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RESEARCH ARTICLE

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A novel risk score to predict diagnosis with coronavirus disease 2019 (COVID-19) in suspected patients: A retrospective, multicenter, and observational study

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Abstract

The aim of the study was to explore a novel risk score to predict diagnosis with COVID-19 among all suspected patients at admission. This was a retrospective, multicenter, and observational study. The clinical data of all suspected patients were analyzed. Independent risk factors were identified via multivariate logistic regression analysis. Finally, 336 confirmed COVID-19 patients and 139 control patients were included. We found nine independent risk factors for diagnosis with COVID-19 at admission to hospital: epidemiological exposure histories (OR:13.32; 95%CI, 6.39-27.75), weakness/fatigue (OR:4.51, 95%CI, 1.70-11.96), heart rate less than 100 beat/minutes (OR:3.80, 95%CI, 2.00-7.22), bilateral pneumonia (OR:3.60, 95%CI, 1.83-7.10), neutrophil count less than equal to 6.3×10^9/L (OR: 6.77, 95%CI, 2.52-18.19), eosinophil count less than equal to 0.02×10^9/L (OR:3.14, 95%CI, 1.58-6.22), glucose more than equal to 6 mmol/L (OR:2.43, 95%CI, 1.04-5.66), D-dimer ≥ 0.5 mg/L (OR:3.49, 95%CI, 1.22-9.96), and C-reactive protein less than 5 mg/L (OR:3.83, 95%CI, 1.86-7.92). As for the performance of this risk score, a cut-off value of 20 (specificity: 0.866; sensitivity: 0.813) was identified to predict COVID-19 according to reciever operator characteristic curve and the area under the curve was 0.921 (95%CI: 0.896-0.945; $P < .01$). We designed a novel risk score which might have a promising predictive capacity for diagnosis with COVID-19 among suspected patients.

KEYWORDS
clinical characteristics, COVID-19, predicting risk score, suspected cases

1 | BACKGROUND

Since December 2019, an increasing number of coronavirus disease 2019 (COVID-19) cases were identified all over the world for last few months.[1,2] So far more than one million patients have been diagnosed with COVID-19 worldwide. It is estimated that the overall mortality now is about 5.7% globally.[3] The elders and patients with comorbidities often develop to acute respiratory distress syndrome, shock or organ failure, and finally yield poorer clinical outcomes.[4] Respiratory failure, immunosuppression, as well as systemic infection and inflammation are already recognized as main clinical characteristics of COVID-19 patients.[5]

This outbreak has caused enormous adverse impacts around the world. The epidemiologic situation is still severe but medical system

capacity is limited at present. As a result, it is necessary to improve hospital management and stratification of patients as early as possible. The real-time reverse transcription-polymerase chain reaction (RT-PCR) has competent ability to detect virus and is the most reliable diagnostic method for COVID-19 now.

However, given the incidence of RT-PCR false-negative results, shortage of PCR kit, and possible delayed diagnosis due to time consuming process of RT-PCR,[6] an early efficient identification of confirmed COVID-19 patients is important for early diagnosis and treatments. It can also help decrease the risks of spread of viral infection. Previous few studies about the differentiation of confirmed COVID-19 and suspected cases had some limitations, including relatively small sample size, insufficient clinical utility, and so on. The current study is conducted aiming to explore the potential early risk factors, and to develop a risk score used for predicting the probability of diagnosis among all suspected COVID-19 patients at early stage.

2 | MATERIALS AND METHODS

2.1 | Study design

This was retrospective, multi-center, observational study on patients admitted into 26 COVID-19 designated hospitals from 21 January to February 72 020, in Sichuan province, China. Among these 26 hospitals, Chengdu Public Health Clinical Medical Center reported the highest number of cases. Meanwhile, data of suspected patients admitted to Chengdu Public Health Clinical Medical Center and West China hospital in the same period were also collected.

This study was conducted in accordance with the amended Declaration of Helsinki. This study was approved by the West China Hospital of Sichuan University Biomedical Research Ethics Committee (No. 2020-272). Written informed consent was waived because of the urgent need to collect clinical data and retrospective observational design. All patient data were anonymously recorded to ensure confidentiality.

Two doctors reviewed the medical records of all patients independently. Any disagreement was resolved through the third doctor and team discussion until consensus reached.

2.2 | Inclusion and exclusion criteria

All patients enrolled in this study were diagnosed with confirmed or suspected COVID-19 according to the Chinese Guidance for COVID-19 (7th edition).[7] The epidemiological exposure histories include (a) history of travel or residence in Hubei province; (b) contact history of patients with suspected or confirmed COVID-19. The clinical manifestations are as follows: (a) fever, and/or respiratory symptoms, (b) having imaging features of pneumonia, (c) normal or decreased white blood cell (WBC) counts, and normal or decreased lymphocyte counts.

Suspected case is defined as satisfying anyone of the epidemiological exposure histories and two of clinical manifestations. Patients without epidemiological exposure histories can be also diagnosed with suspected COVID-19 only if the three clinical manifestations are met. The confirmed case is defined as positive result of the nucleic acid of SARS-CoV-2 by fluorescence RT-PCR. Meanwhile, the suspected patients with finally RT-PCR negative results were included into control group. To be specific, if patients had received at least two RT-PCR tests taken at least 24-hour apart and the results were all negative, they were included into control group.

There was no exclusion criterion.

2.3 | Data collection and outcome measurements

Baseline data, including demographic characteristics, comorbidities, basic vital signs, symptoms, and signs, chest computed tomography (CT) scan images, and laboratory examinations data were retrospectively collected from electronic medical records. These laboratory examinations were all recorded within 24 hours after admission to hospitals.

Continuous variables were categorized for further analysis. The threshold value of each continuous variable was determined by the clinically relevant cut-off value, or upper limit or lower limit of normal range. Two doctors completed the data collection independently. The primary outcome is diagnosis of COVID-19.

3 | STATISTICAL ANALYSIS

Data were analyzed by using IBM SPSS Statistical version 23.0 (SPSS, Chicago, IL). Data were expressed as mean ± standard deviation or median (interquartile range [IQR]) for continuous variables, as well as counts and percentages for categorical variables. The difference between the two groups was tested using a two-tailed independent Student's t tests for normally distributed continuous variables, the Mann-Whitney U-test for nonnormally distributed continuous variables, and χ^2 test or Fisher's Exact test for categorical variables. The data were tested by the Kolmogorov-Smirnov normality test and Bartlett's test for homogeneity of variance. Variables with $P < .10$ were included in univariate and multivariate logistic regression analysis. The odds ratio (OR) and confidence interval (CI) were used to evaluate risk factors

The score for each independent risk factor was assigned as integer value close to the regression coefficient. The total risk score of each patient is the sum of each single score. To assess the relationship between the risk score and diagnosis, we did the receiver-operating characteristics (ROC) curve and reported area under the ROC curve (AUC). The optimal cut-off point of the risk score was based on the Youden's index of ROC curve while sensitivity and specificity were reported. $P < .05$ was considered statistically significant.

4 | RESULTS

4.1 | Baseline patient characteristics

A total of 475 patients who met the inclusion criteria were retrospectively enrolled in the study. The patients in our study consisted of 264 males and 211 females. They had a median age of 40 years old (IQR 30–52 years old). Totally 252 (53.1%) patients had epidemiological exposure histories. The most common comorbidities were hypertension (n = 66, 13.9%) and diabetes (n = 39, 8.2%). The most common symptoms were fever (n = 314, 66.1%), productive cough (n = 170, 35.8%), and dry cough (n = 166, 34.9%). The chest CT scan of 448 (94.3%) patients showed abnormal signs. Some abnormal laboratory test results were also found, such as lymphocytopenia (n = 181, 38.1%) and elevated C-reactive protein (CRP) (n = 139, 29.3%).

There were 336 (70.7%) patients finally confirmed with COVID-19. And 265 (78.9%) patients had mild cases at admission. The median age of confirmed patients was higher than that of control group (43 vs 34 years; $P < .01$). About 39.9% of confirmed patients has at least one comorbidity. However, that of control patients was significantly lower (25.2%, $P < .01$). At admission, heart rate of patients with COVID-19 was lower than that of control group (88 vs 104; $P < .01$). There were some other significant differences between confirmed cases and control cases in terms of, history of alcohol ($P < .01$), epidemiological exposure histories ($P < .01$), hypertension ($P < .01$), chronic liver disease ($P < .01$), diabetes mellitus ($P = .02$), rhinorrhea ($P < .01$), dry cough ($P < .01$), weakness/fatigue ($P < .01$), and bilateral white blood cell count ($P < .01$), neutrophil count ($P < .01$), lymphocyte count ($P < .01$), platelet count ($P < .01$), eosinophil count ($P < .01$), monocyte count ($P < .01$), aspartate aminotransferase ($P < .01$), total bilirubin ($P < .01$), creatinine ($P < .01$), glucose ($P = .02$), and stool occult blood positive ($P = .01$). The detailed baseline characteristics of patients are all shown in Table 1.

4.2 | Risk factors and risk score

The factors with a $P < .10$ in Table 1 were added into the logistic regression model analysis.

Finally, the independent risk factors were as follows: epidemiological exposure histories (OR:13.32, 95%CI, 6.39-27.75), symptoms of weakness/fatigue at admission (OR:4.51, 95%CI, 1.70-11.96), heart rate less than 100 beat/min at admission (OR:3.80; 95%CI, 2.00-7.22), imaging characteristics of bilateral pneumonia (OR:3.60, 95%CI, 1.83-7.10), neutrophil count less than equal to 6.3×10^9/L at admission (OR: 6.77, 95%CI, 2.52-18.19), eosinophil count less than equal to 0.02×10^9/L at admission (OR:3.14, 95%CI, 1.58-6.22), glucose more than equal to 6 mmol/L at admission (OR:2.43, 95%CI, 1.04-5.66), D-dimer more than equal to 0.5 mg/L at admission (OR:3.49; 95%CI, 1.22-9.96), and C-reactive protein less than 5 mg/L at admission (OR:3.83, 95%CI, 1.86-7.92). (Table 2)

Thus, the detailed risk score was calculated and formed (Table 3). The number of patients, sensitivity and specificity of each cut-off point was shown in Table 4. A cut-off value of 20 (specificity: 0.866; sensitivity: 0.813) was identified to predict according to ROC curve and area under the curve (AUC) was 0.921 (95%CI: 0.896-0.945; $P < .01$) (Figure 1).

5 | DISCUSSION

To our knowledge, this is the first predictive tool used for predicting the possibility of diagnosis with COVID-19 among all suspected patients at admission to hospital. We found nine independent risk factors for diagnosis with COVID-19 and the score of each indicator varies from 2 to 13 points. The total score varies from 2 to 45 points for each patient. Higher total score represents increased probability of COVID-19.

So far, several studies have also demonstrated some similar risk factors among all suspected patients. Chen et al[8] have found COVID-19 patients had more exposure to Wuhan city, lower neutrophil count and lower CRP compared with control group. Another research demonstrated that bilateral involvement via chest CT occurred in 78.95% of COVID-19 patients but only 26.67% of non-COVID-19 pneumonia patients.[9] However, some other results are not identical between our study and above studies. For example, the differences of incidences of fever between two groups are significant in above studies but not significant in our study. We speculate that this result is associated with disease types of control group. In current study, most of RT-PCR test negative patients were finally diagnosed with influenza or bacterial pneumonia, which could also result in fever. However, we could not perform further comparison due to lack of original data of above studies. Our study has larger sample size and includes more laboratory indexes, and explore independent risk factors after multivariate analysis.

Compared with control group, confirmed patients had lower occurrence of rhinorrhea, but higher rate of diarrhea, nausea, and vomiting. It is consistent with previous studies, which demonstrated SARS-Cov-2 need to bind to the angiotensin converting enzyme 2 (ACE-2) receptor for cell entry.[10] Most of ACE-2 receptor located in gastrointestinal tract and lower airway. Therefore, it is understandable that most of symptoms in COVID-patients are nonspecific. The rates of hypertension and diabetes were both higher in confirmed cases, which was found in previous studies [11] and current study. However, they are not independent risk factor. The interference of ACE2 increasing drugs, deficient sample size of hypertension and diabetes patients might be reasons. It is unexpected that the increased level of serum glucose is an independent risk factor, even after adjusting for diabetes history. However, we should be cautious about this finding. The 95% CI is near to nonsignificance (1.04-5.66). Meanwhile, the uses of corticosteroid are also not clear before admission. And oxidative stress could also affect levels of glucose. We also found normal heart rate is a risk factor in our score. The exact effects of coronavirus on heart are not completely clear so far. Generally, tachycardia correlates with fever and is common in community acquired pneumonia,[12] which accounted for the majority of control

TABLE 1 Comparisons of clinical characteristics between confirmed patients and control group

Variables	Overall (n = 475)	RT-PCR test positive (confirmed cases) (n = 336)	RT-PCR test negative (control cases) (n = 139)	*P* value
Demographic characteristics				
Sex (male)	264 (55.6)	182 (54.2)	82 (59.0)	.30
Age, y	40 (30-52)	43 (32-54)	34 (26-49)	<.01
≥60	79 (16.6)	60 (17.9)	19 (13.7)	.26
History of alcohol	90 (18.9)	77 (22.9)	13 (9.4)	<.01
Smoking history	76 (16)	55 (16.4)	21 (15.1)	.73
Epidemiological exposure histories	252 (53.1)	234 (69.6)	18 (12.9)	<.01
Close contact with animals	4 (0.8)	3 (0.9)	1 (0.7)	1.00
Comorbidities				
At least one comorbidity	169 (35.6)	134 (39.9)	35 (25.2)	<.01
COPD	10 (2.1)	9 (2.7)	1 (0.7)	.32
Asthma	7 (1.5)	5 (1.5)	2 (1.4)	1.00
Hypertension	66 (13.9)	57 (17)	9 (6.5)	<.01
Cardiovascular disease	22 (4.6)	16 (4.8)	6 (4.3)	.83
Chronic liver disease	36 (7.6)	32 (9.5)	4 (2.9)	.01
Diabetes mellitus	39 (8.2)	34 (10.1)	5 (3.6)	.02
Cancer	7 (1.5)	4 (1.2)	3 (2.2)	.71
cerebrovascular disease	4 (0.8)	3 (0.9)	1 (0.7)	1.00
Chronic renal disease	12 (2.5)	10 (3)	2 (1.4)	.52
Vital signs on admission				
Temperature (°C)	37 (36.5-37.6)	36.9 (36.5-37.6)	37.1 (36.7-37.6)	.06
≥37.3	168 (35.4)	114 (33.9)	54 (38.8)	.31
Respiratory rate (breath/min)	20 (20-21)	20 (20-21)	20 (20-21)	1.00
Heart rate (beat/min)	92 (82-104)	88 (80-98)	104 (91-114)	<.01
≥100	161 (33.9)	74 (22)	87 (62.6)	<.01
Systolic pressure (mm Hg)	125 (115-136)	126 (116-137)	123 (113,133)	.16
≥140	91 (19.2)	70 (20.8)	21 (15.1)	.15
Diastolic pressure (mm Hg)	80 (73-88)	80 (72-87)	81 (75.3,90)	.07
≥90	105 (22.1)	70 (20.8)	35 (25.2)	.30
Symptoms and Signs				
Fever	314 (66.1)	216 (64.3)	98 (70.5)	.19
Headache	51 (10.7)	39 (11.6)	12 (8.6)	.34
Rhinorrhea	29 (6.1)	14 (4.2)	15 (10.8)	<.01
Shortness of breath/ dyspnea	45 (9.5)	33 (9.8)	12 (8.6)	.68
Wheeze	25 (5.3)	15 (4.5)	10 (7.2)	.23
Dry cough	166 (34.9)	132 (39.3)	34 (24.5)	<.01
Hemoptysis	3 (0.6)	3 (0.9)	0 (0)	.56
Diarrhea	23 (4.8)	19 (5.7)	4 (2.9)	.20
Rash	2 (0.4)	2 (0.6)	0 (0)	1.00
Earache/ear pain	1 (0.2)	1 (0.3)	0 (0)	1.00
Enlargement of lymph nodes	2 (0.4)	0 (0)	2 (1.4)	.09

TABLE 1 (Continued)

Variables	Overall (n = 475)	RT-PCR test positive (confirmed cases) (n = 336)	RT-PCR test negative (control cases) (n = 139)	*P* value
Weakness/Fatigue	98 (20.6)	83 (24.7)	15 (10.8)	<.01
Muscle ache/Myalgia	53 (11.2)	39 (11.6)	14 (10.1)	.63
Stuffy nose	15 (3.2)	11 (3.3)	4 (2.9)	1.00
Sore throat	70 (14.7)	54 (16.1)	16 (11.5)	.20
Chest pain	33 (6.9)	27 (8)	6 (4.3)	.15
Productive cough	170 (35.8)	122 (36.3)	48 (34.5)	.71
stomachache	8 (1.7)	6 (1.8)	2 (1.4)	1.00
Nausea/Vomiting	15 (3.2)	14 (4.2)	1 (0.7)	.10
arthralgia	9 (1.9)	6 (1.8)	3 (2.2)	1.00
Skin ulcer	0 (0)	0 (0)	0 (0)	NA
Unconsciousness	1 (0.2)	1 (0.3)	0 (0)	1.00
Chest CT scan images				
Abnormal chest image	448 (94.3)	316 (94)	132 (95)	.70
Bilateral pneumonia	311 (65.5)	246 (73.2)	65 (46.8)	<.01
Ground-glass opacity	254 (53.5)	181 (53.9)	73 (52.5)	.79
Presence with consolidation	81 (17.1)	61 (18.2)	20 (14.4)	.32
Laboratory examinations				
White blood cell count, $\times 10^9$/L	6 (4.48-7.65)	5.37 (4.11-6.87)	7.4 (6.2-9)	<.01
≤9.5	431 (90.7)	317 (94.3)	114 (82)	<.01
Neutrophil count, $\times 10^9$/L	4.13 (2.80-5.59)	3.53 (2.58_4.9)	5.3 (4.1-6.7)	<.01
≤6.3	410 (86.3)	307 (91.4)	103 (74.1)	<.01
Lymphocyte count, $\times 10^9$/L	1.17 (0.80-1.55)	1.08 (0.75-1.45)	1.4 (1-1.7)	<.01
≤1.1	181 (38.1)	137 (40.8)	44 (31.7)	.06
Platelet count, $\times 10^9$/L	176.5 (141-225.2)	168 (137-213)	193 (152.5-237.5)	<.01
≤100	34 (7.2)	19 (5.7)	15 (10.8)	.05
Eosinophil count, $\times 10^9$/L	0.02 (0.00-0.58)	0.01 (0-0.03)	0.06 (0.02-0.11)	<.01
≤0.02	231 (48.6)	194 (57.7)	37 (26.6)	<.01
Monocyte count, $\times 10^9$/L	0.42 (0.29-0.62)	0.37 (0.26-0.53)	0.53 (0.4-0.77)	<.01
≤0.1	19 (4)	18 (5.4)	1 (0.7)	.02
Alanine aminotransferase, U/L	23 (15-37)	23 (15-39)	23 (12.5-34.5)	.14
≥40	69 (14.5)	56 (16.7)	13 (9.4)	.04
Aspartate aminotransferase, U/L	25 (18.2-35)	27 (20-37)	19 (15-25)	<.01
≥35	76 (16)	68 (20.2)	8 (5.8)	<.01
Total bilirubin, μmol/L	9.7 (6.8-14.9)	9.2 (6.5-14)	10.5 (8.5-16.8)	<.01
≥20.5	34 (7.2)	22 (6.5)	12 (8.6)	42
Direct bilirubin, μmol/L	3.4 (2.5-4.7)	3.4 (2.4-4.6)	3.5 (2.6-5.7)	.23
≥3.5	146 (30.7)	109 (32.4)	37 (26.6)	.21

(Continues)

TABLE 1 (Continued)

Variables	Overall (n = 475)	RT-PCR test positive (confirmed cases) (n = 336)	RT-PCR test negative (control cases) (n = 139)	*P* value
Blood urea nitrogen, mmol/L	3.9 (3.1-5.0)	3.86 (3.1-4.84)	4.2 (3.2-5.4)	.20
≥7	21 (4.4)	14 (4.2)	7 (5)	.68
Creatinine, μmol/L	67 (54-80)	65.5 (52.5-77.7)	78 (61.5-88.5)	<.01
≥110	10 (2.1)	6 (1.8)	4 (2.9)	.69
Creatine kinase, U/L	70 (48-117)	71 (48-126)	68 (47.8-96.8)	.43
≥200	29 (6.1)	25 (7.4)	4 (2.9)	.06
Albumin, g/L	42.7 (39-45.9)	42.9 (39.1-46)	42.1 (37.9-45.3)	.47
≤35	35 (7.4)	27 (8)	8 (5.8)	.39
Glucose, mmol/L	5.87 (5.11-7.08)	6.01 (5.2-7.3)	5.5 (5-6.4)	.02
≥6	140 (29.5)	116 (34.5)	24 (17.3)	<.01
C-reactive protein, mg/L	18.6 (4.2-43.6)	15.4 (5.7-30.8)	23.5 (2.8-59.7)	.08
≥5	139 (29.3)	68 (20.2)	71 (51.1)	<.01
APTT, s	31.3 (28.1-34.7)	31.4 (28.2-35.2)	30.5 (30-33.4)	.25
PT, s	12.3 (11.6-13.2)	12.4 (11.6-13.2)	11.8 (11.3-12.8)	.06
Fibrinogen, g/L	3.79 (2.71-4.65)	3.77 (2.8-4.6)	4.23 (2.66-5.09)	.42
≥4	97 (20.4)	82 (24.4)	15 (10.8)	<.01
INR	1.03 (0.96-1.10)	1.03 (0.96-1.1)	0.99 (0.95-1.08)	.19
D-dimer, mg/L	0.45 (0.19-1.57)	0.475 (0.19-1.76)	0.37 (0.13-0.83)	.11
≥0.5	103 (21.7)	93 (27.7)	10 (7.2)	<.01
Procalcitonin, μg/L	0.06 (0.03-0.12)	0.056 (0.029-0.11)	0.06 (0.04-0.13)	.09
≥0.5	11 (2.3)	7 (2.1)	4 (2.9)	.85
Stool occult blood positive	12 (2.5)	4 (1.2)	8 (5.8)	.01

Note: Data are shown as median with interquartile range (IQR) for continuous variables or number with percentage for categorical variables.

Abbreviations: APTT, activated partial thromboplastin time; COPD, chronic obstructive pulmonary disease; CT, computed tomography; INR, international normalized ratio; PT, prothrombin time; n, numbers; RT-PCR, real time polymerase chain reaction.

cases. The median heart rates are similar between our study and previous studies about COVID-19.[4]

There are also some indicators, such as comorbidities, symptoms, and alanine aminotransferase, which were significantly different between two groups in univariate analysis, but not in multivariate analysis. The chronic comorbidities and cough are also risk factors for influenza.[13] It has been reported 2% to 11% of patients with COVID-19 had liver comorbidities and 14% to 53% cases had liver injury,[14] which was consistent with our results. Similarly, severe COVID-19 cases often have higher rates of liver dysfunction. Dysregulated innate immune response, immunocompromised status and cytokine storm might be the reasons. However, other researchers suspect that COVID-19-induced hepatic damage is a clinical distraction and it is not necessary for physicians to excessively focus on indicators of liver injury.[15] The viral control is most important and major issue during treatment of COVID-19. Based on our results, we believed these parameters had relatively limited effects on the identification of COVID-19 from suspected patients. However, our findings remain to be confirmed in the future.

It's worth noting that some changes in white blood cell counts was inconsistent with previous studies. It is reported that coronavirus might mainly act on lymphocytes and cause lower percentages of lymphocytes, monocytes and eosinophils.[16] Zhang et al[17] even found lymphopenia and eosinopenia were observed in most COVID-19 patients and eosinophil counts correlate positively with lymphocyte counts. However, we only found normal or decreased neutrophil count and decreased eosinophil count were independent factors for diagnosis with COVID-19. One possible reason is that we only included the first laboratory examinations after admission. The change of white blood cell counts, due to systemic inflammation and dysregulation of immune response, is not significant in such a short time. Moreover, about 23% (15/66) of patients who was mild at admission would progress to severe COVID-19 during hospital stay.[18] In the current study most of patients were mild at admission. It is acknowledged that decrease of white blood cell counts were more common in patients with severe diseases.

The serum level of procalcitonin was normal and similar between two groups. However, the level of C-reactive protein was

TABLE 2 Risk factors associated with confirmed cases among patients with suspected COVID-19

Risk factors	Univariate OR(95%CI)	*P* value	Multivariate OR	*P* value
History of alcohol	2.88 (1.54-5.38)	<.01		
Epidemiological exposure histories	15.42 (8.92-26.65)	<.01	13.32 (6.39-27.75)	<.01
At least one comorbidity	1.97 (1.27-3.06)	<.01		
Hypertension	2.95 (1.42-6.14)	<.01		
Chronic liver disease	3.55 (1.23-10.24)	.02		
Diabetes mellitus	3.02 (1.16-7.89)	.02		
Dry cough	2.00 (1.28-3.12)	<.01		
Weakness/Fatigue	2.71 (1.50-4.89)	<.01	4.51 (1.70-11.96)	<.01
Bilateral pneumonia	3.11 (2.06-4.70)	<.01	3.60 (1.83-7.10)	<.01
White blood cell count, $\times10^9$/L (≤9.5)	3.66 (1.94-6.90)	<.01		
Neutrophil count, $\times10^9$/L (≤6.3)	3.7 (2.16-6.33)	<.01	6.77 (2.52-18.19)	<.01
Eosinophil count, $\times10^9$/L (≤0.02)	3.77 (2.44-5.81)	<.01	3.14 (1.58-6.22)	<.01
Alanine aminotransferase, U/L (≥40)	1.94 (1.02-3.67)	.04		
Aspartate aminotransferase, U/L (≥35)	4.16 (1.94-8.90)	<.01		
Glucose, mmol/L (≥6)	2.53 (1.54-4.14)	<.01	2.43 (1.04-5.66)	.04
Fibrinogen, g/L (≥4)	2.67 (1.48-4.82)	<.01		
D-dimer, mg/L (≥0.5)	4.94 (2.49-9.81)	<.01	3.49 (1.22-9.96)	.02
Heart rate (beat/min) (<100)	5.44 (3.46-8.55)	<.01	3.80 (2.00-7.22)	<.01
Without Rhinorrhea	3.16 (1.35-7.38)	<.01		
C-reactive protein, mg/L (<5)	3.89 (2.44-6.21)	<.01	3.83 (1.86-7.92)	<.01

Abbreviations: CI, confidence interval; OR, odds ratio.

significantly higher in control group. Less than 5 mg/L C-reactive protein is even an independent risk factor for COVID-19. It has been demonstrated that pneumonia caused by 2009 H1N1 influenza alone had significantly lower C-reactive protein level than mixed bacterial and viral infection pneumonia.[19] Additionally, patients with Middle East respiratory syndrome coronavirus (MERS-CoV) also often have lower C-reactive protein level among patients with acute febrile illness.[20]

TABLE 3 The risk score for diagnosis with COVID-19 among suspected patients

Independent risk factors	Score
Epidemiological exposure histories	13
Neutrophil count, $\times10^9$/L, ≤6.3	7
Weakness/fatigue	5
Bilateral pneumonia	4
Heart rate (beat/min), <100	4
C-reactive protein, mg/L, <5	4
Eosinophil count, $\times10^9$/L, ≤0.02	3
D-dimer, mg/L, ≥0.5	3
Glucose, mmol/L, ≥6	2

To sum up, all indicators in this novel risk score are easy to get at admission to hospital. ROC analysis suggests it is promising for the risk stratification among suspected patients. We believed this study reflected the "real world" situation, to some degree. It is crucial for physicians to differentiate COVID-19 from other similar diseases because it is highly infectious. This risk score might help physicians make appropriate decisions about early diagnosis and treatments. Furthermore, it might become a suitable supplement to RT-PCR and help researchers reveal detailed pathophysiological mechanisms of COVID-19 in future.

Nevertheless, there are still several limitations in the study. First, it was a retrospective observational study, unavoidable subjective selection bias existed. Second, the sample size was relatively small, and the number of patients was not equal between groups. Third, drugs and therapies before admission might have disturbed our results. Forth, we did not explore the variation trend of laboratory examinations in few days after admission among suspected patients.

TABLE 4 The performance of risk score

Total score	No. of patients	No. of confirmed patients	Sensitivity	Specificity
2	1	0	1.000	0.000
3	4	0	1.000	0.007
4	5	0	1.000	0.036
5	1	0	1.000	0.072
7	12	0	1.000	0.079
8	7	1	1.000	0.165
9	6	0	.997	0.209
10	4	1	.997	0.252
11	28	1	.994	0.273
12	8	2	.991	0.468
13	5	3	.985	0.511
14	4	2	.976	0.525
15	28	10	.970	0.540
16	7	2	.940	0.669
17	7	5	.935	0.705
18	8	5	.920	0.719
19	23	13	.905	0.741
20	15	13	.866	0.813
21	8	6	.827	0.827
22	18	14	.810	0.842
23	7	6	.768	0.871
24	20	16	.750	0.878
25	9	7	.702	0.906
26	1	1	.682	0.921
27	13	11	.679	0.921
28	24	18	.646	0.935
29	10	9	.592	0.978
30	11	10	.565	0.986
31	22	22	.536	0.993
32	28	28	.470	0.993
33	16	15	.387	0.993
34	21	21	.342	1.000
35	27	27	.280	1.000
36	11	11	.199	1.000
37	20	20	.167	1.000
38	12	12	.107	1.000
39	6	6	.071	1.000
40	8	8	.054	1.000
41	3	3	.030	1.000
42	4	4	.021	1.000
43	2	2	.009	1.000
45	1	1	0.000	1.000

Abbreviation: n, numbers.

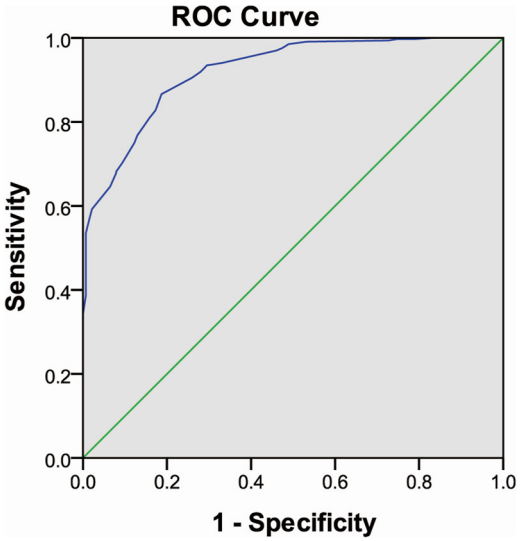

FIGURE 1 Receiver operating characteristic (ROC) curve for prediction of diagnosis with COVID-19. Area under the curve (AUC) was 0.921 (95%CI: 0.896-0.945, $P < .01$)

Further well-designed, multi-center studies with better comparability are warranted to update this risk score.

6 | CONCLUSIONS

We found a novel risk score, which is based on nine easy-to-get parameters in clinical practice. It has a promising predictive capacity for diagnosis with COVID-19 among all suspected patients. Our findings need to be confirmed in further studies.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

DH, TW, HY, RY, and ZL conceived the idea, designed, and supervised the study, drafted the manuscript, and had full access to all of the data and took responsibility for the integrity of the data. DH, TW, ZC, and RY collected data. DH and RY analyzed data and performed statistical analysis. All of the authors reviewed and approved the final version of the manuscript.

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