted the results. All authors participated in interpretation data, manuscript writing, and review of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The data will be available from the corresponding author on a reasonable request. After the publication of this study, the participant data without names and identifiers will be made available after approval from the corresponding authors and Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology.

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science. Written informed consent was waived due to the rapid emergence of this infectious disease with the permission of the Medical Ethical Committee.

Consent for publication

Not applicable.

Competing interests

We declare that we have no conflicts of interest.

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Tables
Table 1. Demographic, clinical, radiographic, laboratory findings of survivors and non-survivors with COVID-19

| Indicators                          | Total          | Survivors      | Non-survivors   | P value |
|-------------------------------------|----------------|----------------|-----------------|---------|
| **Characteristics**                 |                |                |                 |         |
| Age, years                          | 68(63-74)      | 68(63-73)      | 69(62-77)       | 0.100   |
| **Sex**                             |                |                |                 |         |
| Male                                | 655(65.96%)    | 464(65.17%)    | 191(67.97%)     | 0.401   |
| Female                              | 338(34.04%)    | 248(34.83%)    | 90(32.03%)      |         |
| **Comorbidities**                   |                |                |                 |         |
| Hypertension                        | 401(40.38%)    | 292(41.01%)    | 109(38.79%)     | 0.521   |
| Diabetes                            | 174(17.52%)    | 134(18.82%)    | 40(14.23%)      | 0.087   |
| Coronary heart disease              | 104(10.47%)    | 72(10.11%)     | 32(11.39%)      | 0.554   |
| Cerebrovascular disease             | 39(3.93%)      | 27(3.79%)      | 12(4.27%)       | 0.727   |
| Pulmonary tuberculosis              | 22(2.22%)      | 13(1.83%)      | 9(3.20%)        | 0.184   |
| Hepatitis                           | 17(1.71%)      | 10(1.40%)      | 7(2.49%)        | 0.234   |
| Chronic bronchitis                  | 19(1.91%)      | 11(1.54%)      | 8(2.85%)        | 0.177   |
| Chronic obstructive pulmonary disease| 9(0.91%)      | 5(0.70%)       | 4(1.42%)        | 0.280   |
| **Initial symptoms**                |                |                |                 |         |
| Fever                               | 718(78.13%)    | 523(78.88%)    | 195(76.17%)     | 0.373   |
| Cough                               | 632(68.77%)    | 471(71.04%)    | 161(62.89%)     | 0.017*  |
| Dyspnea                             | 409(44.50%)    | 280(42.23%)    | 129(50.39%)     | 0.026*  |
| Expectoration                       | 399(43.42%)    | 293(44.19%)    | 106(41.41%)     | 0.445   |
| Diarrhoea                           | 199(21.65%)    | 140(21.12%)    | 59(23.05%)      | 0.524   |
| Fatigue                             | 170(18.50%)    | 119(17.95%)    | 51(19.92%)      | 0.490   |
| Chest tightness                     | 147(16.00%)    | 106(15.99%)    | 41(16.02%)      | 0.992   |
| Chills                              | 97(10.55%)     | 72(10.86%)     | 25(9.77%)       | 0.628   |
| Condition      | N1       | N2       | N3       | P-Value |
|----------------|----------|----------|----------|---------|
| Myalgia        | 82(8.92%)| 67(10.11%)| 15(5.86%)| 0.043*  |
| Anorexia       | 71(7.73%)| 50(7.54%)| 21(8.20%)| 0.736   |
| Headache       | 56(6.09%)| 43(6.49%)| 13(5.08%)| 0.424   |
| Vertigo        | 40(4.35%)| 21(3.17%)| 19(7.42%)| 0.005*  |
| Others         | 124(13.49%)| 104(15.69%)| 20(7.81%)| 0.002*  |

**Vital signs**

| Measure                  | N1       | N2       | N3       | P-Value |
|--------------------------|----------|----------|----------|---------|
| Temperature, °C          | 36.6(36.3-37.1) | N = 712 | 36.5(36.2-36.9) | N = 281 | 36.8(36.4-37.6) | <0.0001* |
| Heart rate, bpm          | 92(80-105) | N = 712 | 88(78-99) | N = 281 | 102(90-115) | <0.0001* |
| Respiratory rate, bpm    | 20(20-23) | N = 712 | 20(20-21) | N = 281 | 26(21-33) | <0.0001* |
| Mean arterial pressure, mmHg | 95(86.67-104.33) | N = 711 | 96.67(89.33-105.67) | N = 281 | 88.67(79-99) | <0.0001* |

**CT findings**

| Finding                  | N1       | N2       | N3       | P-Value |
|--------------------------|----------|----------|----------|---------|
| Patchy shadows           | 586(77.41%)| 544(77.83%)| 42(72.41%)| 0.344   |
| Ground-glass opacity     | 338(44.65%)| 307(43.92%)| 31(53.45%)| 0.161   |
| Fibrous stripes          | 262(34.61%)| 253(36.19%)| 9(15.52%) | 0.001*  |
| Pleural thickening       | 212(28.01%)| 188(26.90%)| 24(41.38%)| 0.018*  |
| Nodules                  | 60(7.93%) | 55(7.87%) | 5(8.62%)  | 0.800 a |
| Lymphadenia              | 214(28.27%)| 192(27.47%)| 22(37.93%)| 0.089   |
| Bilateral pulmonary      | 735(97.09%)| 677(96.85%)| 58(100.00%)| 0.413 a |
| Right lung               | 12(1.59%) | 12(1.72%) | 0(0.00%)  | 0.614 a |
| Left lung                | 10(1.32%) | 10(1.43%) | 0(0.00%)  | 1.000 a |

**Laboratory examinations**

| Test                     | N1       | N2       | N3       | P-Value |
|--------------------------|----------|----------|----------|---------|
| Blood routine            |          |          |          |         |
| Leukocytes, # (N = 993), ×10^9/L | 6.12(4.66-8.28) | N = 712 | 5.63(4.43-7.14) | N = 281 | 8.91(6.00-13.03) | <0.0001* |
| Monocytes, % (N = 993)   | 8.10(5.40-10.40) | N = 712 | 8.90(7.00-10.90) | N = 281 | 4.60(2.70-7.50) | <0.0001* |
| Neutrophils, % (N = 993) | 73.60(63.70-83.90) | N = 712 | 69.00(60.30-77.35) | N = 281 | 87.10(79.90-92.20) | <0.0001* |
| Eosinophils, % (N = 993) | 0.30(0.00-1.30) | N = 712 | 0.70(0.00-1.70) | N = 281 | 0.00(0.00-0.10) | <0.0001* |

**Immune cell subsets**
| Lymphocytes, # (N = 993), ×10^9/L | 0.94 (0.64-1.34) | N = 712 | 1.09 (0.76-1.46) | N = 281 | 0.63 (0.44-0.85) | <0.0001* |
| CD3+CD19- T cells, # (N = 207), /μL | 782.00 (394.00-1060.00) | N = 153 | 905.00 (682.00-1173.00) | N = 54 | 276.50 (132.75-408.50) | <0.0001* |
| CD3+CD8+ T cells, # (N = 207), /μL | 248.00 (112.50-350.50) | N = 153 | 280.00 (206.00-384.00) | N = 54 | 62.00 (29.25-127.00) | <0.0001* |
| CD3-CD19+ B cells, # (N = 207), /μL | 137.00 (78.00-205.00) | N = 153 | 156.00 (117.00-209.00) | N = 54 | 73.50 (40.25-143.00) | <0.0001* |
| CD3-CD16+CD56+ NK cells, # (N = 207), /μL | 160.00 (72.50-278.50) | N = 153 | 209.00 (128.00-313.00) | N = 54 | 36.50 (16.00-74.75) | <0.0001* |
| T cells+ B cells+ NK cells, # (N = 207), /μL | 1134.00 (687.00-1533.00) | N = 153 | 1337.00 (995.00-1662.00) | N = 54 | 406.00 (269.75-692.50) | <0.0001* |

**Inflammatory cytokines and biomarkers**

| IL-6 (N = 796), pg/mL | 14 (3.42-49.38) | N = 594 | 6.85 (2.82-24.18) | N = 202 | 61.35 (29.27-151.45) | <0.0001* |
| IL-10 (N = 778), pg/mL | 5.00 (5.00-8.90) | N = 579 | 5.00 (5.00-5.85) | N = 199 | 10.30 (6.35-18.70) | <0.0001* |
| IL-8 (N = 779), pg/mL | 14.20 (8.00-27.95) | N = 579 | 11.60 (6.80-20.25) | N = 200 | 28.40 (16.35-61.83) | <0.0001* |
| TNF-α (N = 786), pg/mL | 8.60 (6.60-11.80) | N = 586 | 8.10 (6.10-10.70) | N = 200 | 11.45 (8.1-16.50) | <0.0001* |
| IL-1β (N = 778), pg/mL | 6.92 (7.44) | N = 578 | 6.49 (6.35) | N = 200 | 8.15 (9.88) | <0.0001* |
| IL-2R (N = 774), U/mL | 675.50 (446.25-1078.00) | N = 576 | 599.50 (407.75-873.25) | N = 198 | 1148.00 (740.25-1615.00) | <0.0001* |
| Ferritin (N = 602), μg/L | 751.00 (421.10-1439.05) | N = 420 | 566.90 (351.53-989.13) | N = 182 | 1407.35 (832.68-2400.18) | <0.0001* |
| hs-CRP (N = 980), mg/L | 41.05 (6.90-98.38) | N = 704 | 20.85 (3.58-66.33) | N = 276 | 105.60 (59.33-164.43) | <0.0001* |
| Procalcitonin (N = 890), ng/mL | 0.08 (0.05-0.21) | N = 629 | 0.06 (0.04-0.09) | N = 261 | 0.29 (0.12-0.89) | <0.0001* |

**Organ damage indexes**

| ALT (N = 991), U/L | 24.00 (15.00-39.00) | N = 710 | 23.00 (15.00-38.00) | N = 281 | 27.00 (18.00-42.00) | 0.004* |
| AST (N = 991), U/L | 30.00 (21.00-44.00) | N = 710 | 26.50 (19.00-38.00) | N = 281 | 41.00 (29.00-59.00) | <0.0001* |
| TBIL (N = 993), μmol/L | 10.00 (7.40-13.90) | N = 712 | 9.40 (7.20-12.55) | N = 281 | 12.30 (9.00-18.60) | <0.0001* |
| Test                  | Mean (Range) | N     | Mean (Range) | N     | Mean (Range) | N     | p-value |
|----------------------|--------------|-------|--------------|-------|--------------|-------|---------|
| ALB/GLO (N = 988)    | 0.99(0.83-1.21) | 708   | 1.05(0.89-1.26) | 280   | 0.86(0.75-1.00) | <0.0001* |
| LDH (N = 950), U/L   | 302.00(225.00-442.75) | 673   | 262.00(209.00-328.00) | 277   | 504.00(364.00-669.00) | <0.0001* |
| ALP (N = 952), U/L   | 68.00(56.00-86.00) | 671   | 66.00(55.50-79.00) | 281   | 78.00(60.00-107.00) | <0.0001* |
| Amylase (N = 486), U/L | 63.50(43.00-83.00) | 342   | 67.00(48.00-83.00) | 144   | 52.00(36.00-84.00) | 0.004* |
| LDH (N = 950), U/L   | 82.60(68.80-92.80) | 709   | 85.90(71.60-93.00) | 278   | 72.60(47.83-90.98) | <0.0001* |
| Creatinine (N = 988), μmol/L | 78.00(65.00-93.25) | 712   | 75.00(64.00-88.00) | 281   | 86.00(66.50-114.00) | <0.0001* |
| NT-proBNP (N = 841), pg/mL | 230.00(89.00-744.00) | 589   | 152.00(64.00-335.00) | 252   | 888.50(362.50-2567.00) | <0.0001* |
| Amylase (N = 486), U/L | 7.70(3.60-20.70) | 644   | 5.40(2.80-10.93) | 261   | 35.30(11.20-194.70) | <0.0001* |
| Platelets, # (N = 988), ×10^9/L | 206.00(149.00-273.25) | 712   | 219.00(167.00-285.00) | 281   | 159.00(111.00-223.50) | <0.0001* |
| HbA1c (N = 351), % | 6.40(6.00-7.30) | 251   | 6.30(6.00-7.15) | 100   | 6.65(6.10-7.43) | 0.022* |
| K+ (N = 993), mmol/L | 4.23(3.80-4.61) | 712   | 4.19(3.78-4.55) | 281   | 4.36(3.88-4.86) | 0.001* |
| Ca2+ (N = 992), mmol/L | 2.12(2.04-2.21) | 712   | 2.15(2.07-2.23) | 281   | 2.06(1.99-2.14) | <0.0001* |
| SaO2 (N = 303), % | 95.70(88.00-98.50) | 181   | 98.10(95.90-99.10) | 122   | 85.50(71.00-92.00) | <0.0001* |
| Variable                                      | N = 304 |    | N = 182 |    | N = 122 |    |
|----------------------------------------------|---------|---------|---------|---------|---------|---------|
| PaCO₂ (N = 304), mmHg                        | 37.50(32.28-42.33) | 39.80(34.50-43.35) | 34.60(30.30-37.90) | <0.0001* |
| Actual bicarbonate (N = 304), mmol/L         | 23.75(20.50-25.80) | 24.40(22.25-26.15) | 22.30(19.30-24.90) | <0.0001* |
| Score prediction                              | N = 303 | N = 181 | N = 122 |    |        |    |
| SOFA score                                    | 3.00(2.00-4.00)  | 2.00(2.00-3.00)  | 4.00(3.00-6.00)  | <0.0001* |
| qSOFA score                                   | 0.00(0.00-1.00)  | 0.00(0.00-1.00)  | 1.00(0.25-1.00)  | <0.0001* |
| APACHE II score                               | 13.00(9.00-17.00) | 10.00(7.00-13.00) | 17.00(14.00-20.00) | <0.0001* |
| SIRS score                                    | 1.00(1.00-2.00)  | 1.00(0.00-2.00)  | 2.00(1.00-2.00)  | <0.0001* |

Abbreviation: COVID-19, Coronavirus disease 2019; bpm, Beat per minute; CT, Computerized tomography; CD, Cluster of differentiation; NK cells, Natural killer cells; IL-6, Interleukin 6; IL-10, Interleukin 10; IL-8, Interleukin 8; TNF-α, Tumor necrosis factor α; IL-1β, Interleukin 1β; IL-2R, Interleukin 2 receptor; hs-CRP, High-sensitivity C-reactive protein; ALT, Alanine transaminase; AST, Aspartate transaminase; TBIL, Total bilirubin; ALB, Albumin; GLO, Globulin; LDH, Lactic dehydrogenase; ALP, Alkaline phosphatase; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal of the pro brain natriuretic peptide; CK-MB, Creatine kinase-MB; hs-cTnI, Hypersensitive cardiac troponin I; PT, Prothrombin time; APTT, activated partial thromboplastin time; FDP, Fibrinogen degradation products; PTA, Prothrombin Time Activity; HbA1c, Glycated hemoglobin; PaO₂, Oxygen partial pressure; SaO₂, Oxygen saturation; PaCO₂, Carbon dioxide partial pressure; SOFA, Sequential organ failure assessment; qSOFA, quick SOFA; APACHE II, The acute physiology and chronic health evaluation II; SIRS, The systemic inflammatory response syndrome; IQR, Interquartile range; SD, standard deviation.

Other initial symptoms: hemoptysis, stomachache, palpitation, chest pain, pharyngalgia, nausea, vomiting, catarrh, hemoptysis, cyanosis.

Continuous variables were described as median (IQR) or mean (SD). P values were calculated by Mann-Whitney U non-parameter test for skewed distributed data. Categorical variables were expressed as number (%). P values were calculated by Pearson χ² test, or Fisher's exact test(a). *P < 0.05.
# Table 2. Complications and clinical treatments of survivors and non-survivors with COVID-19

| Indicators                          | Total          | Survivors    | Non-survivors | P value  |
|-------------------------------------|----------------|--------------|---------------|----------|
|                                     | N= 993         | N= 712       | N= 281        |          |
| Complications                       |                |              |               |          |
| ARDS                                | 655(65.96%)    | 383(53.79%)  | 272(96.80%)   | <0.0001*|
| Acute Cardiac injury                | 308(31.02%)    | 84(11.80%)   | 224(79.72%)   | <0.0001*|
| Heart failure                       | 246(24.77%)    | 45(6.32%)    | 201(71.53%)   | <0.0001*|
| Acute kidney injury                 | 167(16.82%)    | 31(4.35%)    | 136(48.40%)   | <0.0001*|
| Hyperkalaemia                       | 150(15.11%)    | 38(5.34%)    | 112(39.86%)   | <0.0001*|
| Acidosis                            | 105(10.57%)    | 42(5.90%)    | 63(22.42%)    | <0.0001*|
| Acute liver injury                  | 85(8.56%)      | 17(2.39%)    | 68(24.20%)    | <0.0001*|
| Alkalosis                           | 67(6.75%)      | 44(6.18%)    | 23(8.19%)     | 0.256    |
| Acute pancreatic injury             | 23(2.32%)      | 11(1.54%)    | 12(4.27%)     | 0.010*   |
| Length of hospital stay             | 18(10-26)      | 22(15-28)    | 8(4-14)       | <0.0001*|
| ICU admission                       |                |              |               |          |
| ICU                                 | 151(15.21%)    | 4(0.56%)     | 147(52.69%)   | <0.0001*|
| Non-ICU                             | 842(84.79%)    | 708(99.44%)  | 134(47.31%)   |          |
| Treatment β                         |                |              |               |          |
| Antibiotics                         | 894(90.03%)    | 630(88.48%)  | 264(93.95%)   | 0.0094*  |
| Glucocorticoid therapy              | 754(75.93%)    | 502(70.51%)  | 252(89.68%)   | <0.0001*|
| Antiviral therapy                   | 874(88.02%)    | 649(91.15%)  | 225(80.07%)   | <0.0001*|
| Intravenous immunoglobulin therapy  | 338(34.04%)    | 227(31.88%)  | 101(35.94%)   | <0.0001*|
| Transfusion                         | 99(9.97%)      | 21(2.95%)    | 78(27.76%)    | <0.0001*|
| Interferon inhalation               | 353(35.55%)    | 298(41.85%)  | 55(19.57%)    | <0.0001*|
| High flow nasal cannula             | 241(24.27%)    | 43(6.04%)    | 198(70.46%)   | <0.0001*|
| Mechanical ventilation              | 365(36.76%)    | 122(17.13%)  | 243(86.48%)   | <0.0001*|
| Non-invasive                         | 311(31.32%)    | 119(16.71%)  | 192(68.33%)   | <0.0001*|
| Invasive                            | 54(5.44%)      | 3(0.42%)     | 51(18.15%)    | <0.0001*|
| Continuous renal replacement therapy | 12(12.08%)    | 2(0.28%)     | 10(3.56%)     | <0.0001*|
| Extracorporeal membrane oxygenation | 7(0.70%)       | 1(0.14%)     | 6(2.14%)      | 0.0026* a|

Abbreviation: COVID-19, Coronavirus disease 2019; ARDS, Acute respiratory distress syndrome; DIC, Disseminated intravascular coagulation; ICU, Intensive care unit.
Categorical variables were expressed as number (%). *P values were calculated by Pearson $\chi^2$ test, or Fisher's exact test(a). *$P < 0.05$.

Table: Treatments include antibiotics (cephalosporin, fluoroquinolones, macrolides), antiviral therapy (Lopinavir/ritonavir, ganciclovir, Riboviron, oseltamivir), transfusion (suspended red blood cells, platelets, plasma).
| Indicators | Univariable Cox regression | Multivariable Cox regression |
|------------|----------------------------|----------------------------|
| **Vital signs** |                               |                            |
| Temperature, °C | 1.340(1.169-1.536) | <0.0001* | 1.332(1.160-1.529) | <0.0001* |
| Heart rate, bpm | 1.036(1.031-1.042) | <0.0001* | 1.037(1.032-1.043) | <0.0001* |
| Respiratory rate, bpm | 1.118(1.105-1.130) | <0.0001* | 1.123(1.109-1.136) | <0.0001* |
| Mean arterial pressure, mmHg | 0.958(0.951-0.966) | <0.0001* | 0.958(0.950-0.966) | <0.0001* |
| **Laboratory examinations** |                               |                            |
| **Blood routine** |                               |                            |
| Leukocytes, # (N = 993), ×10^9/L | 1.075(1.065-1.085) | <0.0001* | 1.095(1.081-1.109) | <0.0001* |
| Monocytes, % (N = 993) | 0.822(0.793-0.852) | <0.0001* | 0.816(0.787-0.847) | <0.0001* |
| Neutrophils, % (N = 993) | 1.106(1.091-1.120) | <0.0001* | 1.107(1.092-1.121) | <0.0001* |
| Eosinophils, % (N = 993) | 0.298(0.224-0.395) | <0.0001* | 0.301(0.227-0.398) | <0.0001* |
| Hemoglobin (N = 993), g/L | 0.994(0.989-1.000) | 0.044* | 0.993(0.987-0.998) | <0.0001* |
| **Immune cells subsets** |                               |                            |
| Lymphocytes, # (N = 993), ×10^9/L | 0.216(0.158-0.297) | <0.0001* | 0.220(0.161-0.302) | <0.0001* |
| CD3⁺CD19⁻ T cells, # (N = 207), /μL | 0.996(0.995-0.997) | <0.0001* | 0.996(0.995-0.997) | <0.0001* |
| CD3⁺CD4⁺ T cells, # (N = 207), /μL | 1.000(0.999-1.001) | 0.786 | 1.000(0.999-1.001) | 0.861 |
| CD3⁺CD8⁺ T cells, # (N = 207), /μL | 0.989(0.986-0.992) | <0.0001* | 0.989(0.985-0.992) | <0.0001* |
| CD3⁺CD19⁺ B cells, # (N = 206), /μL | 0.994(0.990-0.997) | 0.001* | 0.994(0.990-0.998) | 0.002* |
| CD3⁺CD16⁺CD56⁺ NK cells, # (N = 207), /μL | 0.986(0.981-0.990) | <0.0001* | 0.985(0.981-0.990) | <0.0001* |
| T cells+B cells+NK cells, # (N = 207), /μL | 0.997(0.997-0.998) | <0.0001* | 0.997(0.996-0.998) | <0.0001* |
| **Inflammatory cytokines and biomarkers** |                               |                            |

| Protein/Parameter | Sample Size | Lower Bound | Upper Bound | p-Value | Lower Bound | Upper Bound | p-Value |
|------------------|-------------|--------------|-------------|---------|--------------|-------------|---------|
| IL-6 (N = 796), pg/mL | 1.001(1.001-1.002) | <0.0001* | 1.001(1.001-1.002) | <0.0001* |
| IL-10 (N = 778), pg/mL | 1.008(1.006-1.010) | <0.0001* | 1.009(1.006-1.012) | <0.0001* |
| IL-8 (N = 779), pg/mL | 1.000(1.000-1.001) | <0.0001* | 1.000(1.000-1.001) | <0.0001* |
| TNF-α (N = 786), pg/mL | 1.055(1.045-1.066) | <0.0001* | 1.059(1.048-1.070) | <0.0001* |
| IL-1β (N = 778), pg/mL | 1.018(1.005-1.031) | 0.007* | 1.021(1.007-1.036) | 0.004* |
| IL-2R (N = 774), U/mL | 1.001(1.001-1.001) | <0.0001* | 1.001(1.001-1.001) | <0.0001* |
| Ferritin (N = 602), μg/L | 1.000(1.000-1.000) | <0.0001* | 1.000(1.000-1.000) | <0.0001* |
| hs-CRP (N = 980), mg/L | 1.010(1.008-1.011) | <0.0001* | 1.010(1.008-1.011) | <0.0001* |
| Procalcitonin (N = 890), ng/mL | 1.051(1.036-1.066) | <0.0001* | 1.051(1.036-1.067) | <0.0001* |
| **Organ damage indexes** | | | | |
| ALT (N = 991), U/L | 1.001(1.000-1.001) | 0.002* | 1.001(1.000-1.001) | 0.002* |
| AST (N = 991), U/L | 1.001(1.000-1.001) | <0.0001* | 1.001(1.000-1.001) | <0.0001* |
| TBIL (N = 986), μmol/L | 1.006(1.004-1.008) | <0.0001* | 1.007(1.005-1.009) | <0.0001* |
| ALB (N = 988), g/L | 0.875(0.854-0.896) | <0.0001* | 0.874(0.853-0.895) | <0.0001* |
| LDH (N = 950), U/L | 1.003(1.002-1.003) | <0.0001* | 1.003(1.002-1.003) | <0.0001* |
| ALP (N = 952), U/L | 1.003(1.002-1.005) | <0.0001* | 1.004(1.002-1.005) | <0.0001* |
| Amylase (N = 486), U/L | 1.002(1.000-1.004) | 0.021* | 1.002(1.000-1.004) | 0.038* |
| eGFR (N = 987), ml/(min*1.73m^2) | 0.983(0.978-0.988) | <0.0001* | 0.981(0.976-0.986) | <0.0001* |
| Creatinine (N = 988), μmol/L | 1.002(1.002-1.003) | <0.0001* | 1.002(1.002-1.003) | <0.0001* |
| NT-proBNP (N = 841), pg/mL | 1.000(1.000-1.000) | <0.0001* | 1.000(1.000-1.000) | <0.0001* |
| CK-MB (N = 650), U/L | 1.039(1.031-1.047) | <0.0001* | 1.048(1.036-1.060) | <0.0001* |
| hs-cTnl (N = 905), pg/mL | 1.000(1.000-1.000) | <0.0001* | 1.000(1.000-1.000) | <0.0001* |
| **Platelets, # (N = 988), ×10^9/L** | 0.994(0.992-0.995) | <0.0001* | 0.994(0.992-0.995) | <0.0001* |
|-----------------------------------|---------------------|----------|---------------------|----------|
| **PT (N = 980), s**              | 1.046(1.036-1.055)  | <0.0001* | 1.045(1.036-1.055)  | <0.0001* |
| **APTT (N = 930), s**            | 1.025(1.016-1.034)  | <0.0001* | 1.025(1.016-1.034)  | <0.0001* |
| **D-Dimer (N = 971), μg/mL**     | 1.129(1.113-1.144)  | <0.0001* | 1.131(1.115-1.147)  | <0.0001* |
| **FDP (N = 765), g/L**           | 1.018(1.016-1.020)  | <0.0001* | 1.018(1.016-1.021)  | <0.0001* |
| **PTA (N = 980), %**             | 0.959(0.954-0.964)  | <0.0001* | 0.957(0.951-0.962)  | <0.0001* |

**Metabolism indexes**

| **K⁺ (N = 993), mmol/L** | 1.538(1.295-1.826) | <0.0001* | 1.540(1.291-1.837) | <0.0001* |
| **Ca²⁺ (N = 992), mmol/L** | 0.025(0.011-0.058) | <0.0001* | 0.025(0.010-0.058) | <0.0001* |

**Blood gas characteristics**

| **PaO₂ (N = 304), mmHg** | 0.958(0.949-0.967) | <0.0001* | 0.956(0.947-0.966) | <0.0001* |
| **SaO₂ (N = 304), %**    | 0.956(0.949-0.963) | <0.0001* | 0.954(0.947-0.962) | <0.0001* |
| **PaCO₂ (N = 304), mmHg** | 0.946(0.924-0.970) | <0.0001* | 0.950(0.926-0.974) | <0.0001* |
| **Actual bicarbonate (N = 304), mmol/L** | 0.922(0.887-0.958) | <0.0001* | 0.930(0.894-0.967) | <0.0001* |

**Score prediction**

| **SOFA score** | 1.340(1.276-1.408) | <0.0001* | 1.437(1.348-1.532) | <0.0001* |
| **qSOFA score** | 3.435(2.577-4.580) | <0.0001* | 3.471(2.600-4.634) | <0.0001* |
| **APACHE II score** | 1.172(1.137-1.208) | <0.0001* | 1.195(1.156-1.234) | <0.0001* |
| **SIRS score** | 1.854(1.567-2.194) | <0.0001* | 1.924(1.620-2.286) | <0.0001* |

**Complications**

| **ARDS** | 16.051(8.262-31.186) | <0.0001* | 16.216(8.341-31.527) | <0.0001* |
| **Acute Cardiac injury** | 11.435(8.543-15.307) | <0.0001* | 13.023(9.678-17.524) | <0.0001* |
| **Heart failure** | 10.201(7.860-13.238) | <0.0001* | 10.722(8.227-13.974) | <0.0001* |
| Condition                        | HR (95% CI)       | P Value | P Value |
|---------------------------------|-------------------|---------|---------|
| Acute kidney injury             | 5.957 (4.707-7.539) | <0.0001* | <0.0001* |
| Hyperkalaemia                   | 3.999 (3.148-5.081) | <0.0001* | <0.0001* |
| Acidosis                        | 2.658 (2.007-3.520) | <0.0001* | <0.0001* |
| Acute liver injury              | 4.097 (3.114-5.388) | <0.0001* | <0.0001* |
| DIC                             | 5.682 (4.209-7.672) | <0.0001* | <0.0001* |

Abbreviation: COVID-19, Coronavirus disease 2019; HR, Hazard ratio; CI, Confidential interval; bpm, Beat per minute; CD, Cluster of differentiation; NK cells, Natural killer cells; IL-6, Interleukin 6; IL-8, Interleukin 8; TNF-α, Tumor necrosis factor α; IL-1β, Interleukin 1β; IL-2R, Interleukin 2 receptor; hs-CRP, High-sensitivity C-reactive protein; ALT, Alanine transaminase; AST, Aspartate transaminase; TBIL, Total bilirubin; ALB, Albumin; LDH, Lactic dehydrogenase; ALP, Alkaline phosphatase; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal of the pro brain natriuretic peptide; CK-MB, Creatine kinase-MB; hs-cTnI, Hypersensitive cardiac troponin I; PT, Prothrombin time; APTT, activated partial thromboplastin time; FDP, Fibrinogen degradation products; PTA, Prothrombin Time Activity; PaO2, Oxygen partial pressure; SaO2, Oxygen saturation; PaCO2, Carbon dioxide partial pressure; SOFA, Sequential organ failure assessment; qSOFA, quick SOFA; APACHE II, The acute physiology and chronic health evaluation II; SIRS, The systemic inflammatory response syndrome; ARDS, Acute respiratory distress syndrome; DIC, Disseminated intravascular coagulation.

HRs and 95% CIs were calculated by univariable and multivariable Cox regression models. *P < 0.05.