Development and validation of a nomogram for predicting bacterial infections in patients with acute exacerbation of chronic obstructive pulmonary disease

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Abstract. Bacterial infection is a significant contributory factor in the pathogenesis of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) and it has a pivotal role in exacerbating symptoms and precipitating mortality among patients with chronic obstructive pulmonary disease (COPD). The early identification of bacterial infection in individuals with COPD remains a challenge. Therefore, the present study aimed to create and validate a risk assessment tool using easily accessible serum biomarkers to predict bacterial infection in individuals with AECOPD. A retrospective cohort study was carried out at Pingxiang People's Hospital (Pingxiang, China) from January 2023 to December 2023, involving individuals diagnosed with AECOPD. A total of 544 patients with AECOPD were randomly allocated to the two following groups: The training set, which included 70% (n=384) of the patients, and the validation set, which included 30% (n=160) of the patients. Subsequently, a nomogram model was constructed using multivariate logistic regression analysis in the training set. Its discriminatory ability and calibration were internally validated, while decision curve analyses were employed to assess the clinical utility of the nomogram. The incidence of bacterial infection in hospitalized patients with AECOPD was 50% in the training set and 48.1% in the validation set. The nomogram model incorporated independent factors associated with bacterial infection, including C-reactive protein, neutrophil elastase, procalcitonin and eosinophils, identified by univariate and multivariate logistic regression analyses. The area under the curve of the nomogram model was 0.835 [95% confidence interval (CI): 0.795-0.875] in the training set and 0.785 (95% CI: 0.715-0.856) in the validation set. The model demonstrated excellent discrimination and calibration in the validation set [c-statistic: 0.79 (95% CI: 0.68-0.90)]. Furthermore, the discrimination and overfitting bias of the model were assessed through internal validation, revealing a C-index of 0.836 for the initial group and 0.788 for the subsequent validation set. The straightforward risk prediction model for early identification of bacterial infections is valuable for hospitalized patients with AECOPD.

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Abbreviations: AECOPD, acute exacerbations of chronic obstructive pulmonary disease; C-index, concordance index; ESR, erythrocyte sedimentation rate; WBC, white blood cell; NE, neutrophil elastase; CRP, C-reactive protein; PCT, procalcitonin; LDH, lactate dehydrogenase; GOLD, Global Initiative for Chronic Obstructive Lung Disease; AUC, area under the curve; DCA, decision curve analysis

Key words: bacterial infection, AECOPD, risk factors, nomogram, prediction model

Introduction

Chronic obstructive pulmonary disease (COPD) is a complex respiratory disorder characterized by persistent airflow limitation resulting from exposure to noxious particles and gases, leading to an abnormal inflammatory response in the lungs (1). Acute exacerbations in COPD (AECOPD) significantly contribute to the decline in lung function, diminish the quality of life, increase the utilization of emergency healthcare services and heighten the mortality rates associated with COPD (2,3). Infectious pathogens, such as bacteria, viruses and atypical pathogens, can trigger airway inflammation in COPD and lead to acute exacerbations (4,5). These pathogens are associated with acute exacerbations in up to 80% of patients with COPD, with bacteria potentially contributing to 50% of these exacerbations (6).

Delayed diagnosis or delayed initiation of antimicrobial therapy in patients with AECOPD was reported to be associated with increased mortality (1,2,7). Currently, the diagnosis primarily relies on pathogen cultures; however, challenges such as the selection of appropriate specimens, the conditions in which cultures are grown and the proficiency of operators significantly hinder the prompt acquisition of results from cultures and drug sensitivity tests (8). Therefore, early

identification of bacterial infections in patients with AECOPD remains challenging (9). Consequently, clinicians are actively seeking a simple and rapid indicator that can aid the diagnosis of bacterial infections among individuals with AECOPD.

Recently conducted studies have demonstrated that several factors can augment the risk of developing bacterial infections in patients with AECOPD (10,11). The current diagnostic strategy for bacterial infections involves a comprehensive assessment of risk factors, clinical manifestations and laboratory test results (2,4,11). Unveiling the complete spectrum of risk factors associated with bacterial infections in patients with AECOPD is crucial to aid clinicians in identifying such infections (7). Identifying one or more predisposing conditions would be pivotal in initiating further diagnostic investigations, thereby facilitating early diagnosis and treatment (5,6).

The presence of multiple potential risk factors poses a challenge for clinicians in assessing patient risk and there is a dearth of risk-predictive scoring models for bacterial infections in the existing literature. Consequently, there is an urgent need to develop predictive models that can facilitate clinical decision-making. To establish a more precise diagnostic prediction model for bacterial infections in patients with AECOPD, it is essential to incorporate more reliable predictors and include patients from a broader cohort. The primary objective of the present study was to develop and validate a risk prediction model aimed at promptly identifying patients with severe AECOPD who require immediate empirical antibacterial treatment, particularly in healthcare facilities with limited resources.

Patients and methods

Data source. The present retrospective study was carried out using clinical data from patients with AECOPD at Pingxiang People Hospital (Pingxiang, China), from January 2023 to December 2023. Patients who met the criteria of the study design were divided into two groups as follows: 70% were randomly allocated to the training set and the remaining 30% constituted the internal validation set.

The present study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Pingxiang People's Hospital (approval no. PK2023Z67-HS02).

The inclusion criteria for patients with AECOPD were as follows: The diagnosis of AECOPD was established following the guidelines set out by the Global Initiative for Chronic Obstructive Lung Disease (1). AECOPD is characterized by a sudden worsening of symptoms, such as breathlessness, coughing and sputum production, which worsen over <14 days. It is characterized by the presence of at least two of the following symptoms: Increased sputum volume, altered sputum color and exacerbated dyspnea.

Patients were excluded from the present study if they lacked a spirometry report, had been admitted to the hospital within one month before the study, were undergoing treatment with immunosuppressants or had been diagnosed with malignant disease. Patients with chronic respiratory conditions, such as asthma, interstitial lung disease, active tuberculosis and bronchiectasis were also excluded from the study.

Definition of bacterial infection. The diagnosis of bacterial infection was established based on a combination of clinical manifestations, laboratory findings, radiographic imaging, PCR detection and the patient's response to antibiotic treatment. Bacterial infection was confirmed through the isolation of causative agents. Spontaneous sputum samples were incubated on sheep blood, chocolate and MacConkey agar plates (Antu Biological) at 35˚C for 48 h in an atmosphere containing 5% CO_2. A sputum culture was deemed positive if the cultured microorganisms showed potential pathogenicity, exhibited high growth density (semi-quantitative), contained <25 squamous epithelial cells and had >15 leukocytes per high-power microscopic field (magnification, x100) in the Gram-stained sputum sample. The Gram staining involves five steps, all performed at room temperature. First, a sputum smear on a microscope slide was prepared and heat-fixed. Next, crystal violet stain was applied for 1 min, followed by rinsing with water. Iodine solution was then added for 1 min to form a complex with the crystal violet. After another rinse, the sample was decolorized with 95% ethanol for 10-30 sec and rinsed immediately. Finally, counterstaining was performed with safranin for 30 sec and the slide was rinsed and allowed to dry, followed by examination under a microscope.

Risk factors. The predictors utilized for constructing the nomogram model were selected based on prior research studies (10,11). All risk factors, encompassing demographic data, comorbidities, pulmonary function, pharmacological history, status of mechanical ventilation upon admission and history of previous acute exacerbations, were readily accessible from comprehensive early, current and historical medical records. The detailed data are presented in Table I.

Statistical analysis. Statistical analyses were conducted using the statistical software SPSS (version 25.0; IBM Corp.) and R software (version 3.5.2). Continuous variables were presented as the mean ± standard deviation and group comparisons were carried out using the t-test or Mann-Whitney U-test. Categorical variables, presented as numbers and percentages, were compared using the chi-square test or Fisher's exact test, as appropriate. Multivariate analysis included the aggregation of potential biomarkers that were identified as significant using univariate logistic regression analysis. Only variables with $P<0.05$ in the univariate analysis in the training set were included in the multivariate analysis.

Subsequently, the nomogram was created utilizing the 'rms' package in R software, leveraging the outcomes of the multivariate logistic regression analysis of the dependent variable. The discriminatory power was evaluated by calculating the area under the receiver operating characteristic curve (AUC). The calibration of the model was evaluated by comparing the anticipated and actual likelihood of bacterial infection. Furthermore, decision curve analysis (DCA) was employed to assess the clinical utility of the model. Unless explicitly mentioned, a two-tailed $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 706 patients diagnosed with AECOPD were screened, resulting in the exclusion of 162 patients based on predefined exclusion criteria, ultimately

Table I. Characteristics of AECOPD in patients in the training and validation sets.

Variable	Total (n=544)	Validation cohort (n=160)	Training cohort (n=384)	P-value
Age, years	59.75±10.91	59.51±10.94	59.86±10.90	0.733
Sex				0.135
Male	430 (79.0)	120 (75)	310 (80.8)	
Female	114 (21.0)	40 (25)	74 (19.2)	
Albumin, g/l	38.30±12.92	39.30±14.94	37.87±11.97	0.240
$PaCO_2$, mmHg	44.84±10.45	44.48±9.62	44.99±10.78	0.607
PaO_2, mmHg	73.20±14.92	71.94±12.30	73.73±15.87	0.203
Neutrophils, %	67.24±12.85	67.12±12.58	67.28±12.98	0.891
ESR, mm/h	23.46±3.17	23.58±3.22	23.41±3.15	0.566
WBC, $x10^9$/l	10.28±5.75	9.99±5.51	10.40±5.84	0.449
NE, μg/ml	20.51±22.06	20.31±21.66	20.59±22.25	0.892
CRP, mg/l	15.29±10.81	14.66±8.51	15.56±11.64	0.380
D-D dimer, mg/l	0.36±0.85	0.39±1.02	0.35±0.78	0.594
LDH, U/l	208.27±76.02	195.45±63.99	203.61±79.97	0.051
PCT, ng/l	0.39±0.47	0.38±0.35	0.40±0.51	0.639
Drinking				0.905
No	372 (68.4)	110 (68.8)	262 (68.2)	
Yes	172 (31.6)	50 (31.2)	122 (31.8)	
GOLD				0.501
No	366 (67.3)	111 (69.4)	255 (66.4)	
Yes	178 (32.7)	49 (30.6)	129 (33.6)	
Smoking				0.051
No	350 (64.3)	93 (58.1)	257 (66.9)	
Yes	194 (35.7)	67 (41.9)	127 (33.1)	
Diabetes				0.310
No	485 (89.2)	146 (91.2)	339 (88.3)	
Yes	59 (10.8)	14 (8.8)	45 (11.7)	
CAD				0.301
No	430 (79.0)	122 (76.2)	308 (80.2)	
Yes	114 (21.0)	38 (23.8)	76 (19.8)	
Hypertension				0.658
No	264 (48.5)	80 (50.0)	184 (47.9)	
Yes	280 (51.5)	80 (50.0)	200 (52.1)	
Cancer				0.722
No	292 (53.7)	84 (52.5)	208 (54.2)	
Yes	252 (46.3)	76 (47.5)	176 (45.8)	
Anemia				0.152
No	311 (57.2)	99 (61.9)	212 (55.2)	
Yes	233 (42.8)	61 (38.1)	172 (44.8)	
Eosinophils ≥2%				0.859
No	245 (45.0)	73 (45.6)	172 (44.8)	
Yes	299 (55.0)	87 (54.4)	212 (55.2)	

Values are expressed as n (%) or the mean ± standard deviation. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; WBC, white blood cell; NE, neutrophil elastase; CRP, C-reactive protein; PCT, procalcitonin; LDH, lactate dehydrogenase; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAD, coronary artery disease; $PaCO_2$, partial carbon dioxide pressure.

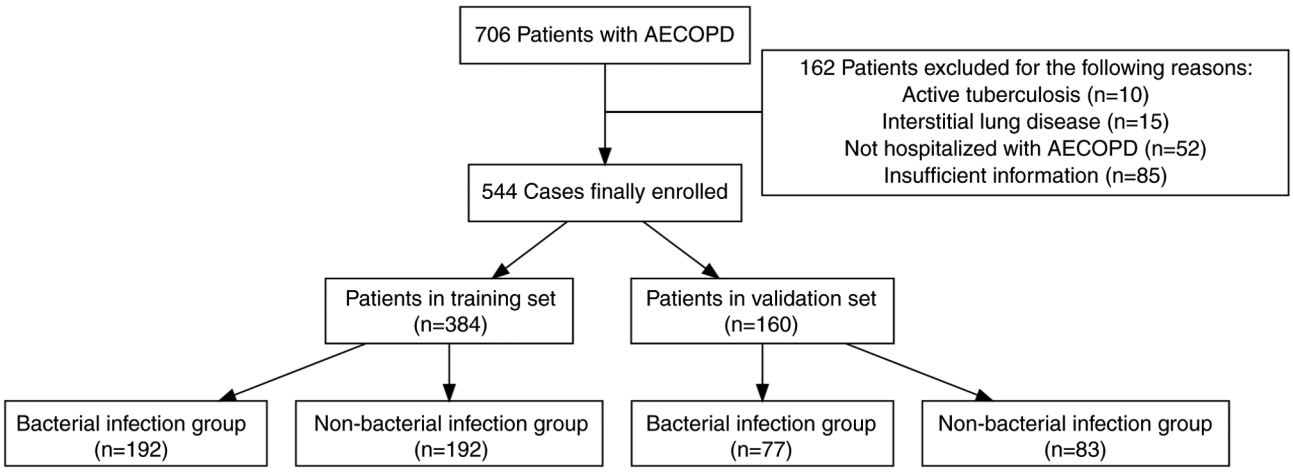

Figure 1. Flow diagram of the study. AECOPD, acute exacerbation of chronic obstructive pulmonary disease.

yielding a final sample size of 544 patients. The basic characteristics of the dataset are summarized in Table I. The training dataset comprised 384 patients, with 192 cases in the bacterial infection group and 192 cases in the non-bacterial infection group, which comprised 310 men and 74 women, aged between 41 and 97 years. The validation dataset comprised 160 patients, with 77 cases in the bacterial infection group and 83 cases in the non-bacterial infection group, which comprised 120 men and 40 women, aged between 44 and 92 years. The flowchart illustrates the strategy for identifying bacterial infections in the AECOPD cohort (Fig. 1). Table I presents the demographic and clinical characteristics of patients in both the training and validation sets.

Risk factors associated with bacterial infections of AECOPD. The characteristics of the patients with AECOPD in the training cohort, both with and without bacterial infection, are compiled in Table II. A total of 21 clinical and basic indicators were included in the univariate analysis to explore their association with bacterial infections. The results revealed that procalcitonin (PCT), PaO_2, neutrophil elastase (NE), C-reactive protein (CRP), the neutrophil percentage and eosinophil percentage ≥2% exhibited a significant association with bacterial infection (P≤0.05; Table III). Subsequent multivariate logistic regression analysis indicated that the following factors were independently associated with bacterial infection: NE, CRP, PCT and eosinophil percentage ≥2% (Table III).

Nomogram development. The logistic regression analysis identified four independent risk factors for bacterial infection in the multivariate analysis: Eosinophil percentage ≥2%, NE, PCT and CRP. Based on the weights assigned to these factors from the training set, a nomogram was generated using the results of the multivariate regression to calculate the risk of bacterial infection (Fig. 2).

Discrimination and calibration. The AUC of the nomogram was calculated to be 0.835 [95% confidence interval (CI), 0.795-0.875] in the training dataset, as demonstrated by the blue curve in Fig. 3. In the validation dataset, the AUC was determined to be 0.785 (95% CI, 0.715-0.856), as indicated by the red curve in the same figure. Further examination of the calibration belt revealed strong concordance of the nomogram in both the training and validation datasets, as illustrated in Fig. 4A and B. The discrimination and overfitting bias of the model were assessed through internal validation. The findings revealed a C-index of 0.836 for the initial group and 0.788 for the subsequent validation set. The calibration plots illustrated a robust agreement between the predictions of the nomogram and the actual occurrence of bacterial infections in patients. The model exhibited excellent goodness-of-fit, as demonstrated by the Hosmer-Lemeshow test results in both the training set and validation set, with P-values exceeding 0.05 (P=0.36 for the training set; P=0.12 for the validation set). Meanwhile, our data (Fig. S1) also showed that the nomogram model had a greater AUC than PCT alone in the training dataset and in the validation dataset.

DCA. The results of the DCA for the risk nomogram in both the training and validation sets were presented to determine the optimal decision threshold for the nomogram (Fig. 5A and B). The nomogram model exhibited a favorable net benefit across both datasets, encompassing predicted risk thresholds ranging from 0-51%.

Discussion

AECOPD is a complex and heterogeneous disease characterized by chronic airway inflammation. Over the past decade, advancements in modern research techniques have significantly enhanced the understanding of the role of bacterial infection in AECOPD (8). Bacterial infections contribute to up to 50% of acute exacerbations of COPD, leading to increased morbidity and mortality (3,4,8,12). Timely intervention is crucial for reducing the impact of bacterial infections on the health outcomes of patients with AECOPD (7). Previous studies have aimed at developing prediction models for identifying patients with bacterial infections (13-15). Therefore, it is imperative to prioritize this distinct patient cohort and develop a concise yet precise prognostic model that enables clinicians to accurately

Table II. Comparison of AECOPD in patients with and without bacterial infection in the training set.

Variable	Total (n=384)	Non-bacterial (n=192)	Bacterial (n=192)	P-value
Age, years	59.86±10.90	59.85±11.27	59.86±10.56	0.989
Albumin, g/l	37.87±11.97	38.86±13.98	36.89±9.48	0.106
$PaCO_2$, mmHg	44.99±10.78	46.00±12.31	43.98±8.92	0.066
PaO_2, mmHg	73.73±15.87	75.38±17.78	72.08±13.54	0.042
Neutrophils, %	67.28±12.98	64.89±12.65	69.68±12.89	<0.001
ESR, mm/h	23.41±3.15	23.26±3.18	23.56±3.12	0.355
WBC, x10^9/l	10.40±5.84	10.07±5.02	10.73±6.56	0.270
NE, μg/ml	20.59±22.25	12.81±10.93	28.38±27.42	<0.001
CRP, mg/l	15.56±11.64	11.27±10.12	19.85±11.49	<0.001
D-D dimer, mg/l	0.35±0.78	0.41±0.90	0.29±0.63	0.126
LDH, U/l	213.61±79.97	213.37±67.82	213.86±90.69	0.953
PCT, ng/l	0.40±0.51	0.30±0.28	0.49±0.65	<0.001
Drinking				>0.999
No	262 (68.2)	131 (68.2)	131 (68.2)	
Yes	122 (31.8)	61 (31.8)	61 (31.8)	
GOLD				0.331
No	255 (66.4)	132 (68.8)	123 (64.1)	
Yes	129 (33.6)	60 (31.2)	69 (35.9)	
Smoking				0.914
No	257 (66.9)	128 (66.7)	129 (67.2)	
Yes	127 (33.1)	64 (33.3)	63 (32.8)	
Diabetes				0.874
No	339 (88.3)	169 (88.0)	170 (88.5)	
Yes	45 (11.7)	23 (12.0)	22 (11.5)	
CAD				0.306
No	308 (80.2)	158 (82.3)	150 (78.1)	
Yes	76 (19.8)	34 (17.7)	42 (21.9)	
Hypertension				0.307
No	184 (47.9)	87 (45.3)	97 (50.5)	
Yes	200 (52.1)	105 (54.7)	95 (49.5)	
Cancer				0.539
No	208 (54.2)	107 (55.7)	101 (52.6)	
Yes	176 (45.8)	85 (44.3)	91 (47.4)	
Anemia				0.412
No	212 (55.2)	110 (57.3)	102 (53.1)	
Yes	172 (44.8)	82 (42.7)	90 (46.9)	
Eosinophils ≥2%				<0.001
No	172 (44.8)	106 (55.2)	66 (34.4)	
Yes	212 (55.2)	86 (44.8)	126 (65.6)	

Values are expressed as n (%) or the mean ± standard deviation. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; WBC, white blood cell; NE, neutrophil elastase; CRP, C-reactive protein; PCT, procalcitonin; LDH, lactate dehydrogenase; GOLD, Global Initiative for Chronic Obstructive Lung Disease; CAD, coronary artery disease; $PaCO_2$, partial carbon dioxide pressure.

assess disease severity and optimize therapeutic strategies for improved patient survival.

Utilizing a multiple logistic regression model, a ranking chart was developed to predict bacterial infections in patients with AECOPD, based on independently correlated and identified risk factors. Each factor was assigned a weighted number of points and the total points for each patient were calculated using the nomogram, which yielded an estimated probability of bacterial infections. Logistic regression analysis revealed that CRP, PCT, eosinophil percentage and NE were

Table III. Logistic regression analysis of predictors for bacterial infections of patients with AECOPD.

	Univariate			Multivariate		
Variable	Coefficient	OR (95%CI)	P-value	Coefficient	OR (95%CI)	P-value
Age, years	0.000	1.000 (0.982, 1.019)	0.989			
Drinking	-0.000	1.000 (0.651, 1.537)	>0.999			
GOLD	0.210	1.234 (0.807, 1.886)	0.331			
Smoking	-0.024	0.977 (0.638, 1.494)	0.914			
Diabetes	-0.050	0.951 (0.510, 1.771)	0.874			
CAD	0.263	1.301 (0.786, 2.155)	0.306			
Hypertension	-0.209	0.811 (0.543, 1.212)	0.307			
Cancer	0.126	1.134 (0.759, 1.695)	0.539			
Anemia	0.169	1.184 (0.791, 1.770)	0.412			
Albumin	-0.017	0.983 (0.962, 1.005)	0.124			
$PaCO_2$	-0.018	0.982 (0.964, 1.001)	0.068			
PaO_2	-0.014	0.986 (0.973, 1.000)	0.046	0.002	1.002 (0.986, 1.019)	0.777
Neutrophil percent	0.031	1.031 (1.014, 1.049)	<0.001	0.019	1.019 (1.000, 1.039)	0.056
ESR	0.030	1.031 (0.967, 1.099)	0.354			
WBC	0.019	1.020 (0.985, 1.056)	0.270			
NE	0.042	1.042 (1.028, 1.057)	<0.001	0.042	1.043 (1.027, 1.059)	<0.001
CRP	0.098	1.103 (1.074, 1.134)	<0.001	0.082	1.085 (1.052, 1.119)	<0.001
D-D dimer	-0.224	0.799 (0.591, 1.080)	0.145			
LDH	0.000	1.000 (0.998, 1.003)	0.953			
PCT	1.559	4.753 (2.373, 9.519)	<0.001	1.674	5.332 (2.263, 12.567)	<0.001
Eosinophils ≥2%	0.856	2.353 (1.559, 3.552)	<0.001	0.830	2.294 (1.403, 3.751)	0.001

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ESR, erythrocyte sedimentation rate; WBC, white blood cell; NE, neutrophil elastase; CRP, C-reactive protein; PCT, procalcitonin; LDH, lactate dehydrogenase; GOLD, Global Initiative for Chronic Obstructive Lung Disease; OR, odds ratio.

significant predictors of bacterial infections in patients with AECOPD. The nomogram incorporating these predictors demonstrated exceptional discriminatory and calibration abilities for predicting bacterial infections in patients at high risk for developing AECOPD, thereby offering valuable clinical guidance for the early identification and initiation of empirical antibiotic treatment.

Consistent with previous studies, NE has been identified as a robust predictor of the development of bacterial infection in patients with AECOPD (14,16,17). NE serves as a relatively specific biomarker for severe bacterial infections and sepsis (14-16). Research findings have indicated that bacterial infection can trigger an immune response in the airways, leading to inflammation (18,19). Of note, one study demonstrated higher levels of neutrophilic inflammation during COPD-mediated bacterial exacerbations compared to non-bacterial exacerbations (18). NE can synergistically impair tracheobronchial ciliary function when combined with bacterial products (16,20). In AECOPD, there is a predominant airway inflammation characterized by neutrophils, with sputum samples from numerous patients showing neutrophil counts exceeding 60% (18,21). Neutrophils play various roles within the innate immune system, including the defense against invading microorganisms (18,22). This demonstrates that NE serves as a highly sensitive and specific predictor of bacterial-associated exacerbation, characterized by an increased bacterial load or positive microbiological findings during acute events.

The eosinophil count/percentage is a readily available and straightforward test that can be utilized for predicting bacterial infection (23,24). However, relying solely on the eosinophil percentage is inadequate to accurately predict bacterial infection, necessitating its combination with other established biological markers to enhance diagnostic accuracy. Thulborn *et al* (24) indicated that an eosinophil percentage <2% demonstrated potential as an indicator of bacterial infection in AECOPD events. Consequently, an eosinophil percentage ≥2% could serve as a reference for guiding antibiotic usage in the treatment of AECOPD.

Numerous previous literature reports have consistently demonstrated that both PCT and CRP serve as common clinical indicators for predicting the occurrence of bacterial infection in AECOPD (25,26). The predictive capability of CRP alone for bacterial infection is limited, necessitating the integration of other established biological markers to enhance its diagnostic accuracy in identifying bacterial infections (27). The present study further confirmed, through univariate and multivariate analyses, that PCT is a robust predictor of bacterial infection and an increasing concentration of PCT was associated with a higher risk of infection. Consequently, PCT was identified as a pivotal contributor in the current model.

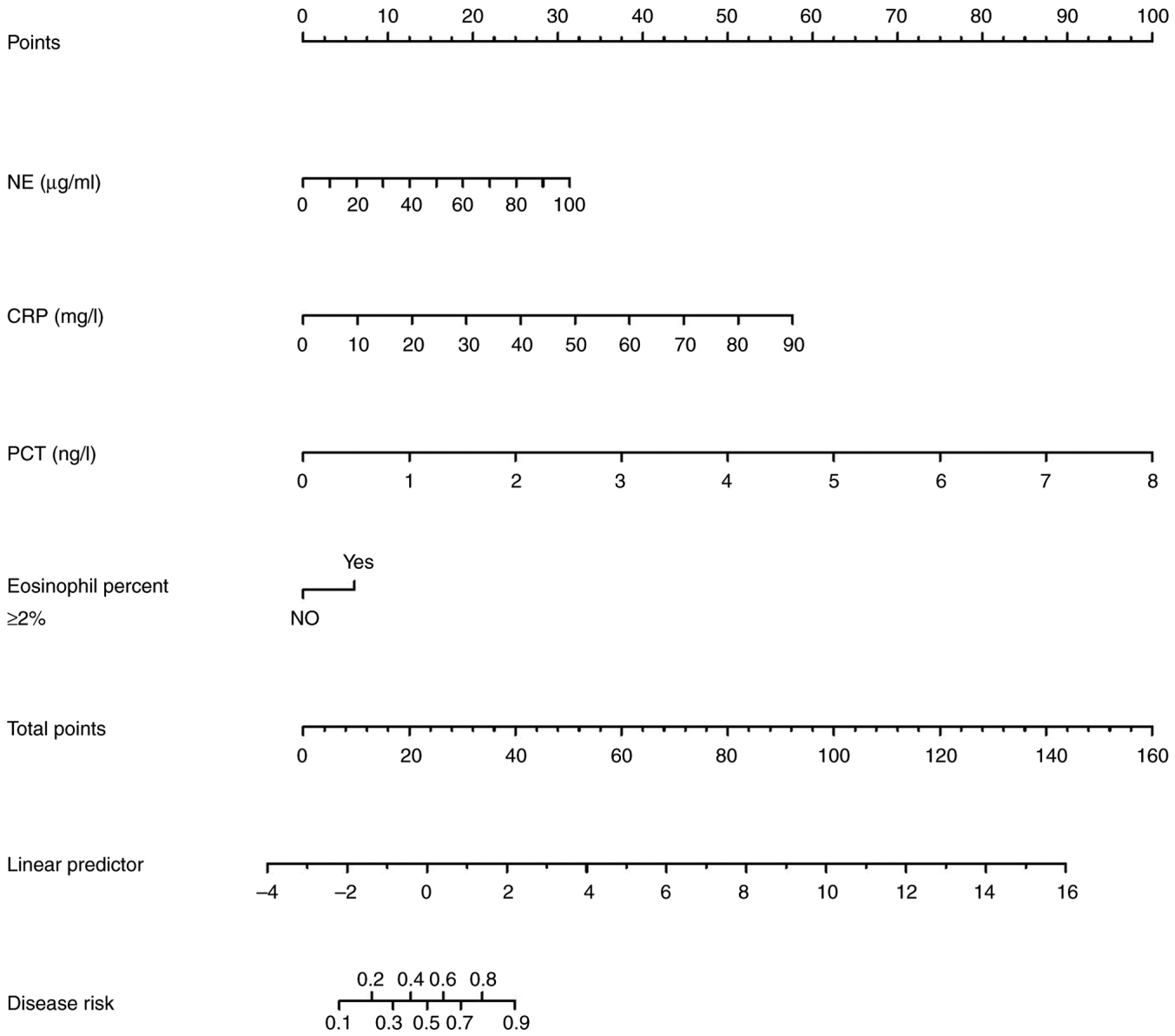

Figure 2. Nomogram for predicting bacterial infections of patients with AECOPD. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; NE, neutrophil elastase; CRP, C-reactive protein; PCT, procalcitonin.

The two most important biomarkers for detecting infection are PCT and CRP, both of which are inflammatory markers.

Plasma levels of PCT are known to be increased in individuals with sepsis or serious bacterial or fungal infections (28). In contrast to these observations, PCT levels tend to be lower in patients exhibiting milder inflammatory reactions (29). Previous studies have demonstrated that compared with CRP, PCT is a superior predictor of early bacterial infection (26,30). It is interesting to know that, owing to the presence of various types of infections in the current model, CRP exhibited a comparatively lower diagnostic value compared with PCT (27,29). It is worth noting that PCT may not be effectively cleared by the kidneys in patients with severe renal failure (25,29,31). Consequently, relying solely on PCT as an indicator for determining the optimal cut-off value to diagnose bacterial infection in patients with AECOPD may not yield significantly different results from those observed in the general population. Meanwhile, a comparative analysis was conducted between the multivariate model and a model using only PCT. The results showed that, while PCT is a significant predictor, the incorporation of other parameters enhances the model's overall predictive ability. Our findings indicate that the nomogram model exhibits a significantly larger AUC compared to the PCT for both the training and validation datasets. Therefore, further research is warranted to fully ascertain the predictive potential of PCT as a biomarker for bacterial infection.

In the present study, a simplified nomogram was pioneered for predicting the risk of bacterial infection in patients with AECOPD. The prediction model was developed using readily available clinical parameters, incorporating risk factors such as NE, CRP, eosinophil percentage and PCT levels. The model's discriminative and calibration abilities were proven to be excellent through internal validation. The criteria for diagnosing bacterial infections were proposed and the clinical

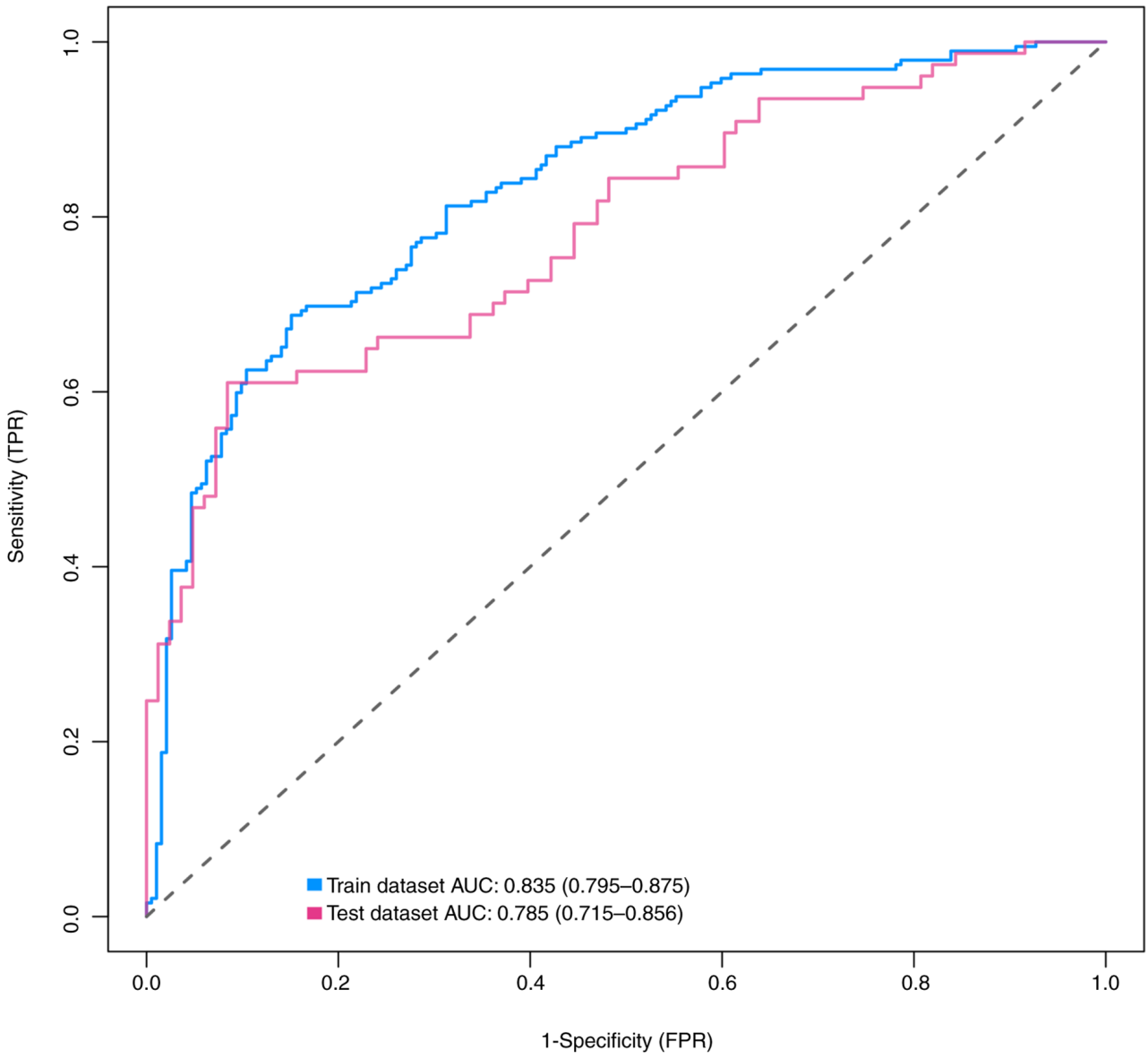

Figure 3. ROC curve indicating the performance of the prediction model using both the training set and validation sets. ROC, receiver operating characteristic; AUC, area under the ROC curve; FPR, false-positive rate; TPR, true-positive rate.

algorithm for patients with lower respiratory tract specimens exhibited favorable validity in distinguishing colonization from true bacterial infection. While previous research studies have identified certain risk factors, such as antibiotic usage, plasma CRP and PCT, as potential indicators of bacterial infection in patients with COPD (26,27), the precise role and complex interplay of these factors in predicting the probability of bacterial infection have not been fully incorporated into current diagnostic standards.

Nomograms are simple yet visually intuitive predictive models that combine various indicators to aid in the diagnosis or prediction of diseases. The nomogram developed in the present study offers clinicians a valuable tool to assess the risk of complications resulting from bacterial infections among patients with COPD. An investigation of alternative methods for diagnosing bacterial infections will be performed in future studies. A patient with AECOPD who presents with two to three additional risk factors, along with impaired lung function, may have a calculated predicted risk of bacterial infection ranging from 8 to 52%, according to the nomogram. In addition, the lack of a predictive model or serum marker currently hinders the differentiation of bacterial infections in patients with AECOPD, which is crucial for determining appropriate antibiotic treatment strategies tailored to specific bacteria types. Since culture and/or PCR methods are used to confirm the infection, it would be reasonable to distinguish the types of bacteria, as they may be strongly associated with disease prognosis. Future research by our group will further investigate the potential of developing models for identifying specific bacterial pathogens, predicting clinical outcomes and customizing treatment strategies for patients with AECOPD.

The present study exhibits certain limitations that should be considered. First, the study was conducted at a single center and was retrospective in nature. The evaluation of the discrimination and calibration of the scoring model was limited to internal validation. To generalize the results, conducting

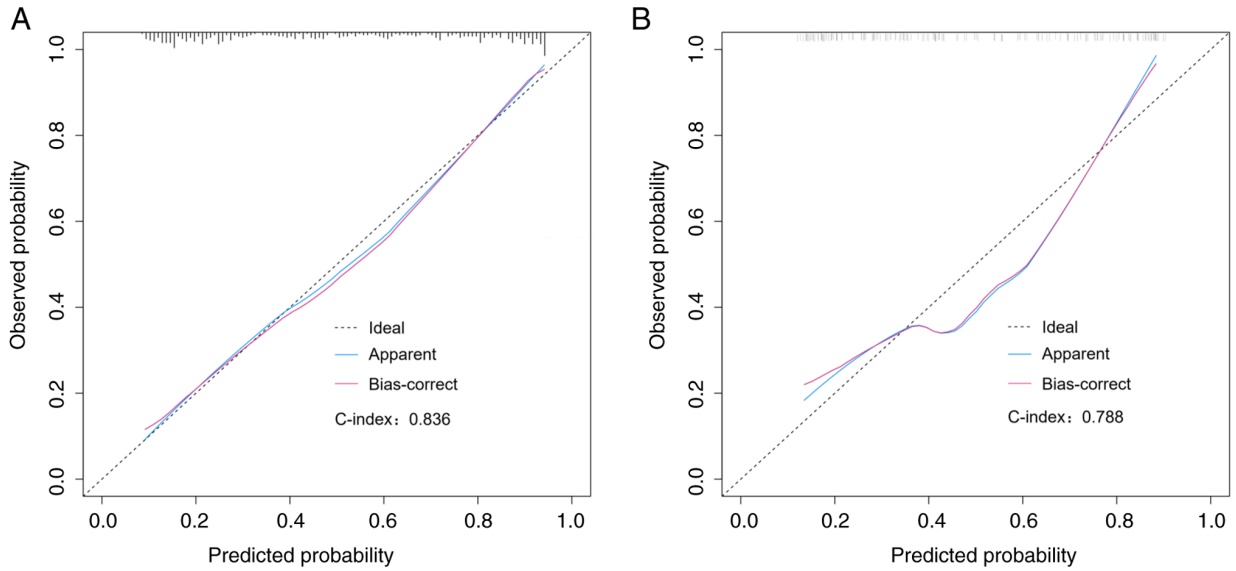

Figure 4. (A) Calibration curve evaluating the ability of the nomogram to predict bacterial infection in the training dataset. (B) Calibration curve evaluating the ability of the nomogram to predict bacterial infection in the testing dataset.

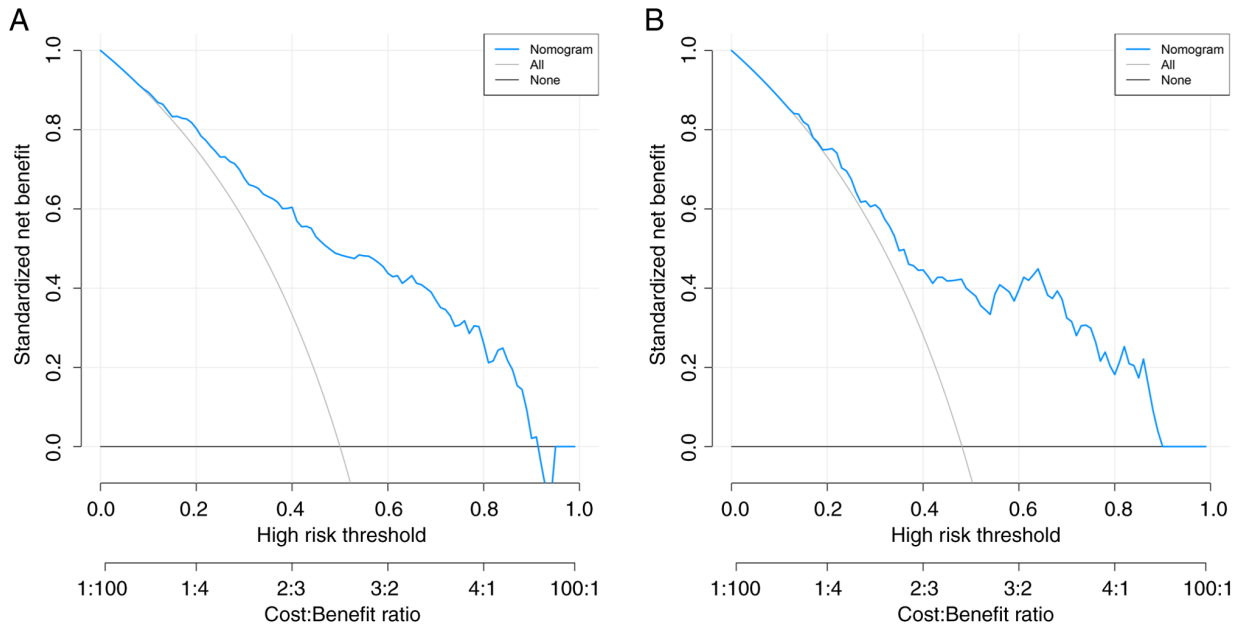

Figure 5. Decision curve analysis for (A) the training cohort and (B) validation cohort demonstrating the benefit in predicting clinically significant bacterial infections for the nomogram. The blue curves depict the net benefit of the model. The gray lines display the net benefits in the alternative strategies of all patients with bacterial infections and the black lines display the net benefits in the alternative strategies of patients without bacterial infections.

multicenter prospective studies for external validation is important. Furthermore, the simplistic binary classification (positive/negative) utilized for categorizing COPD co-morbidities does not accurately capture the true severity of the overall disease burden faced by the patients. Incorporating a system for classifying the severity of these comorbidities could significantly enhance the quality and value of the findings.

The nomogram model integrates four distinct risk factors for bacterial infection and has the potential to provide clinicians and patients with advanced, precise insights into the risk of bacterial infection in AECOPD cases. Additional research is essential to confirm the effectiveness and validity of using the nomogram in real-world clinical settings to enhance the prediction of bacterial infections.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XLC conceived and designed the study. XMW and WQY collected the data and performed the literature search. DZ was involved in writing the manuscript and performed the statistical analyses. All authors have read and approved the final version of the manuscript. XMW and XLC confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The Ethics Committee of Pingxiang People's Hospital (Pingxiang, China; approval no. PK2023Z67-HS02) approved the protocol of the current study and waived the requirement for informed consent owing to the retrospective design of the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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