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Establishing a model for predicting the outcome of COVID-19 based on combination of laboratory tests

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ABSTRACT

Introduction: There are currently no satisfactory methods for predicting the outcome of Coronavirus Disease-2019 (COVID-19). The aim of this study is to establish a model for predicting the prognosis of the disease.

Methods: The laboratory results were collected from 54 deceased COVID-19 patients on admission and before death. Another 54 recovered COVID-19 patients were enrolled as control cases.

Results: Many laboratory indicators, such as neutrophils, AST, γ-GT, ALP, LDH, NT-proBNP, Hs-cTnT, PT, APTT, D-dimer, IL-2R, IL-6, IL-8, IL-10, TNF-α, CRP, ferritin and procalcitonin, were all significantly increased in deceased patients compared with recovered patients on admission. In contrast, other indicators such as lymphocytes, platelets, total protein and albumin were significantly decreased in deceased patients on admission. Some indicators such as neutrophils and procalcitonin, others such as lymphocytes and platelets, continuously increased or decreased from admission to death in deceased patients respectively. Using these indicators alone had moderate performance in differentiating between recovered and deceased COVID-19 patients. A model based on combination of four indicators ($P = 1/[1 + e^{-(-2.658+0.587\times neutrophils - 2.087\times lymphocytes - 0.01\times platelets+0.004\times IL-2R)}]$) showed good performance in predicting the death of COVID-19 patients. When cutoff value of 0.572 was used, the sensitivity and specificity of the prediction model were 90.74% and 94.44%, respectively.

Conclusions: Using the current indicators alone is of modest value in differentiating between recovered and deceased COVID-19 patients. A prediction model based on combination of neutrophils, lymphocytes, platelets and IL-2R shows good performance in predicting the outcome of COVID-19.

1. Introduction

A novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which can cause severe respiratory infection in humans [1,2], has induced a serious outbreak worldwide [3–5]. The disease has been named as Coronavirus Disease-2019 (COVID-19) by the World Health Organization (WHO). According to the report of National Health Commission of the People's Republic of China, more than 80,000 patients are confirmed by SARS-CoV-2 infection, resulting in more than 3000 deaths. COVID-19 has been designated as a public health emergency of international concern by the WHO.

Most patients infected with SARS-CoV-2 have mild illness and present common symptoms such as fever, cough and fatigue, and recover within 2–3 weeks. However, some infected patients progress to severe cases with acute respiratory distress syndrome [6]. And, among them, some patients with severe illness worse in a short period of time and die

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of multiple organ failure, especially in elderly patients with comorbidities [7]. The current published studies have addressed the epidemiology and clinical characteristics of COVID-19 [4,8]. Some studies have compared laboratory tests and imaging features between mild and severe patients [9–11]. There were a few studies exploring laboratory results in deceased COVID-19 patients or comparing laboratory results between deceased and survived patients.

Determination of changes of indicators in deceased COVID-19 patients is crucial, which is helpful for understanding the pathogenesis of the disease. Furthermore, it is important to stratify the risk of death in COVID-19 patients, which is useful for establishing an adequate prophylactic strategy and for a more appropriate therapeutic approach and management. Currently, there are rare studies that focus on establishing prediction model based on combination of routine laboratory tests in COVID-19 patients. Establishing prediction model is important because this can provide a simple and feasible approach to predict the outcome of COVID-19 patients in clinical practice.

2. Methods

2.1. Patients

This study was carried out between January 2020 and March 2020 at Tongji Hospital (the largest hospital in central region of China) in Wuhan, China. The demographic and clinical information, laboratory results and the treatment of deceased COVID-19 patients were collected from electronic medical records. COVID-19 was diagnosed if patients met the following criteria: (1) having typical clinical symptoms; (2) having typical imaging findings; and (3) positive for SARS-CoV-2 real-time RT-PCR. All COVID-19 patients met the criteria of severe illness on admission, since Tongji Hospital was one of designated hospitals for transfer of severe patients with COVID-19 from other hospitals or shelter hospitals. Severe COVID-19 was diagnosed according to the guideline of diagnosis and treatment for SARS-CoV-2 pneumonia made by Chinese National Health Commission: respiratory distress (respiration rate $\geq$ 30 times/min), the oxygen saturation (SpO2) $\leq$ 93%, or the arterial partial pressure of O2 and the fraction of inspired oxygen (PaO2/FiO2) ratio $\leq$ 300 mmHg.

The collected laboratory indicators included six aspects: (1) blood routine (leucocytes, neutrophils, lymphocytes, and platelets); (2) liver and kidney function (aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, albumin, γ-glutamyl transpeptidase (γ-GT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), and creatinine); (3) heart function (amino-terminal pro-brain natriuretic peptide (NT-proBNP) and high-sensitivity cardiac troponin T (Hs-cTnT)); (4) coagulation function (prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen, and D-dimer); (5) cytokine profiles (IL-1β, IL-2 receptor (IL-2R), IL-6, IL-8, IL-10, and TNF-α); and (6) infection markers (procalcitonin, ferritin, C-reactive protein (CRP)). The laboratory results of deceased patients were collected at two time points (on admission, and within 3 days before death). Patients missed any of the above laboratory tests were excluded.

In order to establish the model for predicting the death of COVID-19 patients, we also collected clinical information and laboratory results from another group of matched patients (recovered group). COVID-19 patients in recovered group were matched for the following criteria: gender-consistency, age (±3 years), and 1:1 pairing. This study was approved by the ethical committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China (TJ-C20200128).

2.2. The laboratory procedures

Routine laboratory tests. The blood routine, liver and kidney function, heart function, coagulation function and infection markers were performed by automated analyzers according to the manufacturers' instructions.

Real time RT-PCR. The clinical samples obtained from patients at admission or during the hospital stay were maintained in viral-transport medium. SARS-CoV-2 was confirmed by using TaqMan One-Step RT-PCR Kits from Shanghai Huirui Biotechnology Co.,Ltd and Shanghai BioGerm Medical Biotechnology Co.,Ltd. Briefly, RNA was extracted from clinical samples. 5 μL of RNA was used for real-time RT-PCR, which targeted the ORF1ab and N gene. Real-time RT-PCR was performed using the following conditions: 50 °C for 15 min and 95 °C for 5 min, 45 cycles of amplification at 95 °C for 10 s and 55 °C for 45 s. The positive SARS-CoV-2 real time RT-PCR result was defined if both ORF1ab and N cycle thresholds were <35.

Cytokine profile analysis. Serum samples were collected from study participants. The levels of IL-1β, IL-2R, IL-8, IL-10, and TNF-α in serum were measured according to an automatic procedure of a solid-phase two-site chemiluminescent immunometric assay via IMMULITE 1000 Analyzer (Siemens). The level of IL-6 was measured by electrochemiluminescence method (Roche Diagnostics).

2.3. Statistical analysis

The results are presented as mean ± standard deviation (SD) and median and range. Paired *t*-test or Mann-Whitney *U* test was used to compare the difference of continuous variables. Chi-square test was used for categorical data. Statistical significance was determined as $p < 0.05$. A prediction model for predicting the outcome of death was established by using multivariate logistic regression method. All variables with statistical significance ($p < 0.001$) were taken as candidates for multivariable logistic regression analyses, and the regression equation (predictive model) was obtained. The regression coefficients of the predictive model were regarded as the weights for the respective variables and a score for each patient was calculated. Receiver operating characteristic (ROC) analysis was performed on these scores to assess the ability and the optimal cutoff value for discriminating between recovered and deceased COVID-19 patients. Area under the ROC curve (AUC), sensitivity, specificity, together with their 95% confidence intervals (CIs) were calculated. AUCs of different indicators were compared by using DeLong test. Data were analyzed by using SPSS version 19.0 (SPSS, Chicago, IL), GraphPad Prism 6.0 (San Diego, CA, USA), and MedCalc version 11.6 (Medcalc, Mariakerke, Belgium).

3. Results

3.1. The clinical characteristics of recovered and deceased patients

The demographic and clinical characteristics of recovered and deceased COVID-19 patients are shown in Table 1. The mean age had no statistical difference between recovered and deceased patients. Mortality in males (66.7%) was higher than in females. Fever, cough, and shortness of breath were the most common symptoms in both recovered and deceased patients. Bilateral pneumonia was the predominant imaging feature and approximately one fifth of cases had ground-glass opacity in both survived and deceased patients. Over half of the patients had comorbidities such as hypertension, diabetes, and cardiovascular disease in deceased patients. The percentages of patients with cardiovascular disease and chronic obstructive pulmonary disease in deceased group were significantly higher than those in recovered group. The treatment strategies had no significant difference between these two groups. The median times from onset to admission were 9 days (range 3–23 days) and 9.5 days (range 3–24 days) in recovered and deceased patients, respectively. The median time from onset to death was 28 days (range 8-45 days).

Table 1
The demographic and clinical characteristics of recovered and deceased patients with COVID-19.

	Recovered (n = 54)	Deceased (n = 54)	*p* value
Age (years)	70.9 (10.6)	71.1 (10.1)	0.904
Male sex	36 (66.7%)	36 (66.7%)	1
Signs and symptoms on admission			
Fever	36 (66.7%)	38 (70.3%)	0.836
Cough	37 (68.5%)	35 (66.7%)	0.838
Shortness of breath	34 (63.0%)	37 (68.5%)	0.685
Fatigue	15 (27.8%)	13 (24.1%)	0.827
Expectoration	8 (14.8%)	11 (20.4%)	0.614
Anorexia	6 (11.1%)	8 (14.8%)	0.776
Diarrhoea	10 (18.5%)	7 (13%)	0.598
Headache	8 (14.8%)	5 (9.3%)	0.556
Nausea and vomiting	2 (3.7%)	3 (5.6%)	1
Muscle ache	3 (5.6%)	2 (3.7%)	1
Pharyngalgia	2 (3.7%)	1 (1.9%)	1
Imaging features			
Unilateral pneumonia	5 (9.3%)	3 (5.6%)	0.716
Bilateral pneumonia	49 (90.7%)	51 (94.4%)	0.716
Ground-glass opacity	11 (20.3%)	10 (18.5%)	1
Comorbidities			
Hypertension	28 (51.9%)	22 (40.7%)	0.335
Diabetes	9 (16.7)	15 (27.8%)	0.247
Cardiovascular disease	3 (5.6%)	12 (22.2%)	0.023
COPD	0	6 (11.1%)	0.027
Cerebrovascular disease	4 (7.4%)	3 (5.6%)	1
Chronic kidney disease	3 (5.6%)	3 (5.6%)	1
Chronic liver disease	2 (3.7)	1 (1.9%)	1
Malignancy	3 (5.6%)	2 (3.7%)	1
Treatment			
Antibiotics	46 (85.2%)	50 (92.6%)	0.359
Antiviral treatment	10 (18.5%)	8 (14.8%)	0.797
Corticosteroids†	25 (46.3%)	30 (55.6%)	0.442
Intravenous immunoglobin	25 (46.3%)	31 (57.4%)	0.336
CRRT or CVVHDF	10 (18.5%)	18 (33.3%)	0.279
Oxygen support*	51 (94.4%)	54 (100%)	0.243
ECMO	0	4 (7.4%)	0.118
Days from onset to admission (Days)	9 (3-23)	9.5 (3-24)	0.411
Days from onset to death (Days)	/	29 (8-45)	/

Data are presented as numbers (%), mean (SD), or median (range). †Corticosteroids mean using methylprednisolone (40-80 mg per day) for 3–5 days. *Oxygen support means that nasal cannula oxygen therapy, non-invasive mechanical and invasive mechanical ventilation are used orderly if oxygen saturation cannot be maintained. COVID-19: novel coronavirus disease-2019; COPD: chronic obstructive pulmonary disease; CRRT: continuous renal replacement therapy; CVVHDF: continuous venovenous hemodiafiltration; ECMO, extracorporeal membrane oxygenation.

3.2. Comparison of laboratory results between recovered and deceased patients on admission

We observed that many laboratory indicators had significant difference between recovered and deceased patients on admission. For blood routine, the numbers of leucocytes and neutrophils in deceased patients were significantly higher than in recovered patients, but the numbers of lymphocytes and platelets in deceased patients were significantly lower than in recovered patients (Fig. 1A). The numbers of leucocytes and neutrophils in 46.3% (25/54) and 70.4% (38/54) of deceased patients on admission were over the upper limit of the normal range respectively. The number of lymphocytes and platelets in 87.0% (47/54) and 33.3% (18/54) of deceased patients on admission were below the lower limit of the normal range. The normal ranges of laboratory tests are shown in Supplementary Table 1.

For liver, kidney and heart function, AST, ALT, γ-GT, ALP, LDH, NT-proBNP and Hs-cTnT in deceased patients were all significantly higher than in recovered patients. In contrast, total protein and albumin in deceased patients were significantly lower than in recovered patients (Fig. 1C, E). The levels of AST, ALT, γ-GT, ALP, LDH, NT-proBNP and Hs-cTnT in 44.4% (24/54), 38.9% (21/54), 24.1% (13/54), 13.0% (7/54), 90.7% (49/54), 61.1% (33/54) and 50.0% (27/54) of deceased patients on admission were over the upper limit of the normal range respectively. The levels of total protein and albumin in 44.4% (24/54) and 77.8% (42/54) of deceased patients on admission were below the lower limit of the normal range.

For coagulation function, PT, APTT and D-dimer in deceased patients were all significantly higher than in recovered patients (Fig. 1B). The levels of PT, APTT and D-dimer in 72.2% (39/54), 22.2% (12/54) and 94.4% (51/54) of deceased patients on admission were over the upper limit of the normal range respectively.

For cytokine profiles, IL-2R, IL-6, IL-8, IL-10 and TNF-α in deceased patients were all significantly higher than in recovered patients, while IL-1β had no difference between these two groups (Fig. 1D). For infection markers, CRP, ferritin, and procalcitonin in deceased patients were all significantly higher than in recovered patients (Fig. 1F). The levels of IL-2R, IL-6, IL-8, IL-10, TNF-α, CRP, ferritin and procalcitonin in 79.6% (43/54), 96.3% (52/54), 14.8% (8/54), 42.6% (23/54), 81.5% (44/54), 100% (54/54), 88.9% (48/54) and 94.4% (51/54) of deceased patients on admission were over the upper limit of the normal range respectively.

3.3. Comparison of laboratory results in ***deceased*** patients on admission and before death

For blood routine, the numbers of both leucocytes and neutrophils were significantly increased in patients before death compared with in those on admission. The numbers of leucocytes and neutrophils in 70.4% (38/54) and 88.9% (48/54) of patients before death were over the upper limit of the normal range respectively. The number of lymphocytes had no statistical difference between patients on admission and before death. However, the number of lymphocytes in 85.2% (46/54) of patients before death was below the lower limit of the normal range. The number of platelets was significantly decreased in patients before death compared with in those on admission, and the number of them in 74.1% (40/54) of patients before death was below the lower limit of the normal range (Fig. 2A).

For liver, kidney and heart function, AST but not ALT was significantly increased in patients before death compared with in those on admission. ALP, LDH and creatinine were also significantly increased in patients before death. In contrast, total protein was significantly decreased (Fig. 2C). Although Hs-cTnT had no difference between these two conditions, NT-proBNP was remarkably increased in patients before death compared with in those on admission (Fig. 2E).

For coagulation function, both PT and APTT were significantly increased in patients before death compared with in those on admission. Fibrinogen and D-dimer had no statistical difference between these two conditions (Fig. 2B).

For cytokine profiles, the levels of IL-2R, IL-6, IL-8, IL-10 and TNF-α were all significantly increased in patients before death compared with in those on admission. This trend was more obvious in IL-2R and IL-6. The levels of IL-2R and IL-6 in 92.6% (50/54) and 98.1% (53/54) of patients before death were over the upper limit of the normal range respectively (Fig. 2D).

For infection markers, CRP, ferritin and procalcitonin were significantly increased in patients before death compared with in those on admission (Fig. 2F). The results of ferritin and procalcitonin in 98.1% (53/54) and 98.1% (53/54) of patients before death were over the upper limit of the normal range respectively.

3.4. Establishing the model for predicting the death of patients with COVID-19

ROC analysis showed that most indicators had moderate performance in differentiating between deceased and recovered patients. The AUCs of these indicators (indicators with AUC > 0.8 are shown) were

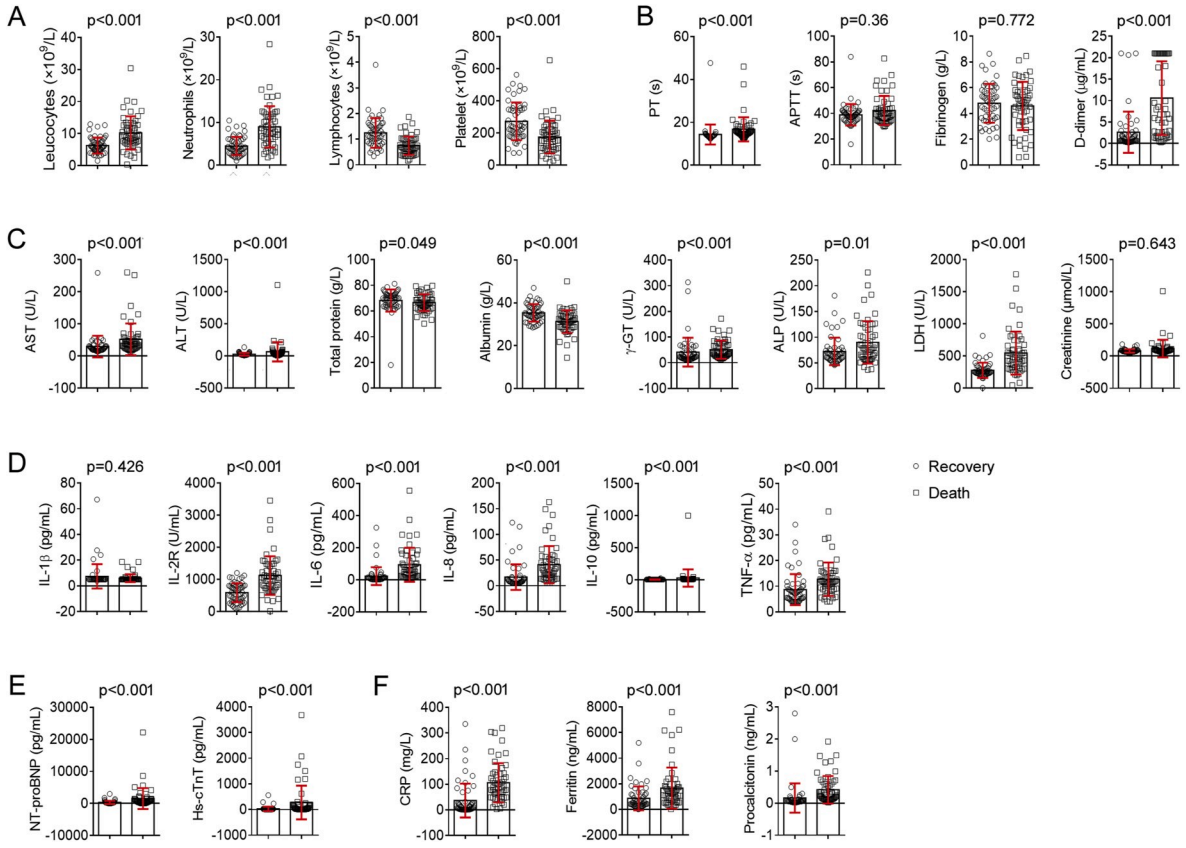

Fig. 1. Comparison of laboratory results between recovered and deceased COVID-19 patient on admission.
(A) Blood routine. (B) Coagulation function. (C) Liver and kidney function. (D) Cytokine profiles. (E) Heart function. (F) Infection markers. The levels of these indicators are shown in bars graphs (mean ± SD). PT, prothrombin time; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GT, γ-glutamyl transpeptidase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; IL-2R, IL-2 receptor; NT-proBNP, amino-terminal pro-brain natriuretic peptide; Hs-cTnT, high-sensitivity cardiac troponin T; CRP, C-reactive protein.

ranged in a descending order from: IL-6 (0.886) > procalcitonin (0.862) > CRP (0.837) > LDH (0.829) > D-dimer (0.827)/IL-8 (0.827) > PT (0.817) > neutrophils (0.817) > IL-2R (0.813) (Fig. 3A). The sensitivities were between 62.96% and 92.59% and the specificities were between 68.52% and 94.44%, when using the optimal cutoff values for distinguishing these two conditions (Fig. 3B).

All variables with statistical significance ($p < 0.001$) selected by univariate analysis were taken as candidates for further multivariable logistic regression analyses. On multivariable logistic regression analysis, neutrophils, lymphocytes, platelets and IL-2R were chosen as prediction model indicators. Based on regression coefficients, we established a mathematical equation as following to predict the death of COVID-19 patients:

$$P = 1/[1 + e^{-(-2.658+0.587\times\text{neutrophils} - 2.087\times\text{lymphocytes} - 0.01\times\text{platelets}+0.004\times\text{IL}-2\text{R})}]$$ P, predictive value; e, natural logarithm.

The score of each patient was calculated, and ROC analysis of score showed that the prediction model had good performance in predicting the death of patients. The AUC of the prediction model was 0.964 (95% CI, 0.909–0.990), and the AUC of the prediction model was significantly higher than the AUC of any other single indicator (Delong test) (Fig. 3A and B). The optimal cutoff value of the prediction model was 0.572, with a sensitivity of 90.74% (95% CI, 79.7–96.9%) and a specificity of 94.44% (95% CI, 84.6–98.8%) (Fig. 3C).

4. Discussion

There are rare studies that assess the risk for mortality of patients with COVID-19 [12,13]. There are a few studies focused on comparison of routine laboratory tests simultaneously between deceased and recovered COVID-19 patients. In the present study, we collected clinical information and laboratory results at different time points in patients died of confirmed SARS-CoV-2 infection. We also compared these data with those obtained in recovered COVID-19 patients. Our study confirmed that many indicators had significant difference between deceased and recovered patients on admission and that some indicators continuously increased from admission to death in deceased patients. A further established prediction model based on combination of four indicators (neutrophils, lymphocytes, platelets and IL-2R) showed satisfactory performance in predicting the death of COVID-19 patients.

Previous study has shown that the older patients with comorbidities had a higher mortality rate in COVID-19 patients [7]. In accordance with this, our results showed that the mean age of deceased patients is over 70 years. This is also similar in SARS and Middle East respiratory syndrome [14,15]. Our previous study has shown that the number and function of $CD4^+$ and $CD8^+$ T cells are inconsistent in older individuals. Although the number of T cells decreases with increasing age, the IFN-γ secretion ability has an increasing trend [16]. However, the expression of type I interferon beta of host immunity in older individuals is decreased [17]. Thus, the high mortality of COVID-19 in older patients may be mainly due to the decrease of number and anti-viral function, but high pro-inflammatory responses in lymphocytes.

One of the important aims of this work is to determine the causes of death in COVID-19 patients. We found that several aspects were associated with the death of patients. First, sepsis is the main cause of death. Many infection markers such as neutrophils, procalcitonin and IL-6 are significantly increased in deceased patients on admission and continuously increase from admission to death. Previous studies have shown that IL-6 and procalcitonin are identified as early markers for bacterial

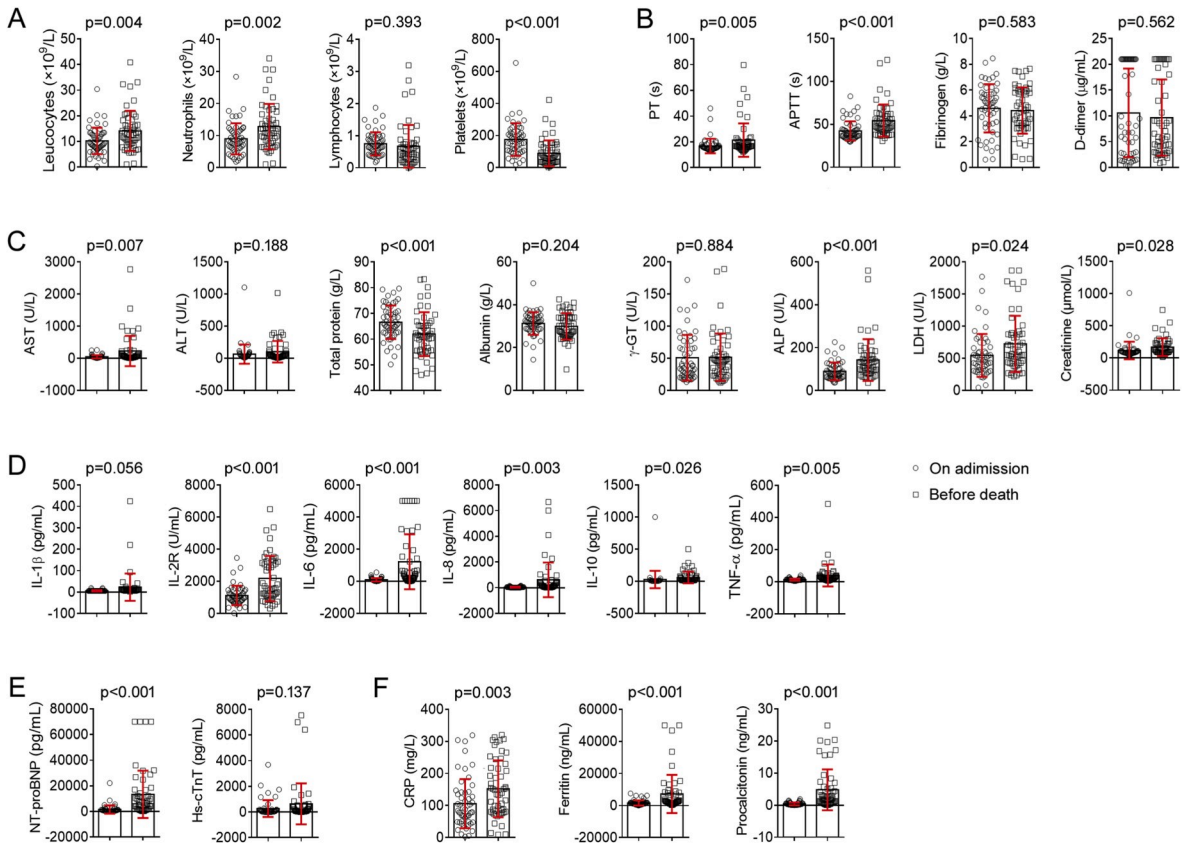

Fig. 2. Comparison of laboratory results in the same COVID-19 patients between on admission and before death.
(A) Blood routine. (B) Coagulation function. (C) Liver and kidney function. (D) Cytokine profiles. (E) Heart function. (F) Infection markers. The levels of these indicators are shown in bars graphs (mean ± SD). PT, prothrombin time; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GT, γ-glutamyl transpeptidase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; IL-2R, IL-2 receptor; NT-proBNP, amino-terminal pro-brain natriuretic peptide; Hs-cTnT, high-sensitivity cardiac troponin T; CRP, C-reactive protein.

sepsis and that admission IL-6 and procalcitonin values differ significantly between survivors and non-survivors among critically ill patients [18–21]. Moreover, procalcitonin, IL-2 and IL-8 levels increase in parallel with the severity of clinical condition of patients [19]. These data indicate that sepsis is commonly occurred in deceased COVID-19 patients. On the other hand, previous study has indicates the role of IL-10 as a negative regulator of immune responses [22]. We found that the number of lymphocytes continuously decreased but IL-10 level continuously increased from admission to death in deceased patients, which suggests the anergy of lymphocyte function in deceased patients. Thus, the anergy of host immunity may be associated with aggravating infection in COVID-19 patients.

Second, impairment of coagulation function is involved with the death of COVID-19 patients. Admission PT and D-dimer in deceased patients are significantly higher than in recovered patients, and PT and APTT continuously increase from admission to death in deceased patients. In contrast, the number of platelets gradually decreases and fibrinogen level also has a decreased trend in deceased patients after admission. These data suggest that the probability of a high risk of hemorrhage is associated with the death of COVID-19 patients, which is in accordance with our previous study showing that over 70% of deceased COVID-19 patients meet the criteria of disseminated intravascular coagulation (DIC) during their hospital stay [23]. The continuous and overwhelming inflammatory responses may be the reason for occurrence of DIC, as sepsis is well established as one of the most common causes of DIC [24].

Third, multi-organ failure is one of the most important causes of death in COVID-19 patients. We found that many biochemical markers such as AST, γ-GT and ALP were all significantly increased in deceased patients on admission. A continuous increase of these markers indicates the damage of liver function in patients. However, creatinine showed no difference in COVID-19 patients between on admission and before death. This may be caused by renal replacement therapy, because one-third of deceased patients were performed continuous renal replacement therapy (CRRT) or continuous venovenous hemodiafiltration (CVVHDF) every few days. Therefore, we speculate that impairment of kidney function is also occurred in deceased patients. Particularly, admission NT-proBNP and Hs-cTnT in some deceased patients were very high, and NT-proBNP in these patients continuously increased from admission to death. These data suggest that heart failure is one of common causes of death in COVID-19 patients. Almost 22% of deceased patients have comorbidity of cardiovascular disease, which may be associated with heart failure in patients. Taken together, multi-organ failure is also the leading cause of death in COVID-19 patients, which is consistent with previous study [13].

Regarding prediction model, four indicators including neutrophils, lymphocytes, platelets and IL-2R are finally chosen as prediction markers. The model indicates that infection, anergy of immunity, hemorrhage and exaggerated inflammatory response may exert synergistic action in predicting the outcome of COVID-19. This is also in accordance with previous studies showing that leukocytosis and neutrophilia, lymphopenia, or increased levels of plasma IP-10 and MCP-3 are associated with disease severity and can be used to predict the outcome of COVID-19 [25–27]. Moreover, some indicators such as IL-6, procalcitonin, CRP, D-dimer and IL-8, which show potential value in distinguishing deceased from recovered patients, are not chosen as prediction markers. This is because that these markers increase in parallel with disease severity and have less synergy effect in predicting the

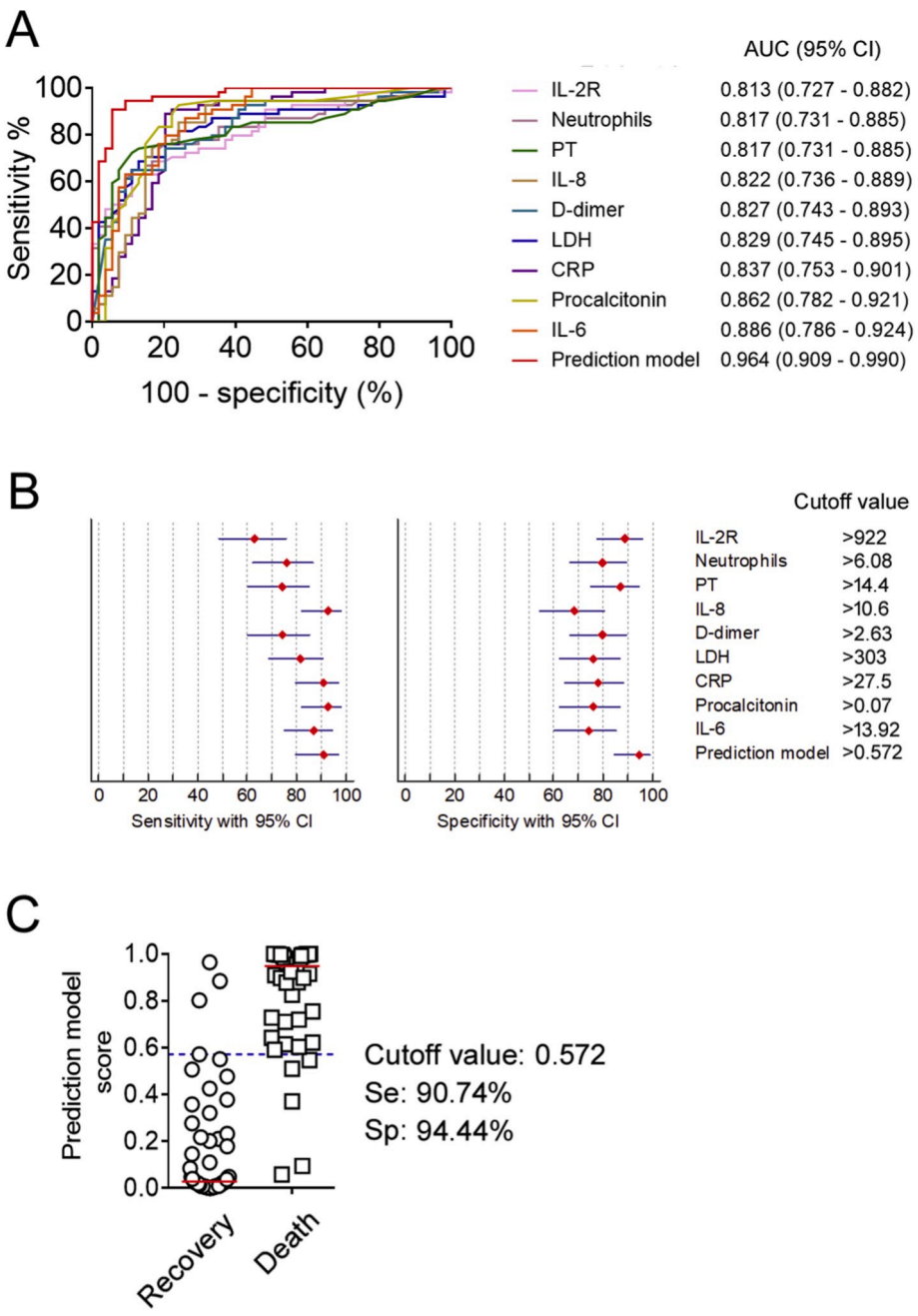

Fig. 3. The performance of single indicator or the prediction model in distinguishing deceased from recovered patients with COVID-19.
(A) Receiver operating characteristic analysis showing the performance of single indicator or the prediction model in distinguishing deceased from recovered patients. (B) Forest plots showing the optimal cutoff values and the sensitivity and specificity. (C) Scatter plots showing the scores of prediction model based on combination of neutrophils, lymphocytes, platelets and IL-2R in recovered and deceased COVID-19 patients. Horizontal lines indicate the median. Blue dotted line indicates the cutoff value in distinguishing these two groups. IL-2R, IL-2 receptor; PT, prothrombin time; LDH, lactate dehydrogenase; CRP, C-reactive protein; Se, sensitivity; Sp, specificity. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

outcome of disease.

Several limitations should be mentioned. First, interpretation of our findings might be limited by the sample size. However, it was difficult to perform all these tests simultaneously in COVID-19 patients, and data of these 54 deceased patients who have performed all these tests simultaneously were very valuable. Nevertheless, this prediction model still needs to be validated in a different group of patients. Second, the values of D-dimer in some patients on admission were over detection limit. Therefore, some results of D-dimer were inaccurate and this could lead to bias. Third, the deceased and recovered groups were only matched for age and sex, while other clinical data such as comorbidities and treatment were not matched. Actually, we found that although the treatment had no difference between deceased and recovered patients, the percentage of patients with diabetes and cardiovascular disease in deceased group was significantly higher than in recovered group. This could affect the results of laboratory tests.

In all, many routine laboratory indicators show high level in deceased COVID-19 patients on admission, and some of them continuously increase from admission to death. Establishment of a prediction model based on combination of neutrophils, lymphocytes, platelets and IL-2R shows good performance in the prognosis of patients with COVID-19.

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Declaration of competing interest

All authors declare no competing interests.

CRediT authorship contribution statement

Feng Wang: Funding acquisition, Writing - review & editing, Data curation. **Hongyan Hou:** Funding acquisition, Writing - review & editing, Data curation. **Ting Wang:** Funding acquisition, Writing - review & editing, Data curation. **Ying Luo:** Funding acquisition, Writing - review & editing, Data curation. **Guoxing Tang:** Funding acquisition, Writing - review & editing, Data curation. **Shiji Wu:** Funding acquisition, Writing - review & editing, Data curation. **Hongmin Zhou:** Funding acquisition, Writing - review & editing, Data curation. **Ziyong Sun:** Funding acquisition, Writing - review & editing, Data curation.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmaid.2020.101782.

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