

Original Article

Correlations of platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio and acute physiology, and chronic health evaluation II score with prognosis of elderly patients with chronic obstructive pulmonary disease and respiratory failure

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Abstract: Objective: To investigate the correlations of platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR) and acute physiology and chronic health evaluation II (APACHE II) score with the prognosis of elderly patients with chronic obstructive pulmonary disease (COPD) and respiratory failure. Methods: A retrospective analysis was conducted on 110 elderly COPD patients with respiratory failure. General information, inflammatory indices (PLR, NLR), and pulmonary function scores were collected. Statistical comparisons were made using t-tests and chi-square tests. ROC curve analysis evaluated the predictive value of the investigated variables. Results: Compared to the good-prognosis group, the poor-prognosis group exhibited significantly higher PLR, NLR levels, as well as higher COPD Assessment Test (CAT) and APACHE II scores. Logistic regression analysis identified PLR, NLR, and APACHE II scores as independent prognostic risk factors for COPD patients with respiratory failure. ROC curve analysis confirmed the high predictive value of these variables in forecasting prognosis. Conclusion: PLR, NLR, and APACHE II scores, exhibiting correlations with prognosis in elderly COPD patients with respiratory failure, can serve as valuable biomarkers for patient prognosis.

Keywords: COPD, respiratory failure, inflammation, prognosis, PLR, NLR

Introduction

Chronic obstructive pulmonary disease (COPD), a prevalent condition requiring effective prevention and treatment strategies [1], is characterized by persistent respiratory symptoms and airflow limitation stemming from chronic airway and lung tissue inflammation due to exposure to harmful gases and particles [2]. COPD is triggered by airway and/or alveolar abnormalities resulting from long-term exposure to such agents, and its acute exacerbations and complications affect disease progression. The primary causes of chronic airflow limitation in COPD are small airway disease and lung parenchymal injury, with the relative contribution varying among individuals [3]. Currently, COPD ranks as one of the top leading causes of death

globally, surpassed by ischemic heart disease and stroke [4]. Projections suggest that the prevalence of COPD will continue to increase in the next 40 years, resulting in over 5.4 million deaths by 2060 [4].

Airway and systemic inflammation play a pivotal role in COPD pathogenesis, and their severity is directly correlated with the severity of the disease [5]. During acute exacerbations of COPD, epithelial cells and macrophages in the airway are activated, leading to the release of chemokines that attract neutrophils. These activated neutrophils secrete proteases such as neutrophil elastase, cathepsin-G, protease 3, matrix metalloproteinase (MMP)-8, and MMP-9, which destroy healthy lung tissue and increase bronchial mucus secretion [6].

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As markers of systemic inflammation, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) reflect the ratio of neutrophils (NEU) and platelets (PLT) to lymphocytes (LYM), respectively [7]. These ratios are considered novel indices that offer insights into the body's inflammatory status [8]. Inflammation typically leads to an increase in NEU and PLT counts and a decrease in LYM, making NLR and PLR crucial for assessing inflammation and cell-mediated immune status.

Compared to traditional inflammatory markers such as white blood cell count, interleukins (IL-1, IL-6, IL-8), and tumor necrosis factor- α , NLR and PLR exhibit advantages in terms of cost-effectiveness and ease of detection, requiring no complex laboratory procedures in clinical settings. Moreover, these markers remain stable even under physiologic variations such as dehydration and exercise, as well as during blood sample handling [9].

The prognostic significance of NLR and PLR in various diseases has been well-established, yet their role in COPD remains understudied. Given the close link between COPD pathogenesis and inflammatory response, a retrospective analysis of NLR and PLR in COPD patients is imperative. This retrospective study aimed to correlate these readily measurable and cost-effective inflammatory indices with COPD severity and prognosis, thereby elucidating their possible value in evaluating and predicting disease outcome.

Methods and data

Patient information

A retrospective analysis was conducted on COPD patients with respiratory failure treated at The First Affiliated Hospital of Xinxiang Medical University from January 2021 to December 2022.

Inclusion criteria: Patients who met the diagnostic criteria for COPD according to the Guidelines for Primary Diagnosis and Treatment of Chronic Obstructive Pulmonary Disease (2018) [10]. Patients with type II respiratory failure, defined by arterial partial pressure of carbon dioxide >50 mm Hg, arterial partial pressure of oxygen <60 mmHg, and symptoms

such as dyspnea, tachypnea, shallow breathing, and altered mental status. Patients aged 60 years or older. Patients with comprehensive clinical records.

Exclusion criteria: Patients with comorbid pulmonary diseases, including pneumonia, bronchial asthma, pulmonary tuberculosis, etc. Patients with abnormal blood coagulation, severe malnutrition, comorbid malignant tumors, mental disorders, severe cardiovascular or cerebrovascular diseases, or other infectious diseases.

This study was conducted with the approval of the Medical Ethics Committee of The First Affiliated Hospital of Xinxiang Medical University.

Criteria for prognosis evaluation

Patients experiencing adverse events, such as cardiac arrest, angina pectoris, myocardial infarction, heart failure, multiple organ dysfunction, or death during hospitalization until discharge, were classified as having a poor prognosis. Otherwise, they were deemed to have a good prognosis.

Blood routine test

Upon admission, EDTA-K2 anticoagulated blood samples (2 mL) were collected from all patients. The Sysmex XT-1800i analyser was utilized to determine the PLT, NEU, and LYM counts. Subsequently, the PLR and NLR were calculated using the following formulas: $NLR = NEU/LYM$; $PLR = PLT/LYM$.

Patient selection

Based on the defined inclusion and exclusion criteria, 110 patients were included in the study, while 48 patients were excluded. According to their prognosis, the 110 patients were categorized into the good-prognosis group ($n = 74$) and the poor-prognosis group ($n = 36$), as depicted in **Figure 1**.

Clinical data collection

Clinical data were gathered from electronic medical records and outpatient re-examination records, encompassing sex, age, body mass index (BMI), disease duration, mechanical ventilation duration, hospital stay, smoking history,

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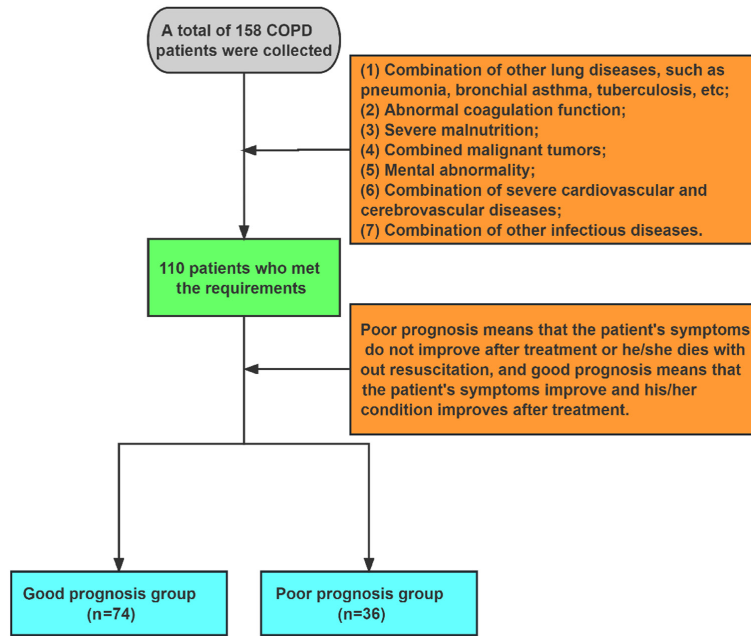


Figure 1. Flow chart.

alcohol consumption history, hypertension history, diabetes mellitus history, COPD assessment test (CAT) score [11], and Acute Physiology and Chronic Health Evaluation II (APACHE II) score [12].

Outcome measures

1: The NLR and PLR levels in the two groups were evaluated before treatment. 2: The CAT and APACHE II scores of the two groups were evaluated. 3: Clinical data of the two groups were compared. 4: Logistic regression was conducted for analysing the risk factors of poor prognosis in elderly COPD patients with respiratory failure.

Statistical analyses

Statistical analyses were performed using SPSS 22.0 software. Categorical variables were presented as frequencies and percentages, and group differences were assessed using a chi-square (χ^2) test. Continuous variables with normal distributions were expressed as mean \pm standard deviation (SD) and were analysed using Student t-test. Receiver operating characteristic (ROC) curves were generated to assess the predictive value of indices for poor prognosis in elderly COPD patients with respiratory failure. Logistic regression analysis was

employed to identify risk factors associated with poor prognosis. A P -value of <0.05 was considered significant.

Results

Clinical data analysis

The two groups showed no significant differences in sex, age, BMI, disease duration, mechanical ventilation duration, hospital stay, smoking history, alcohol consumption history, hypertension history, or diabetes mellitus history (all $P>0.05$, **Table 1**).

Comparison of laboratory indices

The comparison of PLR and NLR levels between the two groups revealed significantly higher values in the poor-prognosis group (PLR: 3.36 ± 0.73 , NLR: 128.16 ± 19.25) compared to the good-prognosis group (PLR: 2.29 ± 0.78 , NLR: 109.09 ± 13.64) (both $P<0.0001$, **Figure 2**).

Comparison of functional scores

The CAT and APACHE II scores were significantly higher in the poor-prognosis group (CAT: 23.83 ± 5.26 , APACHE II: 32.42 ± 5.42) compared to the good-prognosis group (CAT: 20.32 ± 5.45 , APACHE II: 24.22 ± 5.67) ($P<0.0001$, **Figure 3**).

Analysis of predictive value

Using ROC curves, the study evaluated the predictive value of PLR, NLR, CAT score, and APACHE II score in forecasting the prognosis of elderly COPD patients with respiratory failure. The respective areas under the curves were 0.851, 0.799, 0.675, and 0.854 (**Figure 4** and **Table 2**).

Analysis of prognostic risk factors

A logistic regression analysis was conducted to assess prognostic risk factors. The measured data were first categorized (**Table 3**) and then subjected to logistic regression. The re-

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Table 1. Comparison of clinical data from included patients

| Factor | Good-prognosis group (n = 74) | Poor-prognosis group (n = 36) | χ^2 | P |
|---|----------------------------------|----------------------------------|----------|-------|
| Sex | | | | |
| Male | 41 | 18 | 0.284 | 0.593 |
| Female | 33 | 18 | | |
| Age | | | | |
| ≥65 years | 41 | 22 | 0.322 | 0.570 |
| <65 years | 33 | 14 | | |
| BMI | | | | |
| ≥25 kg/m ² | 19 | 10 | 0.055 | 0.814 |
| <25 kg/m ² | 55 | 26 | | |
| Course of disease | | | | |
| ≥5 years | 36 | 14 | 0.930 | 0.334 |
| <5 years | 38 | 22 | | |
| Duration of mechanical ventilation | | | | |
| ≥7 days | 42 | 25 | 1.637 | 0.200 |
| <7 days | 32 | 11 | | |
| Length of stay | | | | |
| ≥2 weeks | 37 | 16 | 0.299 | 0.584 |
| <2 weeks | 37 | 20 | | |
| History of smoking | | | | |
| Yes | 41 | 22 | 0.322 | 0.570 |
| No | 33 | 14 | | |
| History of drinking | | | | |
| Yes | 7 | 5 | 0.489 | 0.484 |
| No | 67 | 31 | | |
| History of hypertension | | | | |
| Yes | 18 | 12 | 0.991 | 0.320 |
| No | 56 | 24 | | |
| History of diabetes mellitus | | | | |
| Yes | 11 | 7 | 0.371 | 0.542 |
| No | 63 | 29 | | |

BMI: Body mass index.

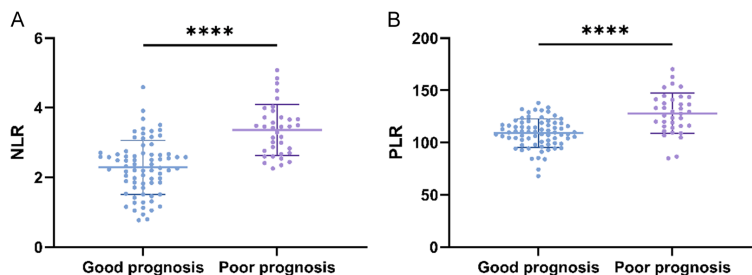


Figure 2. Comparison of peripheral blood PLR and NLR in patients with different prognosis. A: Comparison of peripheral blood PLR between good- and poor-prognosis groups; B: Comparison of peripheral blood NLR between good- and poor-prognosis groups. ****P<0.0001. PLR: platelet-to-lymphocyte ratio; NLR: neutrophil-to-lymphocyte ratio; CAT: COPD assessment test; APACHE II: Acute Physiology and Chronic Health Evaluation II.

sults revealed that PLR (OR: 15.670, 95% CI: 3.358-73.116), NLR (OR: 20.973, 95% CI: 3.719-118.284), and APACHE II score (OR: 57.469, 95% CI: 9.140-361.342) were independent risk factors for prognosis (P<0.01, **Table 4**).

Discussion

COPD, a chronic and complex disease, often has an unfavorable prognosis. Patients with COPD are prone to recurrent

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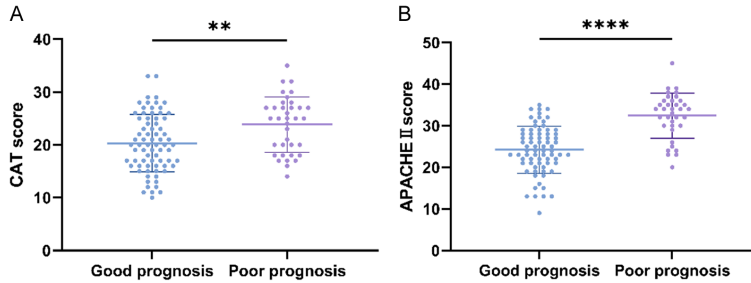


Figure 3. Comparison of CAT and APACHE II scores between patients with different prognosis. A: Comparison of CAT score between good- and poor-prognosis groups; B: Comparison of APACHE II score between good- and poor-prognosis groups. ** $P < 0.01$; **** $P < 0.0001$. CAT: COPD assessment test; APACHE II: Acute Physiology and Chronic Health Evaluation II.

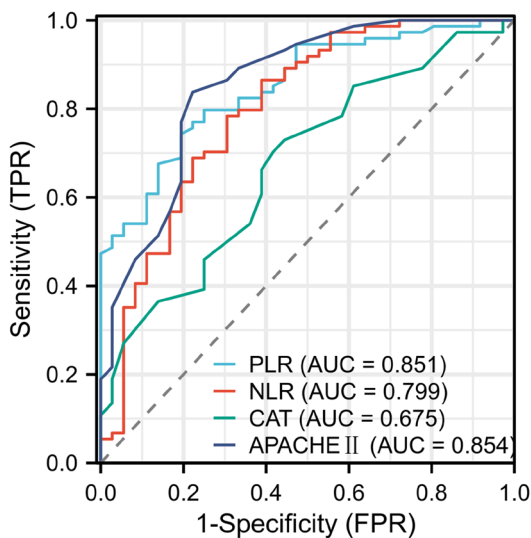


Figure 4. ROC curve of PLR, NLR, CAT score and APACHE II score in forecasting patients' prognosis. PLR: platelet-to-lymphocyte ratio; NLR: neutrophil-to-lymphocyte ratio; CAT: COPD assessment test; APACHE II: Acute Physiology and Chronic Health Evaluation II; PLT: Platelets; LYM: Lymphocytes; ROC: Receiver operating characteristic.

pulmonary infections and hypoxemia, which can trigger pulmonary arteriole spasms, increased blood flow resistance, and pulmonary vascular remodeling, ultimately leading to respiratory failure [13]. The coexistence of COPD and respiratory failure significantly increases mortality rates, emphasizing the importance of timely detection and monitoring of disease progression to improve prognosis [14]. This study analysed the correlations between PLR, NLR, and APACHE II scores with the prognosis of elderly COPD patients with respiratory failure.

APACHE II score, a widely utilized assessment tool in intensive care units, comprehensively evaluates disease severity [15]. This scoring system incorporates various physiologic data, including heart rate, blood pressure, respiratory rate, arterial oxygen saturation, and serum electrolyte levels, alongside factors like age and chronic health status [16]. It provides clinicians with a comprehensive and objective overview of patients' health status, enabling them to formulate more effective treatment plans and predict prognosis.

For elderly COPD patients with respiratory failure, APACHE II score holds particular significance. COPD, a chronic and progressive pulmonary disease, often experiences acute exacerbations that can lead to respiratory failure and further deteriorate the patient's condition [17]. Given the gradual decline in physiologic function and compromised stress and recovery abilities, these patients often face a poor prognosis. Fortunately, APACHE II score, assessed within 24 hours of admission, has been shown to be a strong predictor of prognosis in such cases [18, 19]. This allows doctors to accurately assess a patient's condition and prognosis within 24 hours of hospitalization.

Furthermore, APACHE II score exhibits high prediction accuracy. Prior research has demonstrated its excellent AUC, sensitivity, and specificity in forecasting mortality among COPD patients with respiratory failure [20, 21]. This further confirms the reliability and precision of APACHE II score in forecasting the COPD prognosis.

COPD, a multifaceted respiratory disorder, also encompasses systemic inflammatory components [22]. This inflammatory response is intimately linked to COPD's pathophysiology, acute exacerbations, prognosis, and overall severity [23]. Among the readily accessible markers of systemic inflammation NLR and PLR, derived from routine blood tests, have garnered significant attention in recent years due to their cost-effectiveness [24-26].

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Table 2. Values of ROC curves for PLR, NLR, CAT score, and APACHE II score in forecasting COPD prognosis

| Predictive variable | AUC | 95% CI | Cut-off | Sensitivity | Specificity | Youden index |
|---------------------|-------|-------------|---------|-------------|-------------|--------------|
| PLR | 0.851 | 0.780-0.921 | 2.67 | 74.32% | 80.56% | 54.88% |
| NLR | 0.799 | 0.704-0.894 | 119.11 | 78.38% | 69.44% | 47.82% |
| CAT score | 0.675 | 0.570-0.780 | 23.50 | 70.27% | 58.33% | 28.60% |
| APACHE II score | 0.854 | 0.776-0.933 | 29.50 | 83.78% | 77.78% | 61.56% |

AUC: Area under the curve; CAT: COPD assessment test; APACHE II: Acute Physiology and Chronic Health Evaluation II; PLT: Platelets; LYM: Lymphocytes; ROC: Receiver operating characteristic.

Table 3. Assignment of factors with significant difference between groups

| Factor | Assignment |
|-----------------|--|
| PLR | $<0.267 = 0, \geq 0.267 = 1$ |
| NLR | $<119.11 = 0, \geq 119.11 = 1$ |
| CAT score | $<23.50 = 0, \geq 23.50 = 1$ |
| APACHE II score | $<29.50 = 0, \geq 29.50 = 1$ |
| Prognosis | Good prognosis = 0, poor prognosis = 1 |

PLR: platelet-to-lymphocyte ratio; NLR: neutrophil-to-lymphocyte ratio; CAT: COPD assessment test; APACHE II: Acute Physiology and Chronic Health Evaluation II.

Prior studies have revealed significantly elevated levels of NLR and PLR in COPD patients compared to healthy controls [27]. Moreover, during acute exacerbations of COPD, these levels escalate further, mirroring the exacerbation of systemic inflammation in acute phases of the disease and its subsequent decline during recovery [28]. Notably, NLR and PLR correlate positively with smoking index, GOLD stage, and MMRC score, while exhibiting a negative association with FEV1%, emphasizing their relevance to COPD severity [29].

Specifically, an NLR > 2.8 has been identified as an independent predictor of respiratory-related hospitalization, underscoring its significance in COPD [29]. The current study finds that elevated NLR and PLR serve as independent prognostic risk factors for COPD patients experiencing respiratory failure. This is likely because NLR and PLR reflect the extent of systemic inflammation, which is intricately tied to the severity and prognosis of COPD. Respiratory failure, a critical indicator of COPD progression, often signifies acute worsening, increased severity, and an unfavorable prognosis. High NLR and PLR levels may indicate a more severe inflammatory response, leading to more severe respiratory failure and an unfavorable prognosis.

This study confirms PLR, NLR, and APACHE II scores as independent prognostic factors in COPD patients with respiratory failure, but has some limitations. First, the relatively small sample size of 110 cases and the narrower scope for the prediction model compromise the statistical reliability. In this retrospective design, the impact of marker level fluctuations on prognosis cannot be dynamically tracked, limiting the analysis to

quantitative findings. Furthermore, the study lacks an evaluation of the markers' correlation with pulmonary function measurements, and the specificity of the prediction model may be limited due to its reliance on only three indices. The specific mechanisms underlying elevated marker levels and the clinical significance of monitoring them in guiding treatment also remain unexplored. Finally, this was a single-center study, so the results require validation through multi-center research. Future prospective studies with a larger sample size are needed to delve deeper into the mechanisms and develop a more precise prediction model, thereby enhancing the quality of research and clarifying the clinical value of these inflammatory markers for COPD patients.

In summary, COPD, a multifaceted and chronic disease, is influenced by diverse prognostic factors. Our study provides compelling evidence that PLR, NLR, and APACHE II scores constitute independent prognostic risk factors for elderly COPD patients experiencing respiratory failure. These biomarkers provide invaluable insight into patients' systemic inflammatory status, displaying a strong correlation with disease severity and prognosis. As such, they hold promise as crucial indicators for clinicians, informing disease progression and prognosis,

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Table 4. Analysis of factors impacting patient prognosis

| Factor | β | Standard error | Chi-square value | P value | OR value | 95% CI | |
|-----------------|---------|----------------|------------------|---------|----------|-------------|-------------|
| | | | | | | Lower limit | Upper limit |
| PLR | 2.752 | 0.786 | 12.26 | <0.001 | 15.670 | 3.358 | 73.116 |
| NLR | 3.043 | 0.883 | 11.89 | 0.001 | 20.973 | 3.719 | 118.284 |
| CAT score | 1.393 | 0.731 | 3.633 | 0.057 | 4.028 | 0.961 | 16.877 |
| APACHE II score | 4.051 | 0.938 | 18.651 | <0.001 | 57.469 | 9.140 | 361.342 |

PLR: platelet-to-lymphocyte ratio; NLR: neutrophil-to-lymphocyte ratio; CAT: COPD assessment test; APACHE II: Acute Physiology and Chronic Health Evaluation II.

thus enabling more informed decisions in patient management and treatment strategies.

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Disclosure of conflict of interest

None.

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