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Combined predictive performance of age and neutrophilic percentage on admission for severe novel coronavirus disease 2019

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Abstract

Background: Novel coronavirus disease 2019 (COVID-19) poses a huge threat to the global public health. This study aimed to identify predictive indicators of severe COVID-19.

Methods: We retrospectively collected clinical data on hospital admission of all patients with severe COVID-19 and a control cohort (1:1) of gender- and hospital-matched patients with mild disease from 13 designated hospitals in the Hebei Province between 22 January and 15 April 2020.

Results: A total of 104 patients (52 with severe COVID-19 and 52 with mild disease) were included. Only age, fever, duration from symptom onset to confirmation, respiratory rate, percutaneous oxygen saturation (SpO_2) and neutrophilic percentage were independent predictors of severe COVID-19. Age and neutrophilic percentage performed best in predicting severe COVID-19, followed by SpO_2. 'Age + neutrophilic percentage' (the sum of age and neutrophilic percentage) (area under the curve [AUC] 0.900, 95% confidence interval [CI] 0.825-0.950, $P < .001$) and 'age and neutrophilic percentage' (the prediction probability of age and neutrophilic percentage for severe type obtained by logistic regression analysis) (AUC 0.899, 95% CI 0.824-0.949, $P < .001$) had excellent predictive performance for severe type. The optimal cut-off for 'age + neutrophilic percentage' was >119.1 (sensitivity, 86.5%; specificity, 84.6%; Youden index, 0.712).

Conclusion: The combination of age and neutrophil percentage could effectively predict severe COVID-19. The sum of age and neutrophil percentage was recommended for clinical application because of its excellent predictive value and practicability.

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Abbreviations: AUC, area under the curve; BUN, blood urea nitrogen; CI, confidence interval; COVID-19, novel coronavirus disease 2019; CT, computed tomography; FiO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen; ROC, receiver operator characteristic; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SpO_2, percutaneous oxygen saturation.

What's known

- Increasing studies showed that most patients with COVID-19 were asymptomatic or mild, about 20% of patients develop critical pneumonia, multiple organ dysfunction or even death.
- The early recognition of severe forms of COVID-19 is absolutely essential for timely triaging of patients.
- Age, comorbidities and inflammatory indicators were associated with the severity of COVID-19.

What's new

- We analysed the predictive value of a variety of indicators that were easily accessible to patients upon admission for severe COVID-19 and found that the sum of age and neutrophil percentage was an excellent predictive and clinical practicable indicator for severe COVID-19.

1 | BACKGROUND

In December 2019, the first novel coronavirus disease 2019 (COVID-19) epidemic began in Wuhan, posing a huge threat to the global public health.[1,2] Studies have shown that most patients with COVID-19 are asymptomatic or mild and about 20% of patients develop critical pneumonia leading to multiple organ dysfunction or even death.[3,4] The treatment of severe cases has become a major challenge, and the early recognition of severe forms of COVID-19 is essential for timely triaging of patients. However, there are no reliable indicators to predict disease severity. The objective of this study was to identify predictive indicators of severe COVID-19.

2 | METHODS

2.1 | Study design and population

This multicenter, retrospective observational trial enrolled 327 patients with COVID-19 from 13 designated hospitals in the Hebei Province, China between 22 January and 15 April 2020. The inclusion criteria were diagnosis of COVID-19 by laboratory confirmation and local health authority. Patients aged ≤18 years, those with hospital length of stay ≤24 hours, and pregnant patients were not included. Finally, 52 patients with severe COVID-19 and a control cohort (1:1) of gender- and hospital-matched patients with mild type were included in the final analysis. Severe-type patients were categorised based on the Chinese Clinical Guidelines for COVID Pneumonia Diagnosis and Treatment (7th edition)[5] and should meet at least one of the following criteria: (a) respiratory distress, a respiratory rate >30 breaths per minute, (b) percutaneous oxygen saturation (SpO_2) <93% under resting conditions or (c) partial pressure of oxygen (PaO_2)/fraction of inspired oxygen (FiO_2) ≤300 mmHg (1 mmHg = 0.133 kPa). Patients with mild type should meet the following criteria: (a) mild clinical symptoms or (b) mild or no lesions on imaging.

2.2 | Data collection

Data were collected by accessing clinical medical records, nursing records and laboratory and radiological examination records. In the case of missing or uncertain data, we obtained them by direct communication with the managing physician. The data were reviewed by a trained team of physicians.

The recorded information included demographic characteristics, exposure history, chronic medical history, surgical history, symptoms from onset to hospital admission, vital signs on hospital admission, chest-computed tomography (CT) findings on admission, laboratory findings on admission, treatment during the illness course, extrapulmonary comorbidities during the illness course, duration of hospital stay, and mortality.

2.3 | Statistical analysis

All analyses were performed using SPSS version 26.0 (IBM, USA). Categorical data were presented as numbers and percentages and compared using Pearson's chi-square test or Fisher's exact probability test. The normality of continuous variables was examined using the Kolmogorov–Smirnov test. Continuous variables without and with a normal distribution were compared using non-parametric tests and independent-sample *t* tests, respectively.[6] Binary logistic regression was performed to identify the independent predictors of severe COVID-19. The prediction probability of the combined predictors for severe type was obtained by logistic regression analysis. The predictive performance of the independent predictors for severe type was analysed using receiver operator characteristic (ROC) curves. Delong's test was used to compare area under the curves

(AUCs) between each predictor using MedCalc version 18.2.1 (MedCalc Software Ltd, Ostend, Belgium). $P < .05$ was considered statistically significant.

3 | RESULTS

3.1 | Epidemiological characteristics and symptoms from onset to hospital admission

By 15 April 2020, 327 patients with COVID-19 were diagnosed, including 57 (17.43%) severe-type patients. Finally, 52 severe-type patients and 52 gender- and hospital-matched mild-type patients were included in this study. The main reasons for exclusion of severe-type patients were lack of clinical data (n = 2) and death within 24 hours (n = 3) (Figure 1).

Severe-type patients were older than mild-type patients ($P < .05$). In the severe type, there were fewer cases of exposure to confirmed patients ($P = .001$), more cases with Wuhan contact history ($P = .070$), and more patients had chronic medical history (hypertension, diabetes, cardiovascular disease and pulmonary disease), surgical history, fever and expectoration symptoms ($P < .05$) than in the mild type (Table 1). The duration from symptom onset to confirmation in severe-type patients was longer than in mild-type patients ($P < .001$) (Table 1). In addition, cases with exposure to confirmed patients had a longer duration from symptom onset to confirmation than those who had no exposure ($P < .05$).

3.2 | Vital signs, laboratory findings and imaging findings on hospital admission

The respiratory rate was higher, and SpO_2 was lower in severe-type patients than in mild-type patients ($P < .05$). More severe-type patients received mechanical ventilation than mild-type patients ($P < .05$) (Table 2).

In severe-type patients, neutrophil percentage, neutrophil count and C-reactive protein were markedly higher, but the lymphocyte percentage and lymphocyte count were lower than in mild-type patients ($P < .05$) (Table 2). Moreover, the white blood cell counts was higher in severe-type patients than in mild-type patients, but the difference was not significant ($P = .063$) (Table 2). Additionally, severe-type patients had lower albumin levels and higher blood urea nitrogen (BUN) than mild-type patients ($P < .001$) (Table 2).

Chest CT imaging on admission showed more bilateral infiltrates, ground-glass opacity and reticular pattern in severe-type patients than in mild-type patients ($P < .05$) (Table 2).

3.3 | Treatment, comorbidities and outcomes

Nearly all patients received antiviral agents and traditional Chinese medicine in both groups. Antibiotic therapy, glucocorticoid treatment and vasoactive drug administration were more common in severe-type patients than in mild-type patients ($P < .001$). Moreover, severe-type patients received more antifungal therapy than mild-type patients, but the difference was not significant ($P = .126$) (Table 3).

All severe-type patients had acute respiratory distress syndrome, and 19 (36.5%), 11 (21.2%) and two (3.8%) of them received mechanical ventilation, prone position ventilation and extracorporeal membrane oxygenation therapy, respectively (Table 3).

More severe-type patients had extrapulmonary comorbidities than mild-type patients ($P < .001$). No mild-type patient had cardiac injury, acute kidney injury or gastrointestinal bleeding. Additionally, two (3.8%) mild-type and four (7.7%) severe-type patients had liver dysfunction (Table 3). The clinical outcome was worse in severe-type patients than in mild-type patients with three (5.8%) deaths among severe-type patients and none among mild-type patients. Furthermore, the length of hospital stay was

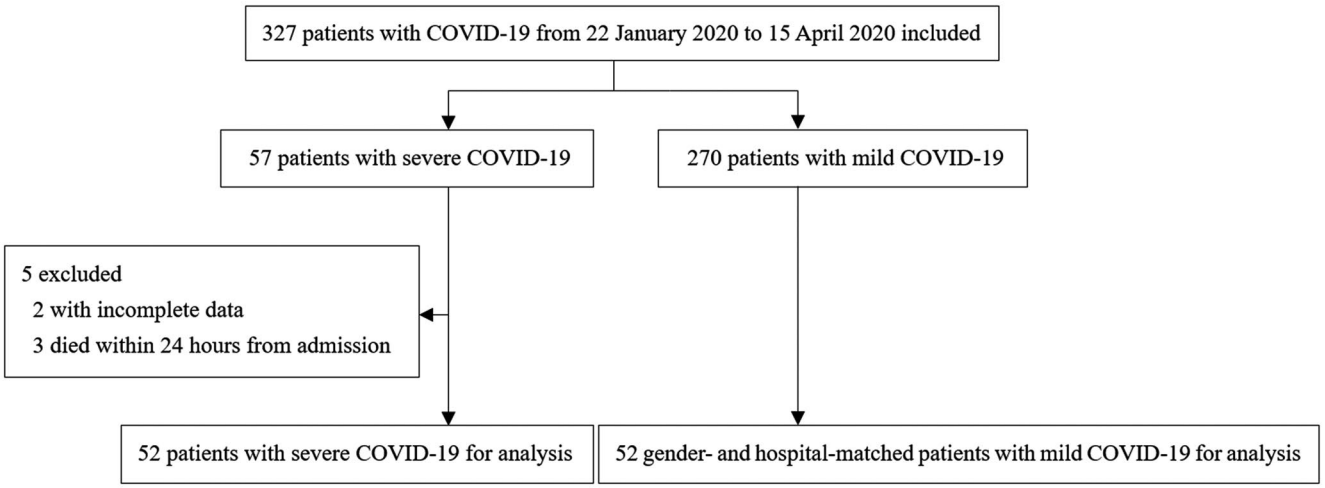

FIGURE 1 Study flow diagram

TABLE 1 Demographics, baseline characteristics and symptoms from onset to hospital admission of the 104 patients with COVID-19

	All patients (n = 104)	Severe group (n = 52)	Mild group (n = 52)	*P* value
Age, y	49.9 ± 16.5	58.8 ± 13.6	41.0 ± 14.2	<.001
Male	54 (51.9%)	27 (51.9%)	27 (51.9%)	1.000
Exposure	88 (84.6%)	40 (76.9%)	48 (92.3%)	.030
Exposure to Huanan seafood market	0 (0.0%)	0 (0.0%)	0 (0.0%)	—
Wuhan contact history[a]	26 (25.0%)	17 (32.7%)	9 (17.3%)	.070
Exposure to patients[b]	61 (58.7%)	22 (42.3%)	39 (75.0%)	.001
Clustering onset[c]	46 (44.2%)	25 (48.1%)	21 (40.4%)	.430
Chronic medical illness	43 (41.3%)	33 (63.5%)	10 (19.2%)	<.001
Hypertension	25 (24.0%)	21 (40.4%)	4 (7.7%)	<.001
Diabetes	13 (12.5%)	11 (21.2%)	2 (3.8%)	.008
Chronic cardiac disease	13 (12.5%)	12 (23.1%)	1 (1.9%)	.001
Chronic pulmonary disease	8 (7.7%)	8 (15.4%)	0 (0.0%)	.010
Cerebrovascular disease	8 (7.7%)	5 (9.6%)	3 (5.8%)	.713
Chronic kidney disease	2 (1.9%)	2 (3.8%)	0 (0.0%)	.475
Chronic liver disease	5 (4.8%)	3 (5.8%)	2 (3.8%)	1.000
Malignancy	1 (1.0%)	1 (1.9%)	0 (0.0%)	1.000
Surgery history	20 (19.2%)	16 (30.8%)	4 (7.7%)	.003
Smoking	7 (6.7%)	4 (7.7%)	3 (5.8%)	1.000
Symptoms				
Fever	83 (79.8%)	49 (94.2%)	34 (65.4%)	<.001
Cough	63 (60.6%)	35 (67.3%)	28 (53.8%)	.160
Expectoration	29 (27.9%)	19 (36.5%)	10 (19.2%)	.049
Dyspnoea	28 (26.9%)	18 (34.6%)	10 (19.2%)	.077
Myalgia	10 (9.6%)	7 (13.5%)	3 (5.8%)	.183
Fatigue	21 (20.2%)	14 (26.9%)	7 (13.5%)	.087
Diarrhoea	11 (10.6%)	6 (11.5%)	5 (9.6%)	.750
Headache	4 (3.8%)	4 (7.7%)	0 (0.0%)	.126
Duration from symptom onset to confirmation, d	4.5 (2.0, 8.8)	6.0 (3.3, 10.0)	2.0 (1.0, 6.0)	<.001

Note: The results are described as median and interquartile ranges, mean and standard deviations or numbers and percentages, as appropriate.

Abbreviation: COVID-19, novel coronavirus disease 2019.

[a]Sojourn in Wuhan or exposure to people who sojourn to Wuhan.

[b]Patients who have confirmed COVID-19 infection or are highly suspected of being infected.

[c]Two or more cases of fever and/or respiratory symptoms within 2 wk in small areas such as home, office, school class, etc.

longer in severe-type patients than in mild-type patients ($P < .001$) (Table 3).

3.4 | Logistic regression analysis of factors independently associated with severe COVID-19

In binary logistic regression, the significant predictors of severe type were age ($P < .001$), fever ($P = .013$), duration from symptom onset to confirmation ($P = .004$), respiratory rate ($P = .016$), SpO_2 ($P = .023$) and neutrophilic percentage ($P = .002$) (Table 4).

3.5 | ROC curve analysis

Age (AUC 0.815, 95% confidence interval [CI] 0.727-0.884, $P < .001$) and neutrophilic percentage (AUC 0.814, 95% CI 0.726-0.884, $P < .001$) had the best predictive value with high specificity for severe type, followed by SpO_2 (AUC 0.811, 95% CI 0.723-0.881, $P < .001$). The performance of fever, duration from symptom onset to confirmation and respiratory rate in predicting severe type were poor (Table 5 and Figure 2).

Given the good performance of age and neutrophilic percentage, we combined these two indicators as 'age and neutrophilic percentage'

TABLE 2 Vital signs, laboratory and imaging findings on hospital admission of the 104 patients with COVID-19

	All patients (n = 104)	Severe group (n = 52)	Mild group (n = 52)	*P* value
Vital signs				
Temperature, °C	36.8 (36.5, 37.6)	36.9 (36.7, 38.0)	36.8 (36.5, 37.3)	.100
Heart rate, beats per minute	86 ± 14	89 ± 16	84 ± 10	.064
Respiratory rate, breaths per minute	20 (19, 22)	21 (19, 24)	20 (18, 21)	.018
SpO_2, %	97.5 (95.0, 98.0)	95.0 (92.3, 97.0)	98.0 (98.0, 99.0)	<.001
Systemic blood pressure, mmHg	131 (120, 140)	132 (121, 140)	130 (118, 140)	.607
Diastolic blood pressure, mmHg	82 (72, 88)	82 (72, 88)	82 (72, 88)	.614
Mean arterial pressure, mmHg	97 (87, 106)	96 (87, 104)	98 (88, 106)	.805
Receiving mechanical ventilation	6 (5.8%)	6 (11.5%)	0 (0.0%)	.035
Blood routine				
White blood cell count, $\times 10^9$/L	5.36 (4.30, 7.20)	5.68 (4.77, 8.07)	5.27 (3.78, 6.84)	.063
Neutrophil count, $\times 10^9$/L	3.63 (2.57, 5.59)	4.42 (3.08, 7.35)	3.31 (2.27, 4.13)	.001
Neutrophilic percentage, %	71.45 (60.40, 81.30)	79.15 (70.43, 89.23)	63.40 (53.53, 72.55)	<.001
Lymphocyte count, $\times 10^9$/L	1.01 (0.66, 1.48)	0.74 (0.49, 1.14)	1.42 (0.93, 1.89)	<.001
Lymphocyte percentage, %	20.40 (12.33, 29.83)	13.35 (6.03, 21.93)	26.90 (19.75, 35.28)	<.001
C-reactive protein, mg/L	13.25 (4.18, 44.17)	43.86 (12.18, 85.39)	4.97 (1.35, 13.75)	<.001
Blood biochemistry				
Albumin, g/L	39.2 ± 5.6	36.4 ± 5.2	42.0 ± 4.4	<.001
Direct bilirubin, mmol/L	3.90 (2.53, 5.80)	4.40 (2.70, 6.18)	3.50 (2.31, 5.69)	.303
Indirect bilirubin, mmol/L	8.35 (6.19, 11.18)	7.90 (5.83, 10.50)	8.70 (6.62, 12.18)	.269
Creatinine, μmol/L	69.0 (56.0, 89.5)	67.0 (56.6 87.8)	72.7 (55.6, 91.5)	.728
Blood urea nitrogen, mmol/L	4.20 (3.03, 5.29)	4.60 (3.84, 6.89)	3.56 (2.73, 4.49)	<.001
Creatine kinase, U/L	67.5 (39.2, 148.3)	80.5 (42.8, 169.5)	61.0 (36.5, 122.8)	.326
Imaging findings				
Bilateral involvement	88 (84.6%)	48 (92.3%)	40 (76.9%)	.030
Consolidation	11 (10.6%)	6 (11.5%)	5 (9.6%)	.750
Ground-glass opacity	93 (89.4%)	51 (98.1%)	42 (80.8%)	.004
Reticular pattern	21 (20.2%)	18 (34.6%)	3 (5.8%)	<.001
Pleural effusion	4 (3.8%)	4 (7.7%)	0 (0.0%)	.126

Note: The results were described as median and interquartile ranges, mean and standard deviations or numbers and percentages, as appropriate.
Abbreviation: COVID-19, novel coronavirus disease 2019.

(the prediction probability of age and neutrophilic percentage for severe type obtained by logistic regression analysis). The predictive value of 'age and neutrophilic percentage' was calculated using the following formula ($\hat{y} = 1/[1 + \exp.(-x\beta)]$: $\hat{y} = 1/[1 + \exp.(10.945 - 0.092 \times \text{age} - 0.091 \times \text{neutrophilic percentage})$. As this combined method was complicated for clinical application and the regression coefficients of age and neutrophilic percentage were similar, we further combined these two indicators as 'age + neutrophilic percentage' (the sum of age and neutrophilic percentage) and explored the predictive value for severe type. Age was in years, and neutrophilic percentage was in % in the two combination methods.

'Age + neutrophilic percentage' (AUC 0.900, 95% CI 0.825-0.950, $P < .001$) and 'age and neutrophilic percentage' (AUC 0.899, 95% CI 0.824-0.949, $P < .001$) presented excellent performances in predicting severe type, and the AUCs were higher than age, neutrophilic percentage, fever, duration from symptom onset to confirmation, respiratory rate, and SpO_2 with significant differences (all $P < .05$). The optimal cut-off for 'age + neutrophilic percentage' was >119.1 (sensitivity, 86.5%; specificity, 84.6%; Youden index, 0.712) (Table 5 and Figure 2).

4 | DISCUSSION

COVID-19 has resulted in considerable morbidity and mortality worldwide since December 2019. Monitoring the severity of COVID-19 and early effective intervention are fundamental measures for reducing mortality.

In this study, we reported the clinical characteristics and risk factors associated with severe COVID-19 including older age, comorbidities, surgical history, symptoms from onset to hospital admission

TABLE 3 Treatment, extrapulmonary comorbidities and outcomes of the 104 patients with COVID-19

	All patients (n = 104)	Severe group (n = 52)	Mild group (n = 52)	*P* value
Oxygen support				
Mechanical ventilation	19 (18.3%)	19 (36.5%)	0 (0.0%)	<.001
Prone position ventilation	11 (10.6%)	11 (21.2%)	0 (0.0%)	<.001
ECMO	2 (1.9%)	2 (3.8%)	0 (0.0%)	.475
CRRT	3 (2.9%)	3 (5.8%)	0 (0.0%)	.241
Antiviral treatment	103 (99.0%)	51 (98.1%)	52 (100.0%)	1.000
Antibiotic treatment	70 (67.3%)	45 (86.5%)	25 (48.1%)	<.001
Antifungal treatment	4 (3.8%)	4 (7.7%)	0 (0.0%)	.126
Glucocorticoids	72 (69.2%)	46 (88.5%)	26 (50.0%)	<.001
Traditional Chinese medicine	101 (97.1%)	50 (96.2%)	51 (98.1%)	1.000
Vasoactive drugs	12 (11.5%)	12 (23.1%)	0 (0.0%)	<.001
Extrapulmonary comorbidities	18 (17.3%)	16 (30.8%)	2 (3.8%)	<.001
Cardiac injury	10 (9.6%)	10 (19.2%)	0 (0.0%)	.001
Acute kidney injury	5 (4.8%)	5 (9.6%)	0 (0.0%)	.067
Liver dysfunction	6 (5.8%)	4 (7.7%)	2 (3.8%)	.674
Gastrointestinal haemorrhage	7 (6.7%)	7 (13.5%)	0 (0.0%)	.019
Clinical outcome				
Died	3 (2.9%)	3 (5.8%)	0 (0.0%)	.241
Length of hospital stay, d	17.0 (14.0, 22.0)	20.5 (16.0, 26.0)	16.0 (12.0, 18.8)	<.001

Note: The results were described as median and interquartile ranges, mean and standard deviations or numbers and percentages, as appropriate.

Abbreviations: COVID-19, novel coronavirus disease 2019; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation.

TABLE 4 Logistic regression to predict severe COVID-19

			95% CI for OR	
	P	OR	Minimum	Maximum
Age	<.001	1.187	1.085	1.298
Fever	.013	440.564	3.559	54534.112
Duration from symptom onset to confirmation	.004	1.461	1.129	1.890
Respiratory rate	.016	1.482	1.075	2.043
SpO_2	.023	0.532	0.308	0.917
Neutrophilic percentage	.002	1.103	1.035	1.176
Constant	.226			

Note: Variables entered on step 1: age, exposure, chronic medical illness, surgery history, fever, expectoration, duration from symptom onset to confirmation, respiratory rate, SpO_2, neutrophilic percentage, lymphocyte percentage, C-reactive protein, albumin, blood urea nitrogen, bilateral involvement, ground-glass opacity, and reticular pattern.

Abbreviations: CI, confidence interval; COVID-19, novel coronavirus disease 2019; OR, odds ratio.

(fever and expectoration), duration from symptom onset to confirmation, vital signs on hospital admission (respiratory rate, SpO_2 and the use of mechanical ventilation), chest CT findings on admission (bilateral infiltrates, ground-glass opacity and reticular pattern), and laboratory findings on admission (neutrophil percentage, neutrophil count, lymphocyte percentage, lymphocyte count, C-reactive protein, BUN and albumin). Older age, fever, duration from symptom onset to confirmation, respiratory rate, SpO_2 and neutrophilic percentage were independent predictors of severe COVID-19. Respiratory rate and SpO_2 are early and readily available indicators

TABLE 5 ROC curves for age, fever, duration from symptom onset to confirmation, respiratory rate, SpO_2, neutrophilic percentage and combined indicators as predictors of severe COVID-19

Indicator	AUC	*P* value	95% CI for AUC		Cut-off value	Sensitivity	Specificity	Youden index
			Minimum	Maximum				
Age	0.815	<.001	0.727	0.884	>53	69.2	82.7	0.519
Fever	0.644	.008	0.544	0.736	≥1	94.2	34.6	0.289
Duration from symptom onset to confirmation	0.711	<.001	0.614	0.796	>2	82.7	51.9	0.346
Respiratory rate	0.633	.017	0.532	0.725	>21	44.2	82.7	0.269
SpO_2	0.811	<.001	0.723	0.881	≤97	76.9	76.9	0.539
Neutrophilic percentage	0.814	<.001	0.726	0.884	>76	63.5	90.4	0.539
Age + neutrophilic percentage	0.900	<.001	0.825	0.950	>119.1	86.5	84.6	0.712
Age and neutrophilic percentage	0.899	<.001	0.824	0.949	≤0.5192	86.5	84.6	0.712

Abbreviations: AUC, area under the curve; CI, confidence interval; COVID-19, novel coronavirus disease 2019; ROC, receiver operating characteristic.

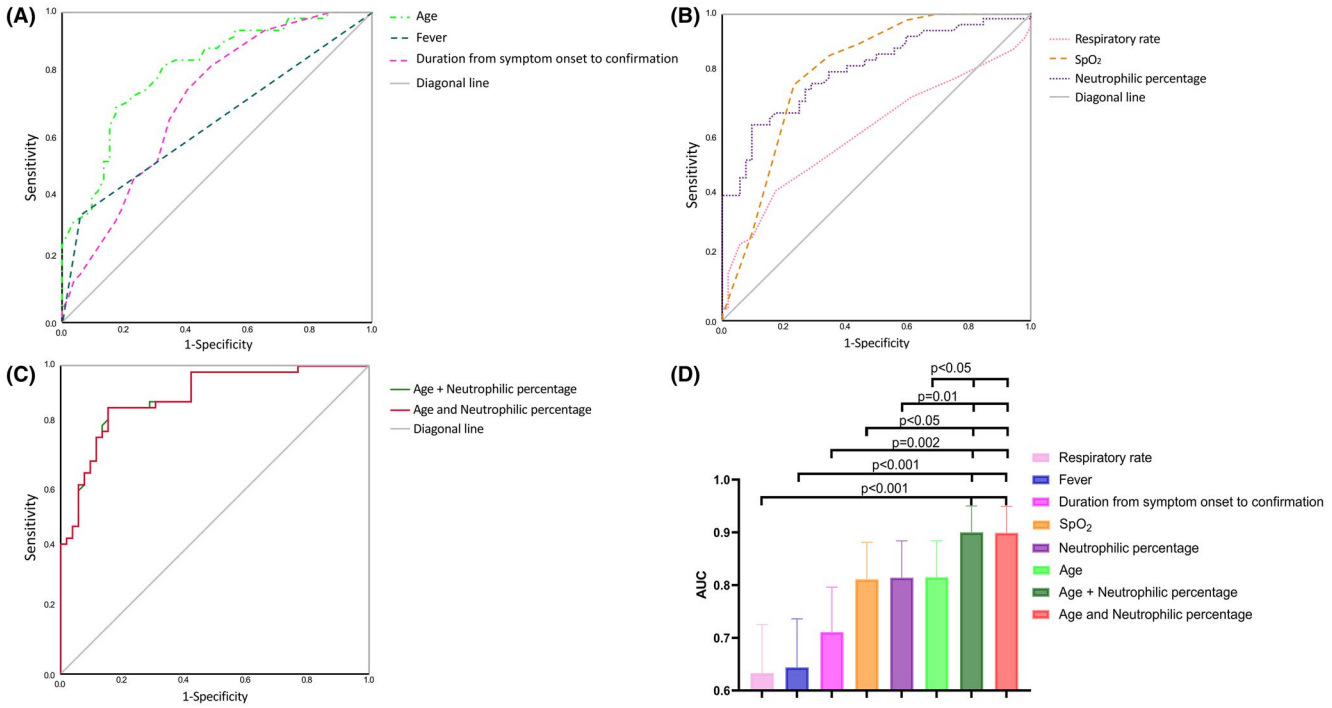

FIGURE 2 ROC curve analysis. The ROC curves for age, fever, duration from symptom onset to confirmation, respiratory rate, SpO_2, the level of neutrophilic percentage on admission (A and B) and the combined parameters of age and neutrophilic percentage (C) in predicting severe COVID-19 and Bar graph of the AUC of each indicator (D). Horizontal lines represent 95% confidence interval for AUCs. Age and neutrophilic percentage, the prediction probability of age and neutrophilic percentage for severe type obtained by logistic regression analysis; age + neutrophilic percentage, the sum of age and neutrophilic percentage; SpO_2, percutaneous oxygen saturation; AUC, area under the curve, COVID-19, novel coronavirus disease 2019; ROC, receiver operator characteristic

of lung injury. The delay in confirmation hinders early treatment of patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that may lead to deterioration of the condition. Consistent with the results of other studies, fever was associated with the development of severe type.[7,8] However, the difference in patient temperature on hospital admission between the groups was small, which may be related to the use of antipyretic drugs before admission. Moreover, the performance of fever, duration from symptom onset to confirmation, and respiratory rate in predicting severe COVID-19 was poor and that of SpO_2 was good.

Older age and neutrophilic percentage performed best in predicting severe COVID-19. SARS-CoV-2 binds to the ACE2 receptor

and enters the alveolar epithelial cells, leading to the release of the inducing factors and chemokines and activation of the abundant immune cells, leading to inflammation and tissue damage.[7,8] Cytokine storm and viral evasion of cellular immune responses are thought to play important roles in disease severity.[9,10] SARS-CoV-2 might mainly act on lymphocytes, especially T lymphocytes, resulting in a significant decrease in the number of T cells, which is further hampered in severe cases.[9] The significant decrease in the number and percentage of peripheral lymphocytes in patients with COVID-19 may be related to the redistribution and increased consumption of lymphocytes and defective haematopoiesis.[11,12] Neutrophils are the main source of chemokines and cytokines. In addition, reduced lymphocyte levels and impaired immune cell function in patients with severe COVID-19 may make them more sensitive to bacterial infection,[13,14] which leads to a significant increase in neutrophil count. The neutrophil percentage had the best predictive performance for severe COVID-19, possibly because it reflects both lymphocytic decline and neutrophil elevation. Older age was associated with both severity and death.[15] Besides older age is associated with reduced immune competence,[16] elderly patients often have coexisting medical conditions, which were associated with severe COVID-19.[2]

The combined parameters of age and neutrophil percentage performed better in predicting severe COVID-19 than these parameters alone and significantly better than single indicators, possibly because age and neutrophil percentage reflect the severity of inflammation and susceptibility of the population, respectively. In this study, we explored two ways in which age and neutrophilic percentage can be combined. 'Age and neutrophilic percentage' were derived from logistic regression analysis, which may be the best method of combination but was complex and clinically impractical. 'Age + neutrophilic percentage', which was the sum of age and neutrophil percentage, was recommended for clinical application because of its excellent predictive value for severe COVID-19 and practicability.

In addition, there were fewer cases of exposure to confirmed patients, and cases with exposure to confirmed patients had shorter duration from symptom onset to confirmation in the severe type, which may be related to the timely follow-up of close contacts of confirmed patients so that their contacts can receive timely diagnosis and treatment. In terms of treatment, antibiotic therapy, glucocorticoid treatment and vasoactive drug administration were more common in the severe type, which is associated with a more intense inflammatory response, more severe haemodynamic disorders and more severe immune impairment in severe-type patients than in mild type. Thus, the clinical outcome was worse in the severe type with more extrapulmonary comorbidities and longer length of hospital stay than in the mild type.

Our study has several potential weaknesses. First, it was a retrospective study, and the number of patients in this study was small. To reduce research bias, the cases in our study were from 13 hospitals in Hebei Province rather than a single centre, and the cases were matched according to the hospitals they were admitted to and their gender. Thus, to some extent, the results of this study may give clinicians a hint for early screening of patients with a tendency to progress to severe disease. Second, the main indicators analysed in this study were those on hospital admission; therefore, many parameters, such as arterial blood gas, erythrocyte sedimentation rate and procalcitonin, were not included in the analysis because of missing data. Nevertheless, our results provide a moderate and important insight on this topic.

5 | CONCLUSIONS

The combination of age and neutrophil percentage could effectively predict severe COVID-19. The sum of age and neutrophil percentage was recommended for clinical application because of its excellent predictive value for severe COVID-19 and practicability.

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DISCLOSURES

The authors declare that there are no conflicts of interests regarding the publication of this paper.

AUTHOR CONTRIBUTIONS

Yuhong Chen and Zhenjie Hu were involved in design. Kun Zhang, Yuhong Chen, Zhigang Cai and Lixia Liu collected the epidemiological and clinical data. Haijun Zhi, Kun Zhang, Yuhong Chen and Zhongheng Zhang summarised the data and performed analysis. Yuhong Chen drafted the manuscript. Xixin Yan, Guijun Zhu and Zhenjie Hu revised the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Ethics Commission of the Fourth Clinical Medical College of Hebei Medical University approved this study(2020KS002).

DATA AVAILABILITY STATEMENT

After publication, we could share the data to other researchers, and a statement will be needed for evaluating the reasonability and validity. With agreement of the corresponding author and designated hospitals to treat patients with COVID-19, raw data will be provided.

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