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ORIGINAL RESEARCH

High Pan-Immune Inflammation Values are Associated with Prolonged Length of Hospital Stay in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Purpose: Inflammation is a major contributor to prolonged hospital stays, increased healthcare costs, and poor prognosis in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). This study aimed to investigate the relationship between the Pan-Immune Inflammation Value (PIV), a novel immune-inflammatory biomarker, and the prolonged hospital stays in patients hospitalized for the first time with AECOPD to provide an effective risk assessment tool for clinical practice.

Patients and Methods: We retrospectively analyzed clinical data from 5810 patients admitted to the Affiliated Dongyang Hospital of Wenzhou Medical University between January 2010 and March 2024, with AECOPD as the primary diagnosis. Prolonged hospital stay was defined as a stay exceeding the 75th percentile for all included patients (length of hospital stay > 10 days). The association between PIV and prolonged hospital stay in patients with AECOPD was assessed using multi-model logistic regression analysis, restricted cubic spline (RCS) curves, and subgroup analysis.

Results: Higher $\log_2$-PIV values were significantly associated with prolonged hospital stay in patients with AECOPD. Multivariate regression analysis revealed that $\log_2$-PIV (≥ 10.08) was an independent predictor of prolonged hospital stay (odds ratio = 1.57; 95% confidence Interval: 1.21–2.02; $P = 0.001$). Furthermore, RCS regression demonstrated a linear correlation between $\log_2$-PIV and the risk of prolonged hospital stay. Subgroup analysis confirmed the consistency of this association across different patient populations.

Conclusion: PIV is a potential biomarker for predicting prolonged hospital stay in patients hospitalized for the first time with AECOPD, providing a new assessment tool for clinical practice. The results of this study can help guide clinical decision-making, optimize treatment strategies, improve patient prognosis, and provide a scientific basis for the rational allocation of healthcare resources.

Keywords: chronic obstructive pulmonary disease, acute exacerbation, pan-immune inflammation value, prolonged hospital stay, biomarker

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory condition that can be categorized into a stable phase and an acute exacerbation phase (acute exacerbation of COPD, AECOPD) based on its clinical course. AECOPD is characterized by a sudden worsening of symptoms, requiring clinical intervention for improvement.[1] However, the high incidence of AECOPD and limited medical resources pose a significant challenge to the global healthcare system.[2–4] Given the low in-hospital mortality rate observed in this patient cohort, length of hospital stay (LHS) was selected as a more sensitive indicator of disease burden. Prolonged LHS for patients hospitalized for the first time with AECOPD correlates with higher medical costs, increased utilization of medical resources, and poorer prognosis.[5–7] Therefore, identifying effective biomarkers for recognizing high-risk patients is of critical importance.

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Several traditional biomarkers have been explored for their prognostic utility in AECOPD. For instance, C-reactive protein (CRP), fibrinogen, and white blood cell count (WBC) have been studied for their associations with disease severity and prognosis.[8,9] These markers reflect various aspects of the inflammatory response and have been shown to correlate with clinical outcomes, although their predictive power may be limited in certain contexts. Additionally, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have gained attention as potential prognostic indicators in COPD and other inflammatory diseases.[10,11] These ratios integrate information from different immune cell populations and have demonstrated some utility in predicting disease progression and treatment response.

The Pan-Immune Inflammation Value (PIV) is a novel immunoinflammatory biomarker that provides a comprehensive reflection of the body's immune and inflammatory response through integrated calculations based on the absolute counts of peripheral blood lymphocytes, neutrophils, monocytes, and platelets. In recent years, PIV has shown potential in the prognostic assessment of various diseases, including malignant tumors,[12,13] autoimmune diseases,[14] and cardiovascular diseases.[15,16]

To date, no studies have investigated the relationship between PIV and prolonged LHS in patients with AECOPD. Our study aimed to explore this association by retrospectively analyzing data from 5,810 patients hospitalized with AECOPD as the primary diagnosis, providing a scientific basis for clinical decision-making, optimizing treatment strategies, and improving patient outcomes.

Materials and Methods

Study Population

This study retrospectively analyzed the clinical data of patients admitted to the Affiliated Dongyang Hospital of Wenzhou Medical University with AECOPD as their primary diagnosis between January 2010 and March 2024. This study was approved by the Ethics Committee of Affiliated Dongyang Hospital of Wenzhou Medical University (No. 2024-YX-250). This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Because all extracted patient information was anonymous and unrelated to clinical care and treatment, patient informed consent was waived upon approval by the Ethics Committee.

COPD was diagnosed based on the ICD codes (J44.0/J44.1/J44.9). Patients with AECOPD were required to have respiratory deterioration, such as dyspnea and severe cough, within the previous 14 days.[17] Inclusion criteria included adult patients (18 years or older) admitted to the hospital for the first time with AECOPD as their primary diagnosis. Exclusion criteria included: (1) patients who had been hospitalized for less than 24 hours; (2) patients who died in the hospital; (3) patients with malignant tumors, acquired immune deficiency syndrome, or autoimmune diseases; (4) patients with acute infections other than those of the respiratory system; and (5) patients with missing absolute counts of peripheral blood lymphocytes, neutrophils, monocytes, and platelets on the first day after admission.

Data Collection

Clinical information of the patients was retrospectively collected from the hospital database. Data collected included patient demographics, such as age, sex, smoking history, drinking history, hypertension, diabetes, and coronary artery disease. Additionally, the initial clinical and laboratory data within 24 hours of admission were also gathered, including pH, PO_2, PCO_2, oxygen saturation (SO_2), blood lactate, WBC count, red blood cell (RBC) count, neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count, red blood cell distribution width (RDW), hemoglobin level, platelet count, mean corpuscular volume, hematocrit, blood urea nitrogen (BUN), creatinine, albumin, glucose, and CRP. Owing to the presence of missing values of less than 15% for smoking history, drinking history, pH, PO_2, PCO_2, SO_2, blood lactate, RDW, BUN, creatinine, albumin, glucose, and CRP, multiple imputations were used to fill in the missing values.[18]

PIV was calculated by multiplying the neutrophil (10^9/L), monocyte (10^9/L), and platelet counts (10^9/L) and dividing the result by the lymphocyte count (10^9/L), as follows:

$$PIV = \frac{\text{Neutrophil count} \times \text{Monocyte count} \times \text{Platelet count}}{\text{Lymphocyte count}}$$

The outcome of the study was prolonged LHS. Since there is currently no universally accepted definition for the appropriate LHS for patients with AECOPD, this study defined LHS as any stay exceeding the 75th percentile of all included patients, which was set as > 10 days.

Statistical Analysis

Statistical analysis and data visualization were performed using IBM SPSS (version 26.0; IBM, Armonk, NY, USA) and R software (version 4.3.2; The R Foundation, Vienna, Austria). The original PIV values exhibited a right-skewed distribution (Shapiro–Wilk test, $P < 0.001$). To satisfy the normality assumption for parametric tests, we applied base-2 logarithmic transformation (log_2-PIV) (Supplementary Figure 1). Patients were then divided into four groups based on the log_2-PIV quartiles. Continuous variables following a normal distribution were expressed as mean ± standard deviation, while skewed data were presented as median (interquartile range). Continuous variables were compared between groups using the Student's *t*-test or Mann–Whitney *U*-test. Count variables were expressed as numbers and percentages, and comparisons were made using the chi-squared or Fisher's exact test. Logistic regression was employed to analyze the binary outcome of prolonged LHS. This method was selected owing to its suitability for binary outcomes, ability to provide clinically interpretable odds ratios for risk assessment, and flexibility in handling both continuous and categorical predictor variables while adjusting for potential confounders.Three unadjusted and multivariable-adjusted logistic regression models were constructed to assess the potential association between log_2-PIV and the risk of prolonged LHS in patients with AECOPD. Model 1 was unadjusted, while Model 2 included age, sex, smoking history, drinking history, diabetes, hypertension, and coronary artery disease (CAD) as covariates. Model 3 incorporated clinical and laboratory variables based on Model 2 and established the optimal regression model using the stepwise regression method to reduce the influence of multicollinearity. Covariates included age, smoking history, diabetes, CAD, $PaCO_2$, SO_2, lactate, monocyte count, basophil count, platelet count, RDW, BUN, hematocrit, and albumin. Additionally, the relationship between log_2-PIV and prolonged LHS in patients with AECOPD was explored using the restricted cubic spline (RCS) model with adjustments based on the same variables. Subgroup analyses were conducted for the outcome event, stratified by age (≤65 and >65 years), gender (female vs male), smoking history (yes vs no), drinking history (yes vs no), diabetes (yes vs no), hypertension (yes vs no), and CAD (yes vs no), to explore the consistency of the association between log_2-PIV and the risk of prolonged LHS in the hospital in patients with AECOPD across different subgroups. To validate the robustness of our findings, we conducted sensitivity analyses by stratifying raw PIV values into quartiles (Q1–Q4) and refitting the regression models. Statistical significance was set at $P < 0.05$.

Results

Data from 7,629 patients with AECOPD as the primary diagnosis were retrospectively extracted from the hospital database. After applying the inclusion and exclusion criteria, 5,810 patients with AECOPD were analyzed in this study, including 4,198 males (72.3%) and 1.612 females (27.7%) (Figure 1). The baseline characteristics are summarized in Table 1. Among the 1,244 patients with prolonged LHS, older age was observed, and they had a lower proportion of smoking and drinking history but were more likely to have hypertension, diabetes, and cardiovascular diseases. Additionally, the log_2-PIV of patients with prolonged LHS (9.18 [8.02; 10.4]) was significantly higher than that of patients with normal LHS (8.71 [7.65; 9.98]), and there were significant differences in multiple clinical and laboratory variables.

Association Between PIV and Prolonged LHS in Patients with AECOPD

As shown in Table 2, patients were divided into four groups based on log_2-PIV quartiles (Q1: log_2-PIV <7.71; Q2: 7.71 ≤ log_2-PIV < 8.80; Q3: 8.80 ≤ log_2-PIV < 10.08; Q4: log_2-PIV ≥10.08). A significant increase in the proportion of patients with prolonged LHS was observed among those with higher log2-PIV values ($P < 0.001$).

Three logistic regression models were used to evaluate the association between log_2-PIV and prolonged LHS in patients with AECOPD (Table 3). The study found that higher log_2-PIV values were associated with an increased risk of prolonged LHS in patients with AECOPD (Model 1: Odds Ratio [OR] = 1.16, 95% Confidence Interval [CI] = 1.12–1.20, $P < 0.001$; Model 2: OR = 1.15, 95% CI = 1.11–1.19, $P < 0.001$; Model 3: OR = 1.15, 95% CI = 1.09–1.22, $P < 0.001$).

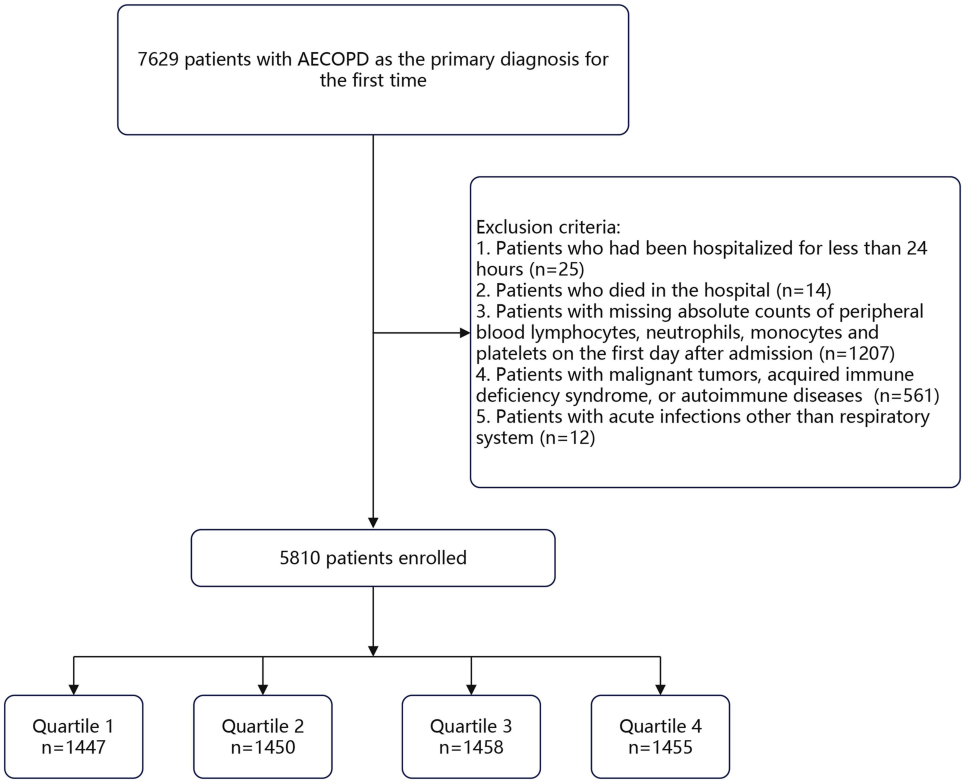

Figure 1 Flowchart of Study Population Selection.

Additionally, we analyzed the log2-PIV as a categorical variable based on quartiles. Compared to the Q1 group, patients with AECOPD in the higher log_2-PIV group (Q4) exhibited a significantly increased risk of prolonged LHS (Model 1: OR = 1.83, 95% CI = 1.53–2.19, $P < 0.001$; Model 2: OR = 1.74, 95% CI = 1.45–2.10, $P < 0.001$; Model 3: OR = 1.57, 95% CI = 1.21–2.02, $P = 0.001$).

Table 1 Baseline Demographics and Clinical Characteristics of Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease Stratified by Length of Hospital Stay

	LHS ≤ 10 days, N = 4,566	**LHS > 10 days, N = 1,244**	**P-value**
Age, years	75.0 [68.0;81.0]	78.0 [71.0;83.0]	<0.001
Sex, n (%)			0.650
Female	1,260 (27.6%)	352 (28.3%)	
Male	3,306 (72.4%)	892 (71.7%)	
Smoking history, n (%)	2,846 (62.3%)	698 (56.1%)	<0.001
Drinking history, n (%)	1,945 (42.6%)	476 (38.3%)	0.007
Comorbidities, n (%)			
Hypertension	1,988 (43.5%)	597 (48.0%)	0.006
Diabetes	465 (10.2%)	203 (16.3%)	<0.001

(*Continued*)

Table 1 (Continued).

	LHS ≤ 10 days, N = 4,566	**LHS > 10 days, N = 1,244**	**P-value**
Coronary artery disease	1,045 (22.9%)	328 (26.4%)	0.012
pH	7.41 [7.39–7.44]	7.41 [7.36–7.44]	<0.001
PaO_2, mmHg	83.8 [71.7–105]	83.3 [68.3–107]	0.049
$PaCO_2$, mmHg	40.7 [37.0–46.4]	42.4 [36.5–54.6]	<0.001
SO_2, %	96.8 [94.7–98.3]	96.4 [93.2–98.3]	<0.001
Lactate, mmol/L	1.30 [1.00–1.70]	1.50 [1.10–2.10]	<0.001
WBC, 10^9/L	7.08 [5.38–9.63]	7.88 [5.89–11.2]	<0.001
RBC, 10^{12}/L	4.32 [3.97–4.69]	4.27 [3.85–4.68]	0.002
Neutrophil count, 10^9/L	4.99 [3.48–7.52]	6.00 [4.20–8.98]	<0.001
Lymphocyte count, 10^9/L	1.16 [0.83–1.58]	0.98 [0.65–1.36]	<0.001
Monocyte count, 10^9/L	0.51 [0.37–0.70]	0.53 [0.37–0.75]	0.049
Eosinophil count, 10^9/L	0.08 [0.02–0.17]	0.05 [0.00–0.14]	<0.001
Basophil count, 10^9/L	0.02 [0.01–0.03]	0.02 [0.01–0.03]	<0.001
RDW, %	13.6 [11.3–16.1]	15.9 [12.8–16.4]	<0.001
Hemoglobin, g/L	131 [120–142]	129 [116–141]	<0.001
Platelet count, 10^9/L	198 [160–247]	187 [142–241]	<0.001
MCV, fL	92.5 [89.5–95.7]	92.8 [89.2–96.3]	0.357
Hematocrit, %	0.41 [0.37–0.45]	0.40 [0.36–0.44]	<0.001
BUN, mmol/L	5.68 [4.51–7.19]	6.30 [4.61–8.43]	<0.001
Creatinine, umol/L	69.0 [58.0–82.0]	71.0 [58.0–91.0]	<0.001
Albumin, g/L	36.8 [33.9–39.4]	35.0 [31.5–38.0]	<0.001
Glucose, mmol/L	6.18 [5.06–7.70]	6.85 [5.51–8.71]	<0.001
C-reactive protein, mg/L	13.1 [2.30–49.3]	28.0 [6.40–68.6]	<0.001
Log_2-PIV	8.71 [7.65–9.98]	9.18 [8.02–10.4]	<0.001

Abbreviations: BUN, blood urea nitrogen; LHS, Length of Hospital Stay; MCV, mean corpuscular volume; PIV: Pan-Immune Inflammation Value; RBC, red blood cell; RDW, red blood cell distribution width; SO_2, oxygen saturation; WBC, white blood cell.

Table 2 Baseline Demographics and Clinical Characteristics of Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease Grouped by Log_2-PIV Quartiles

	Q1 N=1,447	**Q2 N=1,450**	**Q3 N=1,458**	**Q4 N=1,455**	**P-value**
Log_2-PIV	<7.71	7.71–8.80	8.80–10.08	≥10.08	
LHS > 10 days	242 (16.7%)	279 (19.2%)	332 (22.8%)	391 (26.9%)	<0.001
Age, years	74.0 [67.0–80.0]	75.0 [68.0–81.0]	76.0 [68.0–82.0]	77.0 [70.0–82.0]	<0.001

(*Continued*)

Table 2 (Continued).

	Q1 N=1,447	Q2 N=1,450	Q3 N=1,458	Q4 N=1,455	P-value
Sex, n (%)					0.041
Female	442 (30.5%)	400 (27.6%)	389 (26.7%)	381 (26.2%)	
Male	1,005 (69.5%)	1,050 (72.4%)	1,069 (73.3%)	1,074 (73.8%)	
Smoking history, n (%)	843 (58.3%)	875 (60.3%)	920 (63.1%)	906 (62.3%)	0.036
Drinking history, n (%)	620 (42.8%)	604 (41.7%)	595 (40.8%)	602 (41.4%)	0.724
Comorbidities, n (%)					
Hypertension	589 (40.7%)	688 (47.4%)	644 (44.2%)	664 (45.6%)	0.002
Diabetes	140 (9.68%)	170 (11.7%)	172 (11.8%)	186 (12.8%)	0.063
Coronary artery disease	446 (30.8%)	371 (25.6%)	303 (20.8%)	253 (17.4%)	<0.001
pH	7.41 [7.39–7.43]	7.41 [7.38–7.43]	7.42 [7.38–7.44]	7.42 [7.39–7.45]	<0.001
PaO_2, mmHg	84.8 [73.4–106]	84.8 [72.3–106]	82.9 [70.2–106]	82.3 [68.9–104]	<0.001
$PaCO_2$, mmHg	41.0 [37.3–46.0]	41.3 [37.5–47.3]	41.2 [36.8–48.8]	40.3 [36.1–48.1]	0.035
SO_2, %	97.0 [95.0–98.4]	96.9 [94.9–98.4]	96.6 [94.2–98.3]	96.4 [93.8–98.2]	<0.001
Lactate, mmol/L	1.30 [1.00–1.70]	1.30 [1.00–1.80]	1.40 [1.00–1.80]	1.40 [1.10–1.90]	<0.001
WBC, 10^9/L	4.92 [4.08–5.92]	6.42 [5.37–7.43]	8.09 [6.81–9.72]	12.0 [9.52–15.3]	0.000
RBC, 10^{12}/L	4.27 [3.92–4.64]	4.32 [3.97–4.69]	4.33 [3.95–4.71]	4.31 [3.93–4.70]	0.011
Neutrophil count, 10^9/L	3.00 [2.38–3.65]	4.37 [3.65–5.26]	6.18 [5.03–7.64]	10.1 [7.68–13.3]	<0.001
Lymphocyte count, 10^9/L	1.36 [0.99–1.74]	1.24 [0.92–1.61]	1.08 [0.79–1.45]	0.85 [0.59–1.22]	<0.001
Monocyte count, 10^9/L	0.35 [0.28–0.43]	0.46 [0.37–0.56]	0.59 [0.47–0.73]	0.82 [0.62–1.05]	<0.001
Eosinophil count, 10^9/L	0.11 [0.05–0.19]	0.10 [0.04–0.20]	0.07 [0.02–0.16]	0.02 [0.00–0.09]	<0.001
Basophil count, 10^9/L	0.02 [0.01–0.03]	0.02 [0.01–0.03]	0.02 [0.01–0.03]	0.02 [0.01–0.03]	<0.001
RDW, %	14.0 [11.7–16.2]	13.5 [11.4–16.1]	15.2 [11.4–16.2]	15.6 [11.4–16.2]	0.011
Hemoglobin, g/L	131 [120–142]	132 [121–142]	131 [118–143]	129 [117–141]	<0.001
Platelet count, 10^9/L	164 [130–199]	191 [155–232]	202 [162–253]	238 [190–293]	<0.001
MCV, fL	93.2 [90.3–96.3]	92.8 [89.7–96.0]	92.5 [89.1–96.0]	91.7 [88.6–95.0]	<0.001
Hematocrit, %	0.40 [0.37–0.44]	0.41 [0.37–0.46]	0.41 [0.37–0.45]	0.40 [0.36–0.45]	0.012
BUN, mmol/L	5.60 [4.56–7.00]	5.66 [4.42–7.19]	5.77 [4.50–7.45]	6.10 [4.68–8.01]	<0.001
Creatinine, umol/L	68.0 [57.0–80.0]	69.0 [58.0–83.0]	69.0 [58.0–85.0]	70.0 [57.0–87.0]	0.005
Albumin, g/L	38.0 [35.4–40.2]	37.4 [34.9–39.9]	35.9 [33.0–38.6]	34.1 [31.0–37.0]	<0.001
Glucose, mmol/L	5.51 [4.78–7.09]	5.98 [5.02–7.55]	6.45 [5.42–8.10]	7.09 [5.85–8.80]	<0.001
C-reactive protein, mg/L	2.60 [1.00–10.4]	7.30 [1.91–25.3]	25.9 [7.50–55.5]	68.0 [29.3–124]	0.000

Abbreviations: BUN, blood urea nitrogen; LHS, Length of Hospital Stay; MCV, mean corpuscular volume; BUN, blood urea nitrogen; PIV: Pan-Immune Inflammation Value; RBC, red blood cell; RDW, red blood cell distribution width; SO_2, oxygen saturation; WBC, white blood cell.

Table 3 Logistic Regression Analysis of Log_2-PIV in Relation to the Risk of Prolonged Hospital Stay in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

	Model 1		Model 2		Model 3	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Log_2-PIV per unit increase	1.16 (1.12–1.20)	<0.001	1.15 (1.11–1.19)	<0.001	1.15 (1.09–1.22)	<0.001
Quartile*						
Q1	Ref.		Ref.		Ref.	
Q2	1.19 (0.98–1.44)	0.078	1.15 (0.95–1.40)	0.144	1.22 (1.00–1.50)	0.054
Q3	1.47 (1.22–1.77)	<0.001	1.42 (1.18–1.71)	<0.001	1.33 (1.08–1.65)	0.009
Q4	1.83 (1.53–2.19)	<0.001	1.74 (1.45–2.10)	<0.001	1.57 (1.21–2.02)	0.001

Notes: *Log_2-PIV quartile: Q1: Log_2-PIV < 7.71; Q2: 7.71 ≤ Log_2-PIV < 8.80; Q3: 8.80 ≤ Log_2-PIV < 10.08; Q4: Log_2-PIV ≥ 10.08, PIV, Pan-Immune Inflammation Value. Model 1 was unadjusted. Model 2 was adjusted for age, sex, smoking and drinking histories, diabetes mellitus, hypertension, and coronary artery disease (CAD). Model 3 was adjusted for age, smoking history, diabetes, CAD, $PaCO_2$, SO_2, lactate, monocyte count, basophil count, platelet count, red blood cell distribution width, blood urea nitrogen, hematocrit, and albumin.

RCS Regression Model

Figure 2 illustrates three RCS regression models, demonstrating a significant and linear correlation between log_2-PIV and the risk of prolonged LHS in patients with AECOPD in both unadjusted and multivariable-adjusted models. (Model 1: overall $P < 0.001$, P for nonlinearity = 0.734; Model 2: overall $P < 0.001$, P for nonlinearity = 0.557; Model 3: overall $P = 0.022$, P for nonlinearity = 0.180).

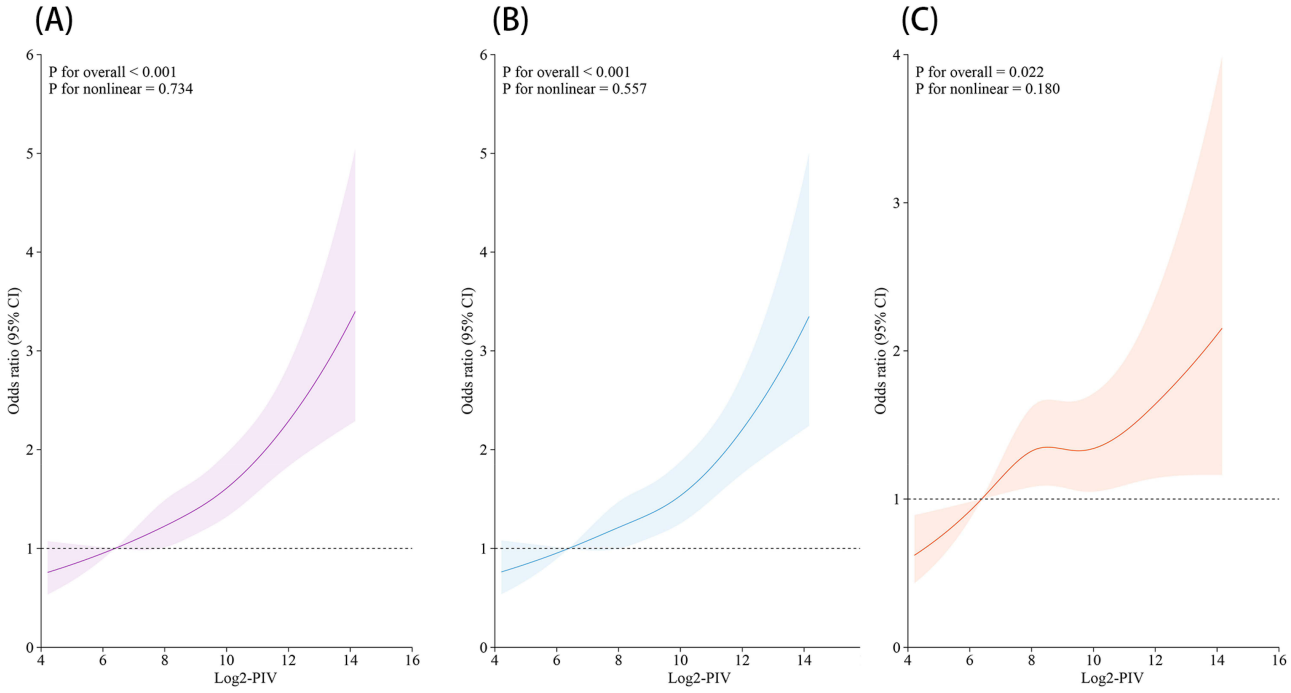

Figure 2 Association between Log_2-PIV and the Risk of Prolonged Hospital Stay in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease Fitted by restricted cubic spline curves. (**A**) Model 1 was unadjusted; (**B**) Model 2 was adjusted for age, sex, smoking history, drinking history, diabetes, hypertension, and CAD. (**C**) Model 3 was adjusted for age, smoking history, diabetes, CAD, $PaCO_2$, SO_2, lactate, monocyte count, basophil count, platelet count, red blood cell distribution width, blood urea nitrogen, hematocrit, and albumin.

Abbreviations: CAD, coronary artery disease; PIV, Pan-Immune Inflammation Value; SO_2, oxygen saturation.

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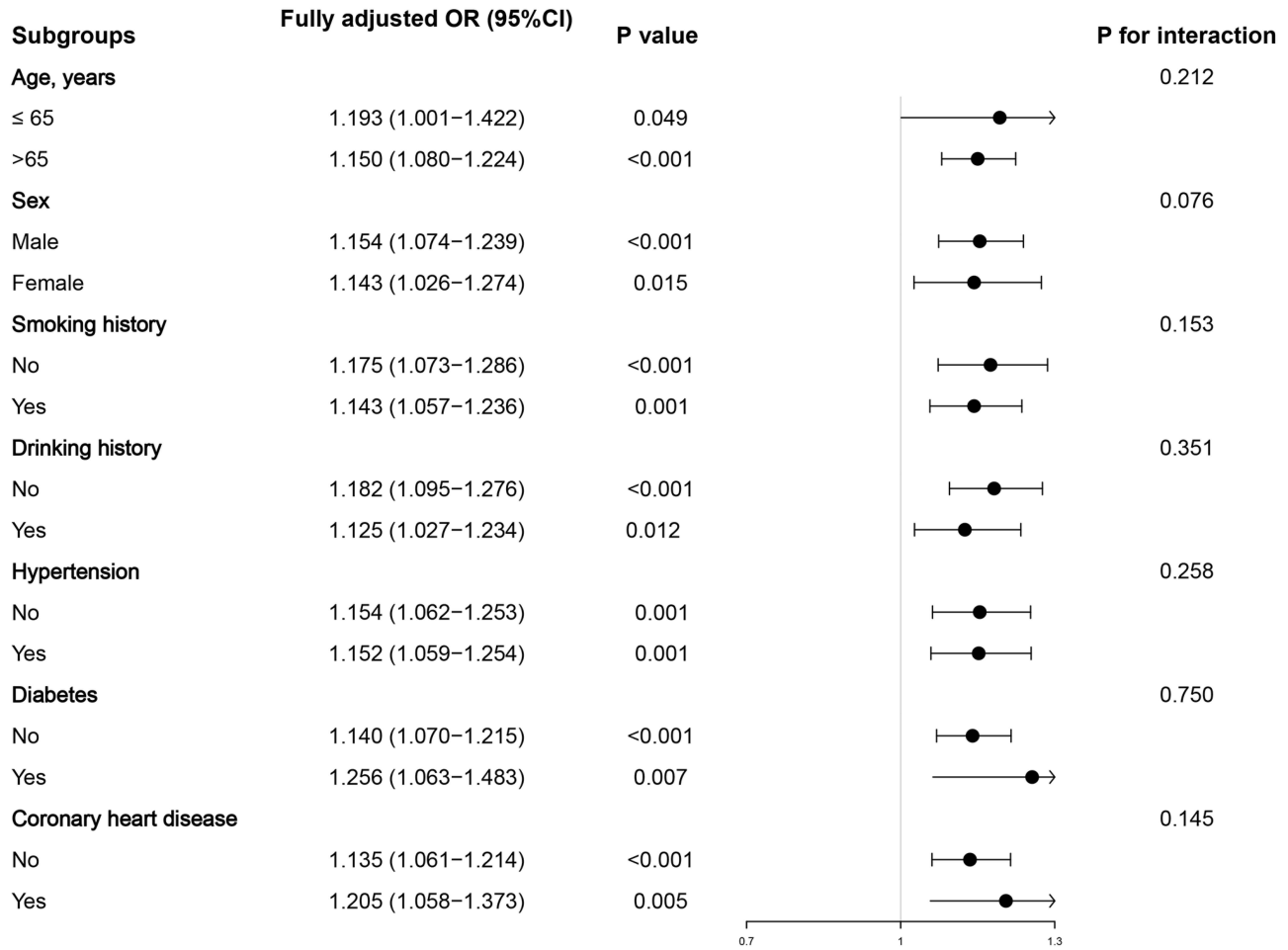

Figure 3 Subgroup Analysis of the Association between Log_2-PIV and the Risk of Prolonged Hospital Stay in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease.
Abbreviation: PIV, Pan-Immune Inflammation Value.

Subgroup Analysis

Subgroup analyses were performed based on age, sex, smoking history, drinking history, diabetes, hypertension, and CAD. Risk stratification analysis was conducted between the log_2-PIV and the risk of prolonged LHS in patients with AECOPD (Figure 3). In all subgroups, there was a consistent relationship between increased log_2-PIV and prolonged LHS in patients with AECOPD (all *P*-values < 0.05). Moreover, in the subgroup analysis, no interaction was observed between log_2-PIV and the risk of prolonged LHS in patients with AECOPD (all *P*-values for interaction > 0.05).

Sensitivity Analysis

Patients were stratified by PIV quartiles (Q1: PIV<210.1; Q2: 210.1≤ PIV < 447.5; Q3: 447.5≤ PIV < 1086.2; Q4: PIV ≥1086.2). Significance trends across the groups remained consistent (Supplementary Table 1), and logistic regression confirmed PIV's association with prolonged hospitalization, aligning with the log_2-PIV model (Supplementary Table 2).

Discussion

COPD is a common respiratory disease that often requires hospitalization. Prolonged LHS not only increases the consumption of medical resources but also impacts patient recovery and quality of life. Timely identification of the risk factors associated with prolonged LHS is crucial for optimizing clinical management. This study aimed to explore the role of PIV in prolonged LHS among patients with AECOPD through a retrospective analysis of 5,810 patients hospitalized for the first time with

AECOPD as the primary diagnosis. This is the first systematic assessment of the relationship between PIV and prolonged LHS in patients with AECOPD. Logistic regression analysis revealed that patients with AECOPD with higher PIV at admission had a significantly increased risk of prolonged LHS. Even after adjusting for other potential confounding factors, the correlation between high PIV and prolonged LHS remained significant. This finding provides clinicians with a potential biomarker and a basis for a more accurate assessment of patient risk in clinical practice.

AECOPD is strongly associated with heightened inflammatory responses, which can be triggered by multiple factors, including viral and bacterial infections, environmental pollution, smoking, and other factors.[19–21] Inflammation plays a multifaceted role in AECOPD. It is central to the pathophysiology of COPD, causing continuous damage to the airways and alveoli, which leads to airflow limitation and airway hyperreactivity.[22] Moreover, inflammation is associated with systemic complications in patients with COPD, such as cardiovascular diseases, skeletal muscle dysfunction, and metabolic syndrome.[23–25] These complications may affect the severity of AECOPD and influence the patient's recovery process. It should be particularly emphasized that, although PIV demonstrates independent predictive value, advanced age and comorbid conditions may exert synergistic effects with PIV by exacerbating systemic inflammatory responses or compromising organ compensatory capacity. Future investigations should conduct stratified analyses to evaluate the predictive performance of PIV across different age groups and specific comorbidity profiles, thereby providing more precise guidance for individualized clinical applications.

PIV is an emerging inflammatory marker that provides a novel perspective for assessing immune responses in the study of various diseases.[16,26] During AECOPD, the inflammatory response intensifies, with various inflammatory immune cells, such as neutrophils, monocytes/macrophages, and lymphocytes, participating in the immune response through both non-specific and specific immune reactions.[27–29] In inflammatory reactions, platelets can be activated by pathogens or inflammatory factors, engaging in the inflammatory process through various mechanisms, such as interaction with white blood cells and the release of inflammatory mediators. These are crucial for maintaining vascular integrity and regulating the inflammatory process.[30,31] Therefore, in the context of AECOPD, PIV may reflect an imbalance between inflammatory and anti-inflammatory immune responses, which may be associated with prolonged LHS.

Previous studies on inflammatory indicators and prognostic predictions in patients with COPD have largely focused on mortality.[32,33] However, mortality rates among patients hospitalized for the first time due to AECOPD were extremely low, making prolonged LHS a more appropriate indicator for medical resource utilizationand the overall disease burden on patients. Compared to traditional inflammatory markers,[34–36] the advantage of PIV lies in its ability to comprehensively reflect dynamic changes in various blood cells, offering clinicians a more comprehensive assessment tool. Additionally, PIV may support clinical decision-making by identifying high-risk patients early, facilitating tailored treatment strategies, optimizing resource allocation, and informing referrals for extended care, pending further validation.

Despite the strong evidence of the relationship between PIV and prolonged LHS in patients with AECOPD, this study has some limitations. First, as a retrospective study, there may have been selection and information biases. The inherent limitations of retrospective data collection can introduce variability in data quality and completeness, potentially affecting the accuracy of our findings. Second, our data were obtained from a single center, which may limit the generalizability of the findings. The specific characteristics of our patient population and institutional clinical practices may have influenced the observed associations. Future prospective multicenter studies are needed to validate these findings and further explore the role of PIV across diverse patient populations and clinical settings. Third, although our sample size was large, we did not divide the dataset into development and validation cohorts. Implementing such an approach could have strengthened validation and enhanced the robustness of our conclusions. Future studies should consider this methodology to confirm the predictive utility of PIV in broader clinical contexts.

Conclusion

This retrospective study identified a significant correlation between high PIV and prolonged LHS in patients hospitalized for the first time with AECOPD, supporting its potential role as a predictive biomarker. Future research should further explore the specific application of PIV in clinical decision-making and investigate how it can be integrated with other clinical parameters and biomarker information to optimize the management of patients with AECOPD. Furthermore, prospective multicenter studies are warranted to validate these findings and establish standardized PIV cutoff values for clinical implementation across diverse healthcare settings.

Abbreviations

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BUN, blood urea nitrogen; CAD, coronary artery disease; COPD, Chronic Obstructive Pulmonary Disease; LHS, length of hospital stay; PIV, Pan-Immune Inflammation Value; RBC, red blood cell; RCS, restricted cubic spline; RDW, red blood cell distribution width; SO_2, oxygen saturation; WBC, white blood cell.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of Affiliated Dongyang Hospital of Wenzhou Medical University (No. 2024-YX-250). As all extracted patient information was anonymous and unrelated to clinical care and treatment, informed consent from patients was waived upon approval by the Ethics Committee.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no conflicts of interest related to this work.

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