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ORIGINAL ARTICLE

A Predictive Model Based on Blood Indicators for Admission to the ICU with AECOPD

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SUMMARY

Background: **AECOPD is the most common cause of death among infectious diseases in developing countries, and also an important cause of mortality and morbidity in developed countries. In recent years, related scoring systems such as the mMRC score and CAT questionnaire have been widely used to assess the severity of AECOPD. However, they both have some shortcomings in predicting the admission of AECOPD patients to the ICU. This study aimed to develop a new prediction model to predict the admission of AECOPD patients to the ICU based on objective blood indicators.**

Methods: **This was a retrospective study. Enrolled patients with AECOPD underwent blood gas analysis as well as biomarker testing for serum inflammatory markers, including white blood cell count (WBC), neutrophils, D-dimer, procalcitonin (PCT), high-sensitivity C-reactive protein (hs-CRP), and erythrocyte sedimentation rate (ESR). General characteristics such as age and gender were also recorded. The main observation was admission to the ICU. Univariate analysis and binary logistic regression analysis were used to explore independent risk factors for admission to the ICU in patients with AECOPD, which could be used as components of a new predictive model. Subject receiver operating characteristic curves (ROC) were used to assess the sensitivity and specificity of the new model, which consisted of all independent risk factors predicting the primary outcome.**

Results: **Initially, 369 patients with AECOPD were admitted to the general ward, of which 119 were subsequently transferred to the ICU (119/369). PaCO2, WBC, D-dimer, PCT, and hs-CRP were independent risk factors for admission to the ICU in patients with AECOPD. The AUC of the new prediction model (combined model consisting of PaCO2, WBC, D-dimer, PCT, and hs-CRP) was 0.94 (95% CI 0.92 - 0.97). The sensitivity was 80.7% and the specificity was 94.8%.**

Conclusions: **The model for predicting the admission of AECOPD patients to the ICU based on blood indicators has a high specificity and sensitivity.**

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease characterized by persistent airflow limitation and is a major cause of morbidity and mortality worldwide. Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is an impor-

tant event in the management of COPD and is a direct cause of high mortality in COPD patients. For patients with AECOPD, the mortality rate during hospitalization requiring admission to the intensive care unit (ICU) due to respiratory distress or progressive deterioration can reach 16.9% - 48.8%. Also, compared to other chronic diseases, patients with acute exacerbations of COPD (AECOPD) have rapidly progressive disease and often require admission to the ICU for treatment. This requires clinicians to work in a timely and accurate manner to assess the severity of AECOPD patients and determine the timing of admission to the ICU to avoid delayed diagnosis and treatment, resulting in irreversible outcomes. Accurate timing of admission to ICU for AECOPD patients can not only reduce the financial burden of patients and avoid the waste of medical resources to some extent but also is crucial to the prognosis of patients.

Over the years, several clinical assessment scores (such as the modified UK Medical Research Council (m-MRC) questionnaire and the COPD Assessment Test (CAT)) have been proposed and validated to achieve this goal. However, due to the complexity and rapid progression of AECOPD patients, the above clinical assessment scores are not adequate for practical clinical work. Several studies have now shown that blood indicators such as biological characteristics and inflammatory biomarkers may correlate with the need for ICU admission in AECOPD patients [8]. To remedy the inadequacy of the assessment system for AECOPD patients requiring ICU admission, this study developed a new model to predict the admission of AECOPD patients to the ICU based on objective blood indicators.

MATERIALS AND METHODS

Patients

We conducted a retrospective study. The study was conducted in a regional teaching hospital with 1,200 beds in China. Adult patients over 40 years of age who were mainly diagnosed with AECOPD from June 2017 to June 2019 were included. Those with a history of hematological diseases, active pulmonary tuberculosis, pulmonary embolism, uremia, advanced lung cancer, refractory heart failure, rheumatic diseases, radiotherapy, immunosuppressive agents, transplantation, medical history, and incomplete history of auxiliary examination were excluded. General clinical data, medical history, history of drinking and smoking, and laboratory inflammatory biomarker tests were recorded.

Blood gas analysis and measurement of blood markers such as serum inflammatory markers

According to our research design, $PaCO_2$, WBC, neutrophils, and D-dimer were measured as part of routine testing on a Denmark ABL555 automatic blood gas analyzer, Sysmex X-E-2100 blood analyzer, and STAGO automatic coagulation analyzer (Asnieres sur Seine, France). Serum CRP and PCT levels were determined using a Rosi-Cobas 8000 automatic biochemical analyzer. Erythrocyte sedimentation rate was determined by hand.

Statistical analyses

SPSS 25.0 statistical software was used for data analysis. Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range (IQR) when the distribution was not satisfied by the Kolmogorov-Smirnov test. Univariate analysis and binary logistic regression analysis were used to explore the independent risk factors in predicting ICU admission in AECOPD patients. ROC curves were used to evaluate the sensitivity and specificity of the independent risk factors and the new model (the joint model consisting of the independent risk factors) in predicting ICU admission and mortality in AECOPD patients. All tests were two-tailed and a p-value < 0.05 was considered statistically significant.

RESULTS

Patient characteristics

A total of 369 eligible patients were included in this study, including 252 males and 117 females, with a median age of 73 (range 65 - 80 years). Among them, 119 patients (32.25%) were transferred to ICU for further treatment. In 272 patients, 73.70% suffered from one or more basic diseases. The general characteristics are shown in Table l.

Univariate analysis to explore the independent risk factors in predicting ICU admission in AECOPD patients

The result revealed $PaCO_2$, WBC, Neutrophils, D-dimer, PCT, and hs-CRP were suspicious risk factors ($p < 0.05$), while ESR was not ($p > 0.05$), (Table 2).

Binary logistic regression analysis to explore the independent risk factors in predicting ICU admission in AECOPD patients

We found $PaCO_2$, WBC, D-dimer, PCT, and hs-CRP were independent risk factors for ICU admission in AECOPD patients, while neutrophils was not an independent risk factor (Table 3).

The ROC curves for independent risk factors and the new model for evaluating ICU admission

The ROC curves for the analyses of independent risk factors and the new model for predicting ICU admission in AECOPD patients were plotted (Figure 1, 2). The AUC of independent risk factors ($PaCO_2$, WBC, D-dimer, PCT, and hs-CRP) were 0.66 (95% CI 0.59 - 0.74), 0.67 (95% CI 0.61 - 0.73), 0.74 (95% CI 0.68 - 0.80), 0.76 (95% CI 0.70 - 0.81), and 0.78 (95% CI 0.73 - 0.83), respectively. The specificities were 64.70%, 50.40%, 52.10%, 63.90% and 69.70%, respectively (Ta-

Table 1. Baseline characteristics of patients with acute exacerbations of chronic obstructive pulmonary disease.

Demographic data	
Number of ICU residents, n (%)	119 (32.25)
Age (year) *	73 (65 - 80)
Male gender, n (%)	252 (68.30)
Female gender, n (%)	117 (31.70)
Suffering from chronic diseases, n (%)	272 (73.70)
Hypertension	167 (45.30)
Cerebrovascular disease	96 (26)
Diabetes mellitus	71 (19.20)
Chronic hepatitis	53 (14.40)
Chronic kidney disease	40 (10.80)
Heart disease	118 (32)
Smoking, n (%)	168 (45.50)
Alcohol intake, n (%)	75 (20.30)

* **Note: Data presented as median (interquartile range).**

Table 2. Single factor analysis results.

	Admission to ICU		Chi-squared/Z	p-value
	Yes	No		
$PaCO_2$ (mmHg) #	64 (43 - 83)	49 (41 - 52)	-5.39	< 0.001 *
WBC (x 10^9) #	11.50 (7.30 - 15.30)	7.50 (6.00 - 10.10)	-5.3	< 0.001 *
Neutrophils (x 10^9) #	9.00 (5.42 - 13.10)	5.19 (3.61 - 7.24)	-6.733	< 0.001 *
D-dimer (ng/mL) #	1,578.70 (642.1 0 - 2,536.10)	543.80 (339.50 - 916.80)	-7.429	< 0.001 *
PCT (mg/mL) #	0.43 (0.19 - 3.50)	0.27 (0.05 - 0.32)	-8.145	< 0.001 *
Hs-CRP (mg/L) #	43.29 (13.80 - 55.30)	2.94 (0.10 - 18.74)	-8.636	< 0.001 *
ESR (mm/hour) #	29.70 (18.32 - 32.46)	25 (9.50 - 38.50)	-0.726	0.468

Note: * - means p < 0.05; # - indicates that SK normality test results in a non-normal distribution, data presented as median (interquartile range). Through single factor analysis, we draw the following conclusions: ESR was not a suspicious risk factor: p = 0.468 > 0.05. Arterial carbon dioxide partial pressure, white blood cell count, neutrophils, D-dimer, procalcitonin, and high-sensitivity C-reactive protein were suspected risk factors (p < 0.05).

Table 3. Results of multivariate analysis.

	B	SE	Wald	df	p	OR	95% CI	
							Lower limit	Ceiling
$PaCO_2$ (mmHg)	0.093	0.012	55.424	1	p < 0.001	1.097	1.071	1.124
WBC (x 10^9)	0.084	0.041	4.313	1	0.038	1.088	1.005	1.178
Neutrophils (x 10^9)	0.013	0.025	0.272	1	0.602	1.013	0.964	1.065
D-dimer (ng/mL)	0.001	0.000	31.637	1	p < 0.001	1.001	1.001	1.002
PCT (mg/mL)	1.147	0.202	32.161	1	p < 0.001	3.148	2.118	4.678
Hs-CRP (mg/L)	0.009	0.004	4.480	1	0.034	1.009	1.001	1.017

Note: The multi-factor results revealed neutrophils were not an independent factor of ICU admission.
Arterial carbon dioxide partial pressure, white blood cell count, D-dimer, procalcitonin, and high-sensitivity C-reactive protein were independent risk factors for subsequent ICU admission in adult AECOPD patients.

Table 4. The ROC curves for independent risk factors and the new model for evaluating ICU admission.

Variable	The critical value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Youden's index
$PaCO_2$ (mmHg) #	50.65	0.66 (0.59 - 0.74)	64.70	89.6	
WBC (x 10^9) #	11.45	0.67 (0.61 - 0.73)	50.40	82.80	0.33
D-dimer (ng/mL) #	1510.46	0.74 (0.68 - 0.80)	52.10	88.80	0.41
PCT (mg/mL) #	0.28	0.76 (0.70 - 0.81)	63.90	92.00	0.56
Hs-CRP (mg/L) #	19.10	0.78 (0.73 - 0.83)	69.70	81.20	0.51
The joint new prediction model *	94.74	0.94 (0.92 - 0.97)	80.70	94.80	0.76

Note: * - means the joint new prediction model consists of arterial carbon dioxide partial pressure, white blood cell count, D-dimer, procalcitonin, and high-sensitivity C-reactive protein.

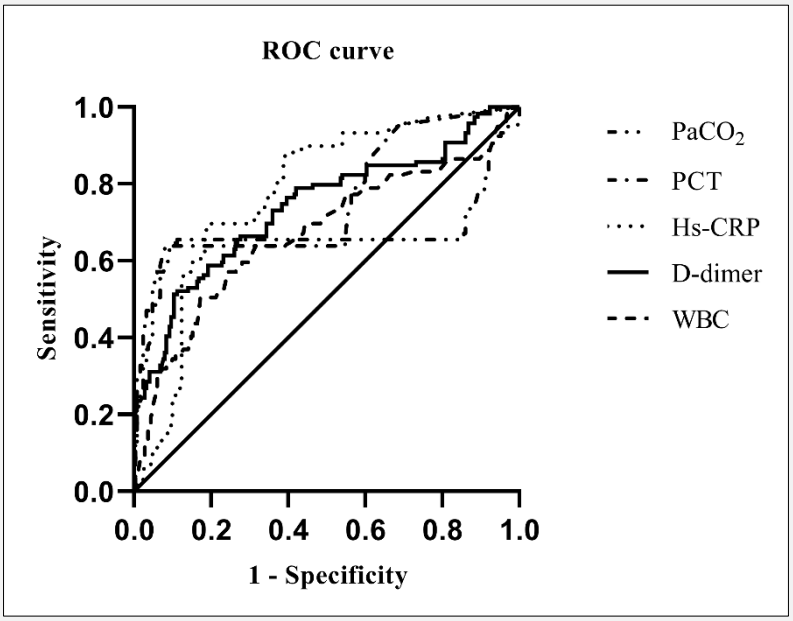

Figure 1. ROC curves of arterial carbon dioxide partial pressure, white blood cell count, D-dimer, procalcitonin, and high-sensitivity C-reactive protein.

ble 4). The joint new prediction model was obtained, and the ROC curve was drawn (Figure 2). The AUC of the new model was 0.94 (95% CI 0.92 - 0.97). The sensitivity was 80.70% and specificity was 94.800% (Table 4).

DISCUSSION

Chronic obstructive pulmonary disease (COPD) is a major chronic disease characterized by irreversible and persistent airflow limitation [9]. It is one of the major causes of rising morbidity, mortality, and healthcare costs worldwide [10]. As a series of problems such as the aging of the society are coming to the fore, the population with COPD is gradually expanding. Currently, patients with COPD, experience at least one acute exacerbation per year, i.e., a deterioration of respiratory

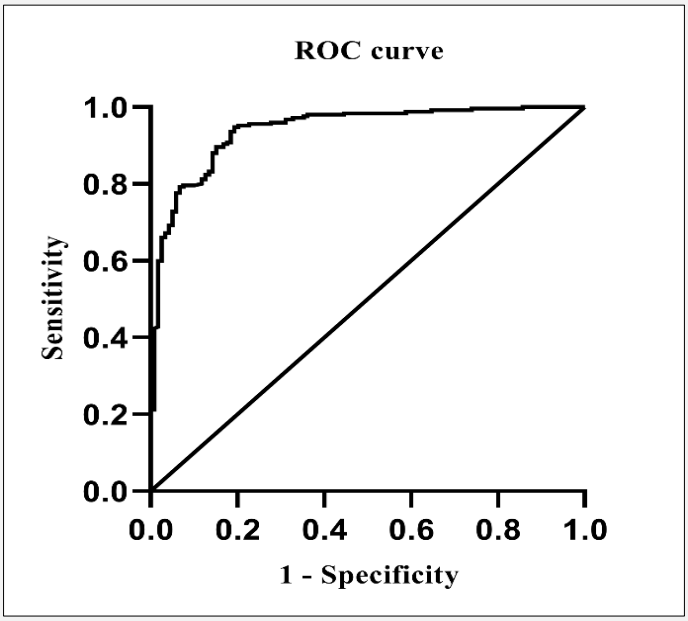

Figure 2. ROC curve analysis of joint new prediction model.

symptoms beyond the day-to-day variant and the resulting need to change their medication [11], often requiring hospitalization for treatment [12]. As the disease progresses, patients with AECOPD who are hospitalized for years eventually need to be admitted to an ICU for the next step of treatment, which imposes a significant economic burden on healthcare systems worldwide. Although, with the improvement of medical treatment, great progress has been made. Numerous clinical scoring systems regarding the severity of COPD patients have been applied to clinical work, such as the mMRC questionnaire and CAT questionnaire. However, there are fewer studies on clinically relevant scoring systems that predict the admission of patients with AECOPD to the ICU. In addition, most of the commonly used clinical scoring systems for COPD patients emphasize the assessment based on patients' subjective symptoms, and although the above scoring systems are more convenient, they lack actual objective indicators. To compensate for the inadequacy of the current clinical scoring system for patients with COPD, we constructed a new predictive model for admission to the ICU in patients with AECOPD using blood indicators. We found that PaCO2, WBC, D-dimer, PCT, and hs-CRP were independent risk factors for predicting admission to the ICU in patients with AECOPD. In recent years, several studies have shown that PaCO2 [13], WBC, D-dimer, PCT [14], and hs-CRP, are strongly associated with the severity of disease during acute exacerbations of COPD, which is consistent with the results of our study. We developed a new joint prediction model by the above independent risk factors. Compared with previous studies on the prediction of AECOPD admission to ICU, the new model had a sensitivity of 80.7% and a specificity of 94.8%, with high accuracy. Therefore, the new model has advantages in predicting ICU admissions in AECOPD patients. Timely and accurate prediction of the timing of ICU admission for AECOPD patients not only can alleviate the economic burden on the health care system and avoid excessive waste of medical resources but also is crucial for patient prognosis. In addition, the new prediction model uses common blood indicators with easily accessible samples.

The main limitation of the study is the small sample size, and we cannot avoid the possibility of selection bias, as the retrospective study was analyzed in a single hospital. This study has more strengths including that our study established a new prediction model which has high sensitivity and specificity.

CONCLUSION

The combination of serum WBC, PaCO2, D-dimer, PCT, and hs-CRP resulted in a new model for predicting admission to the ICU in patients with AECOPD with high sensitivity and specificity.

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Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

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