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ORIGINAL ARTICLE

Procalcitonin (PCT) Improves the Accuracy and Sensitivity of Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation (DECAF) Score in Predicting AECOPD Patients Admission to ICU

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SUMMARY

Background: **The score of Dyspnea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation (DECAF) can be used to predict the in-hospital mortality of patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). It is worth noting that the DECAF score is the first scoring standard combining biomarkers and clinical variables. The application of biomarkers is helpful for improving the accuracy of the scoring system. In recent years, more and more reports and studies paid attentions to procalcitonin (PCT) in respiratory infectious diseases and its clinical value has attracted increasing attention. The study aimed at investigating the effectiveness of the DECAF score combined with PCT in predicting admission of AECOPD patients to intensive care unit (ICU).**

Methods: **We conducted a retrospective study. We analyzed data from 171 non-immune individuals over the age of 40 in this study. All patients received blood routine measurement and DECAF score calculation on admission. The primary outcome used to assess the probability of an AECOPD patient was who would get a bed in general ward or ICU. Receiver operating characteristic curves (ROC) are used to assess the sensitivity and specificity of PCT, WBC, creatinine, and DECAF scores in predicting the risk of admissions to the ICU of COPD patients. We combined PCT, WBC, and creatinine with DECAF scores, observing the sensitivity and specificity of the different combinations in predicting COPD patients with regard to who should be admitted to ICU.**

Results: **After analyzing the data from 171 patients, we found that the probability of entering the ICU was 21.05% (36/171). The area under curve (AUC) of PCT, WBC, creatinine, and DECAF score in individually predicting the probability of entering the ICU of AECOPD patients were 0.71 (95% CI 0.61 - 0.81), 0.64 (95% CI 0.52 - 0.75), 0.74 (95% CI 0.63 - 0.84), and 0.88 (95% CI 0.81 - 0.94), respectively, with statistically significant differences (p = 0.00). The sensitivities of PCT, WBC, creatinine and DECAF scores were 0.61, 0.61, 0.56, and 0.91, respectively. The specificities of PCT, WBC, creatinine, and DECAF scores were 0.76, 0.67, 0.88 and 0.74, respectively. The AUC of Combination 1 (PCT&DECAF scores), Combination 2 (WBC&DECAF scores), and Combination 3 (creatinine&DECAF scores) for predicting AECOPD patients entering the ICU was 0.92 (95% CI 0.86 - 0.97), 0.89 (95% CI 0.84 - 0.94), and 0.91 (95% CI 0.85 - 0.96), respectively, with statistically significant differences (p = 0.00); the sensitivities were 0.92, 0.86, and 0.94, respectively, and the specificities were 0.97, 0.78, and 0.74, respectively.**

Conclusions: **Procalcitonin improves the accuracy and sensitivity of the DECAF score in predicting the probability of AECOPD patients entering the ICU, and PCT was superior to other indexes to improve the sensitivity and specificity of the DECAF score.**

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KEY WORDS

acute exacerbation chronic obstructive pulmonary disease, procalcitonin, DECAF score, prognosis

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is becoming the third leading cause of death worldwide after cardiovascular and cerebrovascular diseases and tumors [1]. Acute exacerbations of the disease often require hospitalization. An acute exacerbation is defined as "an event in the natural course of the disease characterized by a change in the patient's dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication" [2]. Both short - and long-term mortality rates increase after acute exacerbation [3]. There are currently no national guidelines for clinical predictors or scoring systems recommended for exacerbation of COPD [4]. Some studies have evaluated predictors of mortality after COPD progression, but these studies vary in design, criteria, and survey parameters. To date, some studies have assessed existing severity scores, such as CURB-65 and BAP-65, but these scores have limitations [5]. It is necessary to establish reliable mortality predictors for clinical practice in order to better guide clinical diagnosis and treatment. The DECAF score was a significantly stronger predictor of mortality than CURB-65 [6]. The DECAF score can be used as a simple but effective predictor of mortality of patients with acute exacerbation of COPD and can help clinicians more accurately predict whether to admit to the ICU for higher levels of care and treatment to improve outcomes in this common condition [7]. Furthermore, the prognostic indicators included in the DECAF score are objective, and there are few other different explanations.

PCT, an easily measurable laboratory biomarker, is recommended as a promising candidate predictor for ICU admission in COPD patients [8]. Procalcitonin has been a reliable marker of acute bacterial infection in hospitalized patients. Infection is the most common cause of acute exacerbations in COPD patients. Bacterial and fungal cultures of sputum of our patients found that the most common pathogenic bacteria are Hemophilus parahemolyticus, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Candida albicans, Streptococcus aureus, and so on. This suggests that these patients do have an infection. PCT can provide a different prognostic classification for clinicians according to different stratifications [9,10].

Numerous studies have confirmed that both DECAF score and PCT may have some value in the prognosis assessment of COPD patients [11,12]. Based on the above, the main aim of this study was to investigate the effectiveness of PCT combined with the DECAF score in predicting probability of COPD admission to ICU.

MATERIALS AND METHODS

Patients

We did a retrospective study. The study was conducted at a regional class A teaching hospital with 1,200 beds in China. All adult patients over the age of 40 years, who were primarily diagnosed with COPD between January 2017 and December 2018, were included. Those who had a history of hematologic disease, active pulmonary tuberculosis, pulmonary embolism, uremia, advanced lung cancer, refractory heart failure, rheumatic disease, radiotherapy, immunosuppressive agents, transplantation, as well as incomplete medical records, and ancillary examinations were excluded. The statistics included general clinical data, disease history, drinking and smoking history, and laboratory tests. In this study, PCT results, DECAF score, and probability of admission to the ICU were recorded as the primary outcome.

The measurement of PCT and the evaluation of DECAF score

PCT counts were collected by automatic fluorescence immunoanalyzer (VIDAS, France) before treatment. DECAF score was performed in the emergency department or outpatient department for the included patients. The DECAF score included five of the strongest predictors of mortality: Dyspnea, eosinopenia ($< 0.05 * 10^9$/L), consolidation, acidemia (pH < 7.3), and atrial fibrillation. Patients with dyspnea were divided into two groups: those who could bathe and/or dress independently (eMRCD 5a) and those who needed help with both (eMRCD 5b). The total score is 6, except eMRCD 5b is 2, the other indicators are 1. The index's risk level is 0 - 1 for low risk, 2 for medium risk and 3 - 6 for high risk.

Statistical analyses

SPSS 22.0 statistical software was used for data analysis. Measurement data was ex-pressed as mean ± standard deviation (SD) or median and interquartile range (IQR). Classified variables were described as rate. According to the test of normality and homogeneity of variance, chi-square test was used for counting data and T test was used for comparison between groups. Nonparametric test is used for nonnormal distribution data. Univariate analysis was conducted first, and then binary

Table 1. Baseline characteristics of patients with AECOPD.

Demographic data	
Age (year) *	75 (66 - 79)
Age ≥ 65 years, n (%)	136 (79.53)
Male gender, n (%)	51 (29.82)
Coexisting chronic diseases, n (%)	124 (72.51)
Hypertension	71 (41.52)
Cerebrovascular disease	36 (21.05)
Ischemic heart disease	54 (31.58)
Diabetes mellitus	31 (18.13)
Renal dysfunction	19 (11.11)
Pulmonary infectious disease, n (%)	63 (36.84)
Tuberculosis	3 (1.75)
Pneumonia	60 (35.09)
Smoking, n (%)	86 (50.29)
Alcohol intake, n (%)	42 (24.56)
Number of ICU residents, n (%)	36 (21.05)
DECAF score ≥ 3, n (%)	27 (15.79)

* - Data presented as median (interquartile range).

Table 2. Distribution characteristics of infection indicators.

	Mean	Median	Interquartile ranges
WBC	9.30	7.90	5.90 - 11.20
PCT	2.70	0.29	0.07 - 0.85
CRP	26.50	10.50	2.99 - 31.40
Neutrophil	7.60	5.42	3.50 - 8.79
Lymphocyte	1.70	1.41	0.85 - 1.92
NLR	7.80	4.36	1.89 - 8.65
γ-glutamyl transferase	48.4	25	17 - 41
Creatinine	77.6	69	57 - 86

logistic regression analysis was used to determine the variables of independent risk factors for COPD admission to ICU. Odds ratio (ORs) and 95% confidence interval (CIs) of each variable were calculated. ROC curves were used to evaluate the sensitivity and specificity of predicting probability of admission to the ICU in COPD patients. All tests were bilateral and $p < 0.05$ was considered statistically significant.

RESULTS

Patient Characteristics

A total of 171 patients who met the inclusion criteria were included in this study. General characteristics are shown in Table l, including 120 males and 51 females, with a median age of 75 years (interquartile range 66 - 79 years); 80.12% were over 65 years old. Smoking accounted for 50.29% and drinking accounted for 24.56%. Of the patients, 72.52% (124/171) had one or more chronic diseases such as hypertension, cerebrovascular disease, ischemic heart disease, diabetes melli-

Table 3. Single factor analysis results.

		Admission to ICU		Probability of admission to ICU	Chi-square/Z	p-value
		Y	N			
Gender	Men	27	93	22.50%	0.507	0.476
	Women	9	42	17.65%		
Chronic diseases	Y	26	98	20.97%	0.002	0.965
	N	10	37	21.28%		
Smoking	Y	18	68	20.93%	0.002	0.968
	N	18	67	21.18%		
Alcohol abuse	Y	11	31	26.19%	0.884	0.347
	N	25	104	19.38%		
Age #		78 (70 - 83)	75 (65 - 78)		-2.444	0.015 *
γ-glutamyl transferase #		36 (25 - 59)	24 (16 - 40)		-2.885	0.004 *
Creatinine #		93 (68 - 126)	66 (56 - 77)		-4.343	< 0.001 *
WBC #		10.15 (6.70 - 15.55)	7.50 (5.78 - 10.73)		-2.522	0.012 *
Neutrophil #		7.74 (5.07 - 13.32)	5.02 (3.13 - 7.75)		-3.613	< 0.001 *
Lymphocyte #		1.12 (0.62 - 1.55)	1.49 (0.96 - 2.03)		-2.556	0.011 *
NLR #		6.96 (4.76 - 11.39)	3.43 (1.75 - 6.91)		-4.796	< 0.001 *
CRP #		7.25 (3.29 - 24.55)	11.71 (2.97 - 33.09)		-0.938	0.348
PCT #		0.82 (0.20 - 14.42)	0.22 (0.05 - 0.67)		-3.92	< 0.001 *
DECAF Score #		3 (2 - 3)	1 (0 - 2)		-7.188	< 0.001 *

Note: * - means p < 0.05; # - indicates that SK normality test results in a non-normal distribution, data presented as median (interquartile range). Y for yes, N for no.

tus, renal dysfunction at the same time; 36.84% (63/171) of the patients also had pulmonary infectious disease such as tuberculosis, pneumonia. The distribution characteristics of infection indicators are shown in Table 2. The probability of admission to the ICU was 21.05% (36/171).

Univariate analysis of selected indicators

It was found that age, glutamine transferase, creatinine, WBC, neutrophils, lymphocytes, NLR, PCT, and DECAF scores were suspicious risk factors for AECOPD patients which could increase the risk of ICU admission ($p < 0.05$). Gender, CRP, chronic diseases, smoking, and alcohol abuse were not risk factors for AECOPD patients entering ICU ($p > 0.05$) (Table 3).

Binary logistic regression analysis was conducted to determine the independent risk factors of ICU admission for patients with AECOPD

Age, neutrophils, lymphocytes, NLR, and γ- glutamyl transferase were not independent risk factors for admission of AECOPD patients to ICU, each with p-values of 0.433, 0.143, 0.430, 0.054, and 0.568, respectively, all of which were greater than 0.05. Creatinine, PCT, WBC, and DECAF were independent risk factors for admission of AECOPD patients to ICU, each with p-values of 0.034, 0.035, 0.038, and 0 respectively, all less than 0.05. Based on the above conclusions, four indexes including creatinine, PCT, WBC, and DECAF were selected to predict whether patients with AECOPD were admitted to ICU. The prediction accuracy was 90.6%, which means that the above conclusions have good practical application value (Table 4).

ROC curve analysis of risk in COPD patients admitted to the ICU

The AUC of PCT, WBC, creatinine, and DECAF score in predicting probability of AECOPD patients entering the ICU were 0.71 (95% CI 0.61 - 0.81), 0.64 (95% CI 0.52 - 0.75), 0.74 (95% CI 0.63 - 0.84) and 0.88 (95% CI 0.81 - 0.94), respectively, with statistically significant differences ($p = 0.00$). The sensitivity of PCT, WBC, creatinine and DECAF scores were 0.61, 0.61, 0.56 and 0.91, respectively. The specificity of PCT, WBC, creatinine and DECAF scores were 0.76, 0.67, 0.88, and 0.74, respectively. The AUC of Combination 1 (PCT&DECAF scores), Combination 2 (WBC& DECAF scores), and Combination 3 (creatinine& DECAF scores) for predicting entering the ICU of AECOPD patients was 0.92 (95% CI 0.86 - 0.97), 0.89

Table 4. Results of multivariate analysis.

	B	S.E.	Wald	df	p-value	OR	95% CI	
							Lower limit	Ceiling
Age	0.034	0.043	0.614	1	0.433	1.034	0.951	1.126
WBC	-0.228	0.110	4.318	1	0.038 *	0.796	0.642	0.987
Neutrophil	0.163	0.112	2.145	1	0.143	1.177	0.946	1.465
Lymphocyte	0.480	0.609	0.622	1	0.430	1.616	0.490	5.327
NLR	-0.112	0.058	3.712	1	0.054	0.894	0.797	1.002
γ-glutamyl transferase	0.003	0.006	0.325	1	0.568	1.003	0.992	1.015
Creatinine	-0.019	0.009	4.518	1	0.034 *	0.981	0.964	0.999
PCT	-0.129	0.061	4.425	1	0.035 *	0.897	0.799	0.991
DECAF	-1.688	0.367	21.134	1	0 *	0.185	0.090	0.380
Constant	4.959	3.073	2.605	1	0.107	142.475		

Note: * - means p < 0.05.

Table 5. ROC curve analysis of risk in AECOPD patients admitted to the ICU.

Variable	The critical value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Younden's index	p-value
PCT	0.675	0.71 (0.61 - 0.81)	61.10	75.60	0.37	0.00
WBC	9.05	0.64 (0.52 - 0.75)	61.10	66.70	0.28	0.01
Creatinine	91.5	0.74 (0.63 - 0.84)	55.60	88.10	0.44	0.00
DECAF Score	1.5	0.88 (0.81 - 0.94)	91.70	74.10	0.66	0.00
Combination 1		0.92 (0.86 - 0.97)	92.00	97.30	0.89	0.00
Combination 2		0.89 (0.84 - 0.94)	86.10	77.80	0.64	0.00
Combination 3		0.91 (0.85 - 0.96)	94.40	74.10	0.69	0.00

Note: Combination 1, Combination 2, and Combination 3 indicated that PCT, WBC, and creatinine were combined with the DECAF score, respectively, to predict the risk of COPD patients admitted to ICU.

(95% CI 0.84 - 0.94) and 0.91 (95% CI 0.85 - 0.96), respectively, with statistically significant differences (p = 0.00), the sensitivities were 0.92, 0.86, and 0.94 and the specificities were 0.97, 0.78 and 0.74, respectively. It can be seen that PCT improves the accuracy and sensitivity of the DECAF score in predicting risk of admission to the ICU in COPD patients. Moreover, the AUC of PCT combined with the DECAF score is larger than that of the other two indexes combined with DECAF score (Table 5, Figure 1 - 7).

DISCUSSION

AECOPD is a common cause of admission to the intensive care unit (ICU), but the appropriate level of care for ICU patients with AECOPD remains controversial [13]. Understanding the prognosis of the disease and the factors that predict adverse outcomes is important to enable doctors to advise patients on the expected natural course of the disease and the likelihood of complications [14]. Identifying patients at admission who are at high risk of dying in the hospital may be useful for assigning patients to appropriate levels of care, determining the level of positivity of treatment, guiding care goals, and safely leaving the hospital [15]. There are many clinical variables that may have prognostic significance for the treatment of patients with acute exacerbation of COPD [16]. Blood PCT is a simple, widely available index which has been intensively evaluated in recent years in various diseases, including COPD. The studies reviewed showed that the PCT is a valuable predictor of AECOPD mortality. Furthermore, it correlates well, and in some studies is even more accurate, than

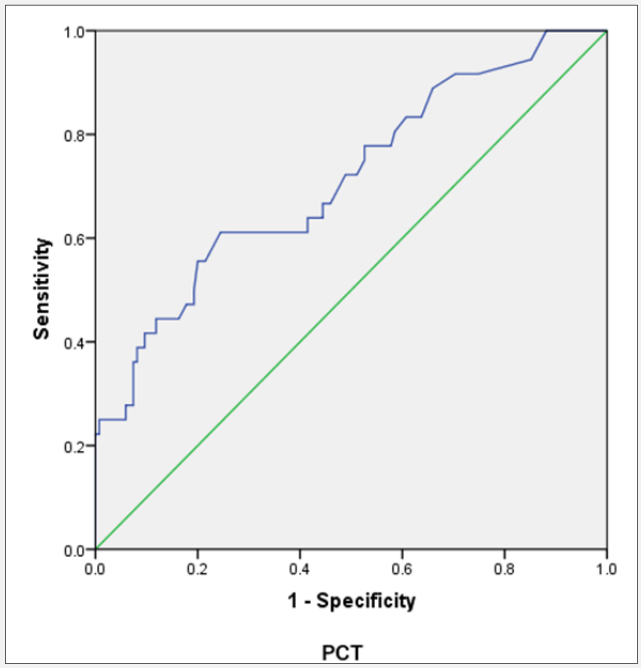

Figure 1. ROC curve of PCT in predicting the risk in AECOPD patients admitted to the ICU.

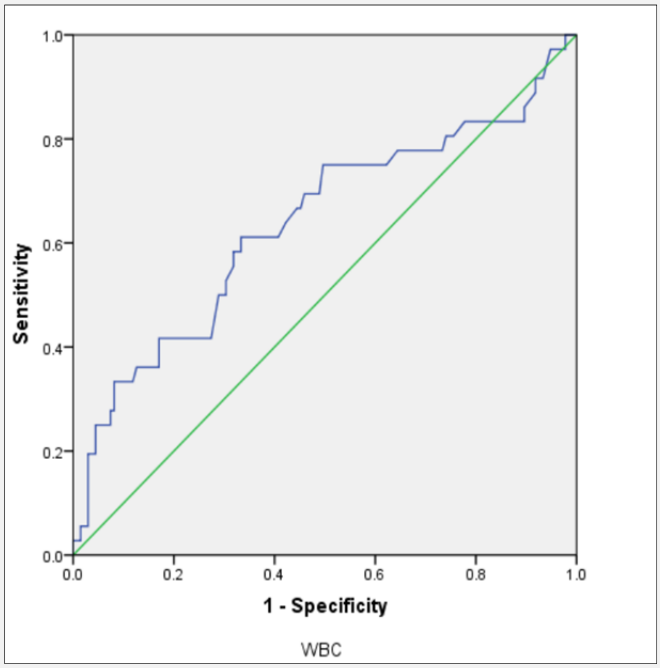

Figure 2. ROC curve of WBC in predicting the risk in AECOPD patients admitted to the ICU.

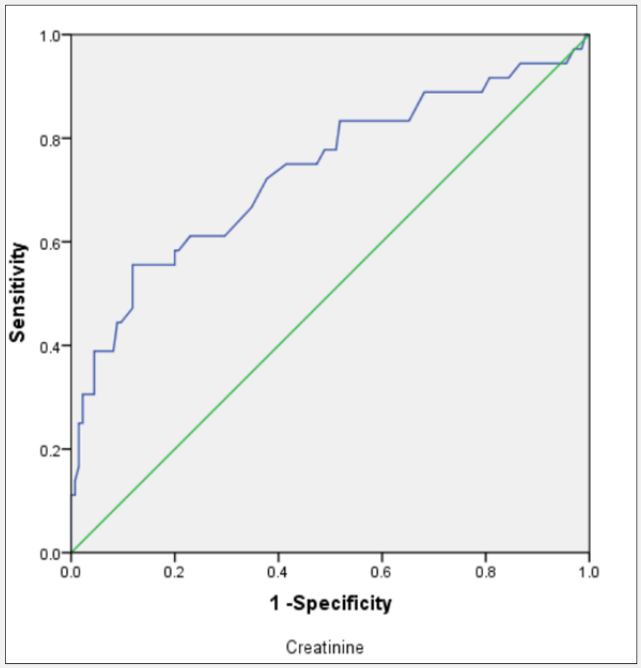

Figure 3. ROC curve of creatinine in predicting the risk in AECOPD patients admitted to the ICU.

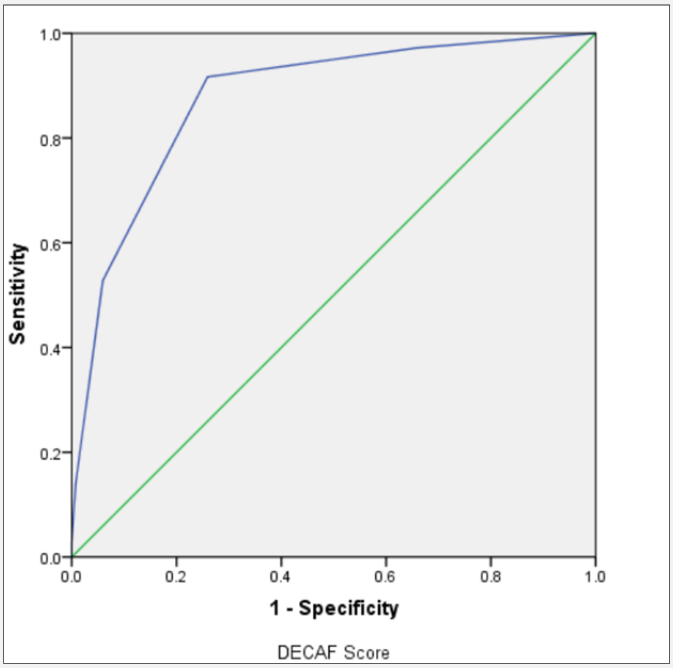

Figure 4. ROC curve of DECAF score in predicting the risk in AECOPD patients admitted to the ICU.

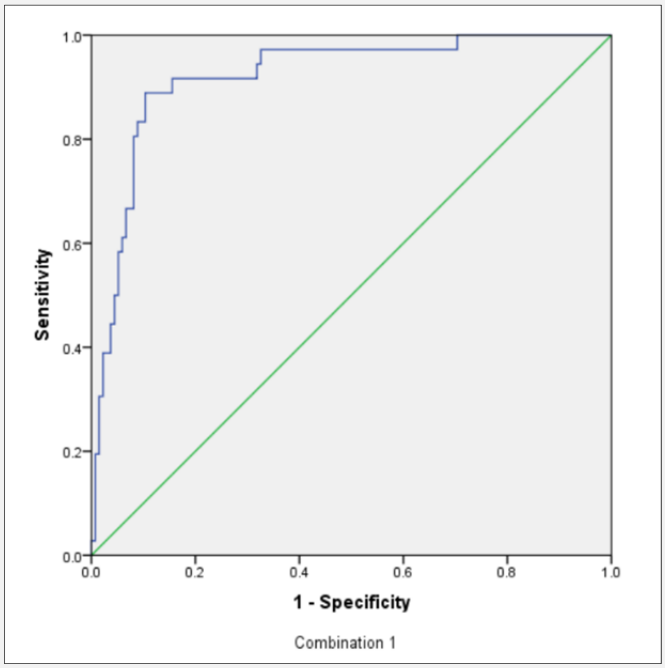

Figure 5. ROC curve of PCT combined DECAF score in predicting the risk in AECOPD patients admitted to the ICU.

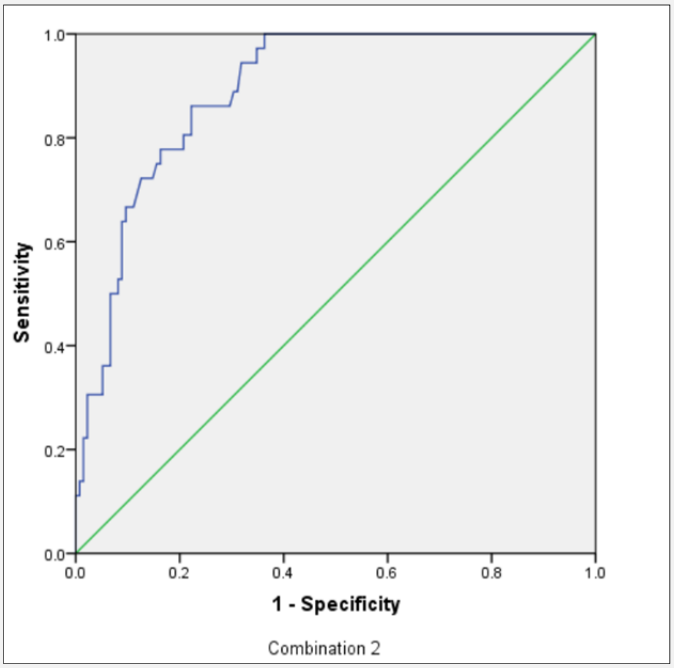

Figure 6. ROC curve of WBC combined DECAF score in predicting the risk in AECOPD patients admitted to the ICU.

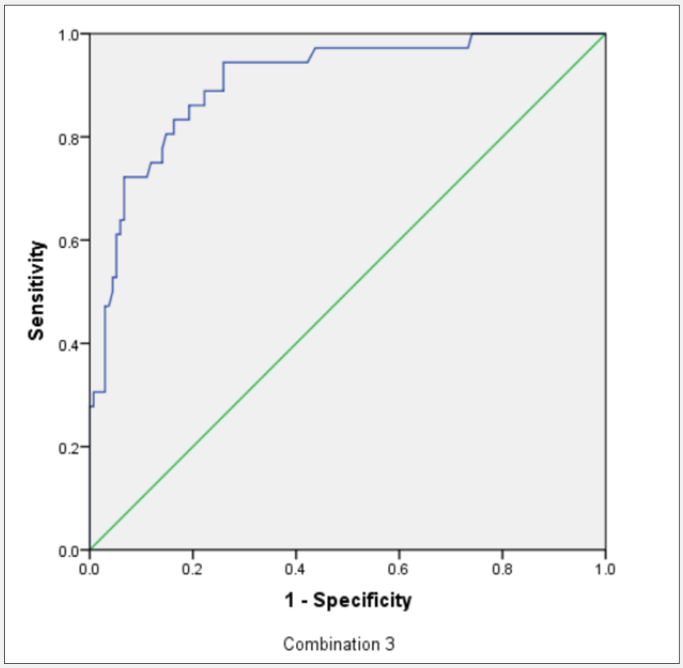

Figure 7. ROC curve of creatinine combined DECAF score in predicting the risk in AECOPD patients admitted to the ICU.

other traditional inflammatory indexes (WBC counts alone). The routine use of the PCT in clinical practice should be further assessed in large, well-designed, prospective studies [17]. Potential prognostic variables include age, FEV1, athletic ability, previous ICU admission including severe deterioration, previous functional status, complications, various physiological and laboratory parameters, and biomarkers [18,19]. CURB-65, BAP-65, and DECAF scoring tools have been proposed to predict AECOPD mortality [20]. CURB-65 scores have been shown to be suboptimal at assessing and guiding the treatment of hospitalized patients with AECOPD. DECAF scores had the highest accuracy in predicting the prognosis of patients among these 3 scores [21].

We found that the DECAF score, PCT, WBC, and creatinine were independent risk factors for admission to the ICU in patients with AECOPD. In this study, ROC analysis was widely used to compare the risk assessment of AECOPD patients admitted to the ICU. PCT improved the accuracy and sensitivity of the DECAF score in predicting ICU admission for AECOPD patients. Moreover, the AUC of PCT combined with the DECAF score is larger than that of the other two indexes combined with the DECAF score. PCT was superior to other indexes to improve the sensitivity and specificity of the DECAF score.

The advantages of this study lie in its innovation and practicality. A prognostic tool is lacking in AECOPD. PCT combined with the DECAF score may be a simple and useful prognostic indicator for admission of AECOPD patients to the ICU. Our results come from a single medical center and larger studies are needed to validate this simple tool.

CONCLUSION

In a word, our results suggest that procalcitonin improves the accuracy and sensitivity of DECAF scores in predicting the risk in COPD patients for admission to the ICU. A simple clinical predictive tool, combined with commonly available indices during hospitalization and accurate classification of clinically relevant risks for AECOPD inpatients can help clinicians manage this common and fatal disease.

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Ethical Approval:
This study was approved by 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 from all individual participants included in this study.

Declaration of Interest:
No conflicts of interest.

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