International Journal of Chronic Obstructive Pulmonary Disease Dovepress

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ORIGINAL RESEARCH

Stability of Neutrophil to Lymphocyte Ratio in Acute Exacerbation of Chronic Obstructive Pulmonary Disease and Its Relationship with Clinical Outcomes: A Retrospective Cohort Study

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Background: More studies have focused on the clinical value of the measurement of the neutrophil-to-lymphocyte ratio (NLR) in acute exacerbations of chronic obstructive pulmonary disease (AECOPD). This study aims to assess the stability of NLR in hospitalized AECOPD patients and its relationship with clinical prognosis.

Methods: This retrospective observational study recruited patients hospitalized with AECOPD from January 2020 to December 2023. Using receiver operating characteristic curves, we determined the optimal NLR cutoff, categorizing NLR stability into four groups: persistent high (NLR ≥ 3.8), increased (NLR < 3.8 at admission but ≥ 3.8 at discharge), decreased (NLR ≥ 3.8 at admission but < 3.8 at discharge), and persistent low (NLR < 3.8). Adverse hospital outcomes included hospital mortality, transfer to the intensive care unit (ICU), invasive mechanical ventilation (IMV), and length of hospital stay (LOS) ≥ 14 days. The associations between NLR stability and these outcomes were analyzed using multivariable logistic regression and Cox hazard analysis.

Results: Among 841 patients hospitalized for AECOPD, the mean age was 72.1±9.5 years, with 644 males (76.6%) and 197 females (23.4%). The proportions and distribution for groups: persistent high, decreased, increased, and persistent low groups were 109 (12.9%), 175 (20.8%), 216 (25.7%), and 341 (40.5%), respectively. The persistent high group had the worst outcomes, including higher IMV use, ICU transfer, LOS > 14 days, and hospital cost, compared to the persistent low group. Compared to the persistent high group, the persistent low group (HR: 0.13; 95% CI: 0.10–0.24) and the decreased group (HR: 0.40; 95% CI: 0.22–0.73) are statistically significant for the risk of death, while the increased group (HR: 0.63; 95% CI: 0.37–1.04) does not show a statistically significant difference.

Conclusion: AECOPD patients who have persistent low NLR group face a low risk of adverse hospital outcomes and mortality after 6 months after discharge. The stability of NLR may serve as a novel biomarker for identifying AECOPD patients at increased risk of poor hospital outcomes.

Keywords: neutrophil-to-lymphocyte ratio, acute exacerbations of chronic obstructive pulmonary disease, outcomes

Introduction

Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) closely correlates with rapid lung function decline, heightened rehospitalization rates, and increased disease-related mortality.[1] Annually, three million individuals succumb to chronic obstructive pulmonary disease (COPD),[2] with a staggering 90% of fatalities occurring in low- and middle-income nations, imposing substantial economic and healthcare burdens.[3] The etiology of AECOPD is multi-faceted, encompassing infectious agents like viruses and bacteria, alongside non-infectious triggers such as smoking and air pollution;yet the precise underlying cellular and molecular mechanisms remain elusive.[4] This prompts the search for

Received: 27 August 2024
Accepted: 7 November 2024
Published: 13 November 2024

new, easily obtainable prognostic biomarkers to facilitate early identification of AECOPD patients at risk of adverse outcomes.

Inflammation and immunity play crucial roles in the pathogenesis and progression of AECOPD. Neutrophils serve as the frontline defense against pathogens, while lymphocytes reflect the body's immune status and regulate inflammation. The ratio thereof comprehensively mirrors the body's immune-inflammatory equilibrium.[5–7] The neutrophil-lymphocyte ratio (NLR) has garnered widespread attention in recent years as a biomarker for predicting hospital outcomes and subsequent exacerbations in AECOPD patients.[8,9] Nevertheless, controversy shrouds the stability of NLR in AECOPD patients, with sole reliance on initial NLR at admission proving inadequate for accurately prognosticating clinical outcomes and prognosis. Moreover, investigations concerning the relationship between NLR stability during hospitalization for AECOPD and patient clinical outcomes remain conspicuously absent.

Hence, this study aims to further delineate the distribution of NLR stability during hospitalization for AECOPD patients and ascertain the correlation between NLR stability and in-hospital outcomes, as well as post-discharge prognosis.

Materials and Methods

Study Design and Study Population

This retrospective observational study recruited patients admitted with the primary diagnosis of AECOPD to the Department of Respiratory and Critical Care Medicine, Yanda Hospital, Hebei, China between January 2020 and December 2023. COPD had been previously diagnosed according to the GOLD guideline, including respiratory symptoms, a history of recurrent lower respiratory tract infections or a history of exposure to risk factors, and forced vital capacity maneuver during spirometry showing the presence of a post-bronchodilator forced expiratory volume in 1 second/forced vital capacity < 0.70.[10] This study was conducted according to the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Hebei Yanda Hospital (2024–07-003), and the need to obtain written informed consent was waived due to its retrospective nature. All patient data were anonymized, and strict confidentiality measures were implemented throughout the study.

Patients were included if they were aged 40 years or older and had a confirmed diagnosis of AECOPD. AECOPD was defined as an event characterized by worsening respiratory symptoms that required additional therapy.[10] The usage of systemic corticosteroids for AECOPD was defined as the administration of oral or intravenous prednisone at a dose of 40 mg per day for at least 5 days.

Exclusion criteria included other respiratory diseases, such as asthma, pulmonary embolism, bronchiectasis, or active pulmonary tuberculosis, as well as comorbidities that could affect the study outcomes, such as hematological malignancies, bone marrow or solid organ transplantation, autoimmune diseases, congenital immunodeficiency diseases, and use of immunosuppressants. For patients with AECOPD who were admitted multiple times during the study period, only the first admission was included.

Measurements and Outcomes

The clinical data were collected from the electronic medical record system at Hebei Yanda Hospital, including baseline demographics, smoking status, onset symptoms to admission time, comorbidities, and treatment in the hospital. We also collected data on vital signs and laboratory tests such as complete blood count, biochemistry, and blood gas analysis. All included patients had at least two blood measurements, with the first measurement taken within 24 hours of admission and the last measurement taken within 24 hours before discharge. Outcomes included hospital mortality, the need for invasive mechanical ventilation (IMV), length of hospital stay (LOS), intensive care unit (ICU) transfer, hospital costs, and 6 months mortality. Adverse hospital outcomes were defined as hospital mortality, ICU admission, use of IMV, and LOS > 14 days.

Based on initial and final NLR levels during hospitalization, NLR stability was classified into four groups:[1] persistent high group: both initial and final NLR above the threshold;[2] persistent low group: both initial and final NLR below the

threshold;[3] decreased group: initial NLR above, but final NLR below the threshold;[4] increased group: initial NLR below, but final NLR above the threshold.

Statistical Analyses

Categorical variables were presented as frequencies and percentages, with group comparisons performed using the chi-square test or Fisher's exact test. Continuous variables were expressed as medians (interquartile ranges, IQR) and mean (standard deviation, SD). Comparisons were performed using one-way ANOVA, the Kruskal–Wallis test, or the *t*-test as appropriate. The optimal cutoff for NLR was determined using receiver operating characteristic (ROC) curves. Covariates and clinically relevant risk factors with a univariate p-value < 0.05 were included in a multivariable logistic regression model to analyze odds ratio (OR) and confidence interval (CI) for adverse hospital outcomes. The Cox proportional hazards regression models were conducted to evaluate the hazard ratio (HR) and 95% CI between NLR stability and 6 months mortality after discharge. Statistical analyses were conducted using R software version 4.3.3, and statistical significance was set at a two-sided p-value of < 0.05.

Results

From January 2020 to December 2023, 1362 patients with AECOPD were screened for eligibility. After exclusions for readmissions, incomplete blood measurement, and concurrent conditions, 841 were eligible for inclusion (Figure 1).

This study involved 841 patients, predominantly male (76.6%). The mean age was 72.1±9.5 years, with a median of 10 days from symptom onset to hospitalization. Hypertension (46.4%), coronary artery disease (23.5%), and diabetes (18.4%) were common comorbidities.74.6% of patients were current smokers or former smokers. Treatments included antibiotics (99.0%) and expectorants (98.3%), with 71.5% receiving inhaled corticosteroids and 18.1% systemic corticosteroids. The median LOS was 12 days, with 32.2% experiencing adverse hospital outcomes (Supplementary Table 1).

Comparison of Characteristics and Outcomes Among Patients with AECOPD in Interquartile NLR

Supplementary Table 1 presents a comparative analysis of patients with AECOPD based on their NLR quartiles. Significant differences were found across NLR quartiles in age (P = 0.006), with older patients having higher NLR. Respiratory rate (RR), white blood cell (WBC), neutrophil, lymphocyte, $PaCO_2$, and lactate levels all showed significant

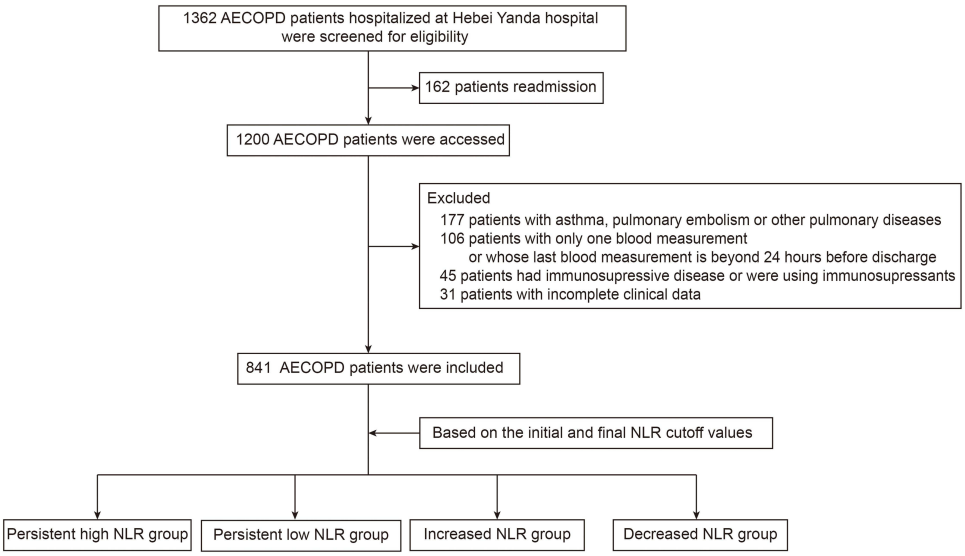

Figure 1 Study flow.
Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; NLR, neutrophil-lymphocyte ratio.

differences, with higher NLR associated with worse values ($P < 0.001$). Higher NLR quartiles had a greater incidence of exacerbations in the previous year ($P = 0.001$), higher Charlson comorbidity index scores ($P = 0.037$), and increased use of systemic corticosteroids ($P = 0.013$). Adverse hospital outcomes, such as ICU transfer, IMV, hospital mortality, and LOS > 14 days were significantly more common in patients with higher NLR ($P < 0.001$).

Multivariate Regression Analysis of Adverse Hospital Outcomes

Using a multivariate logistic model to adjust for confounding factors, results indicated that the NLR (OR: 1.41; 95% CI: 1.53–1.93), exacerbations in the previous year (OR: 1.80; 95% CI: 1.07–3.00), RR (OR:1.10; 95% CI: 1.067–1.14), $PaCO_2$ (OR: 1.14; 95% CI: 1.11–1.17), and lactate (Lac) (OR: 1.65; 95% CI: 1.29–2.12) were identified as independent risk factors for adverse hospital outcomes, as shown in Figure 2.

ROC Curve Analysis of NLR, Eosinophil, C-Reactive Protein, and PLR for Predicting Adverse Hospital Outcomes

The area under the ROC curve for NLR in predicting adverse hospital outcomes was 0.88 (0.84–0.89), with a sensitivity of 72.3%, specificity of 86.8%, Youden's index of 0.59, and an optimal cutoff value of 3.8. For C-reactive protein (CRP), the area under the ROC curve was 0.74 (0.70–0.78), with a sensitivity of 60.0%, specificity of 78.6%, and Youden's index of 0.38. Eosinophil showed an area of 0.55 (0.51–0.59) with a sensitivity of 76.8%, specificity of 30.7%, and Youden's index of 0.08. The platelet-lymphocyte ratio (PLR) had an area of 0.60 (0.56–0.64), sensitivity of 59.8%, specificity of 78.6%, Youden's index of 0.38, as shown in Supplementary Table 2 and Figure 3.

Comparison of Clinical Features of Patients with Different NLR Stability Group

The distribution of NLR at initial admission and before discharge is shown in Figure 4. Table 1 compares clinical features across patient groups based on NLR stability: persistent high group (n=109), decreased group (n=175), increased group (n=216), and persistent low group (n=341). Significant differences include older age in the persistent high group

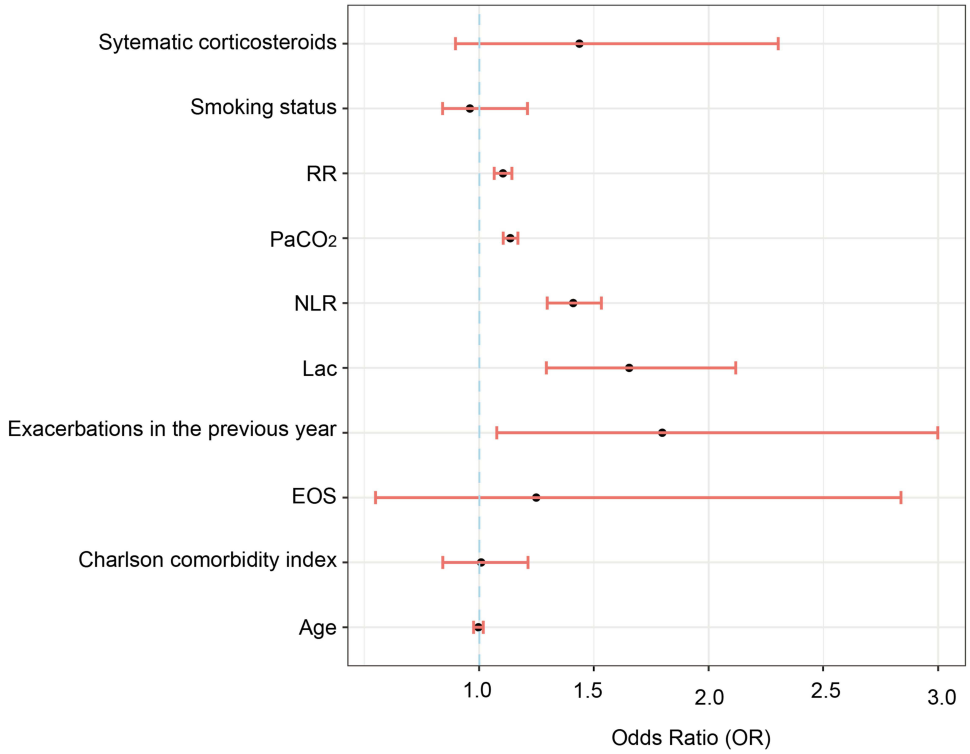

Figure 2 Multivariate regression analysis of adverse hospitalization outcomes.
Abbreviations: RR, respiratory rate; NLR, neutrophil-lymphocyte ratio; Lac, lactate; EOS, eosinophil.

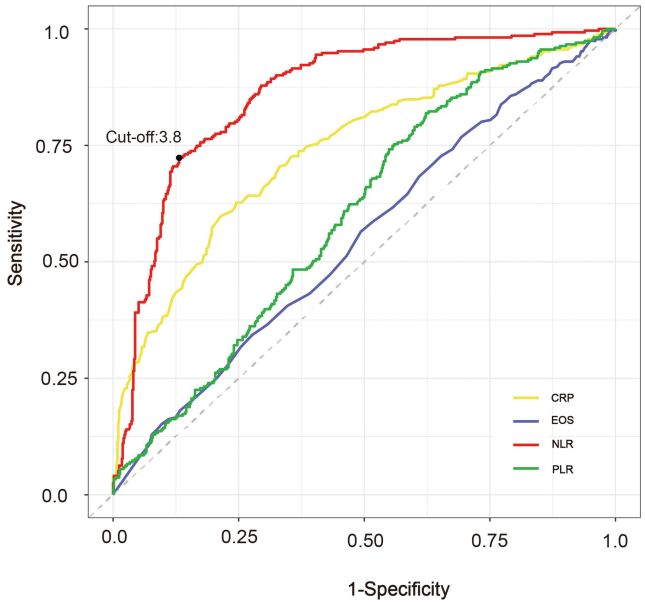

Figure 3 Predictive Efficacy of NLR, EOS, CRP, and PLR in adverse hospital outcomes.
Abbreviations: CRP, C-reactive protein; EOS, eosinophil; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio.

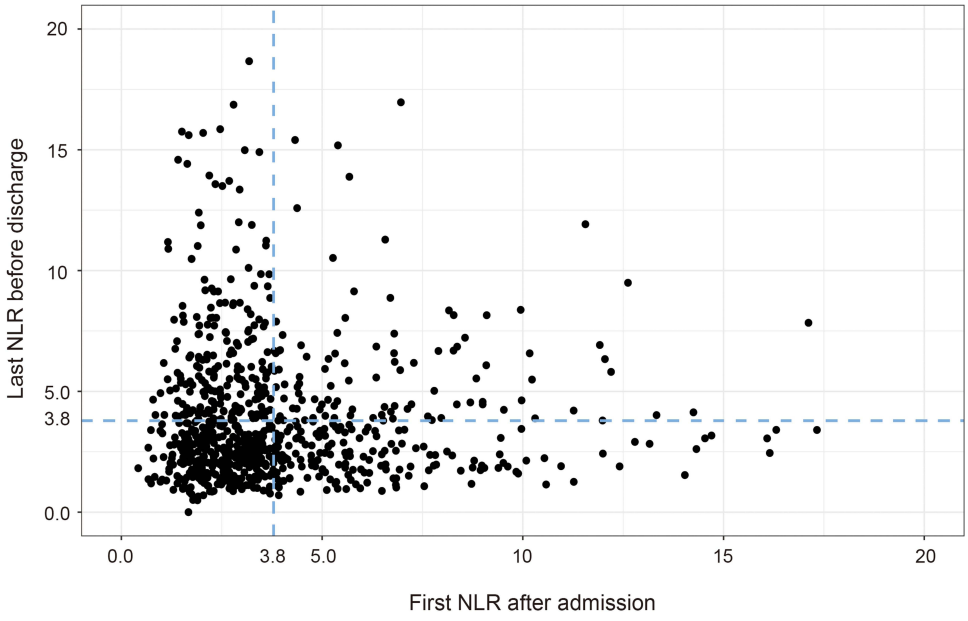

Figure 4 Distribution of first NLR after admission and last NLR before discharge.

(P = 0.008). Compared to the persistent low group, the persistent high group showed higher levels of RR, WBC, neutrophil, $PaCO_2$, and Lac, along with lower lymphocyte and eosinophil counts ($P < 0.001$). Additionally, the persistent low group had lower exacerbations in the previous year (P = 0.001). The persistent high group had the worst hospital outcomes, including higher IMV use, ICU transfer, LOS > 14 days, and hospital cost, compared to the persistent low group, as shown in Table 2.

Longitudinal Analyses

All-cause mortality occurred in 90 (10.7%) patients during 6-month follow-up. The proportions of patients and the distribution for persistent high, decreased, increased, and persistent low groups were 26 (23.9%), 18 (10.3%), 34

Table 1 Comparison of Clinical Features of Patients with Different NLR Stability Groups

Characteristics	Persistent High Group (n=109)	Decreased Group (n=175)	Increased Group (n=216)	Persistent Low Group (n=341)	*P*
Age, year, $\bar{x} \pm s$	74.2±7.1[a]	72.8±8.8[a,b]	72.1±9.7[a,b]	71.0±9.6[b]	0.008
Sex, n, (%)					0.383
Male	88(80.7)	136(77.7)	157(72.7)	263(77.1)	
Female	21(19.3)	39(22.3)	59(27.3)	78(22.9)	
Onset symptoms to admission time, day	9(7–10)	8(7–12)	6(5–10)	6(5–8)	0.068
Comorbidities, n, (%)					
Hypertension	49(45.0)	91(52.0)	95(44.0)	155(45.5)	0.403
Diabetes	17(15.6)	43(24.6)	39(18.1)	56(16.4)	0.116
Coronary heart disease	32(29.4)	45(25.7)	41(19.0)	80(23.5)	0.172
Cerebrovascular disease	17(15.6)	24(13.7)	36(16.7)	40(11.7)	0.394
Smoking status, n (%)					0.063
Non-smoke	21(19.3)	48(27.4)	67(31.0)	78(22.9)	
Former or current smoke	88(80.7)	127(72.6)	149(69.0)	263(77.1)	
Exacerbations in the previous year	27(24.7)[a]	40(22.9)[a]	25(11.6)[a]	36(10.6)[b]	0.001
Charlson comorbidity index, n (%)					0.221
0–1	43(39.4)	60(34.3)	85(39.3)	140(41.1)	
2	35(32.1)	55(31.4)	78(36.1)	110(32.3)	
3	9(8.3)	28(16.0)	30(13.9)	45(13.2)	
≥4	22(20.2)	32(18.3)	23(10.6)	46(13.5)	
Vital signs					
HR (rate/minute)	80(76–88)	82(76–90)	81(73–88)	80(73–89)	0.494
RR (rate/minute)	24(22–28)[a]	24(22–27)[a]	21(19–25)[b]	21(19–24)[b]	<0.001
SBP (mmHg)	131(120–145)	131(120–142)	132(120–140)	134(120–146)	0.568
DBP (mmHg)	75(67–82)	72(66–79)	75(70–82)	75(66–81)	0.063
Laboratory tests					
WBC ($\times 10^9$/L)	7.9(5.8–10.2)[a]	7.6(6.1–9.8)[a]	6.2(5.0–8.0)[b]	6.2(5.0–7.8)[b]	<0.001
NEU ($\times 10^9$/L)	5.8(4.1–8.2)[a]	5.8(4.3–7.7)[a]	4.0(2.9–5.2)[b]	3.8(2.9–5.1)[b]	<0.001
LYM ($\times 10^9$/L)	1.1(0.8–1.4)[a]	1.0(0.8–1.4)[a]	1.5(1.2–1.9)[b]	1.5(1.1–2.0)[b]	<0.001
EOS ($\times 10^9$/L)	0.18(0.07–0.26)[a]	0.17(0.05–0.29)[a]	0.210.14–0.35[b]	0.20(0.14–0.29)[b]	<0.001
PLT ($\times 10^9$/L)	204(159–273)	207(153–266)	213(163–258)	199(154–246)	0.193
HB (g/L)	125(105–139)	126(108–141)	127(103–141)	130(108–143)	0.507
PLR	225.8(167.2–315.4)[b]	210.1(157.6–291.8)[b]	137.3(105.2–199.2)[b]	123.8(99.1–184.1)[b]	0.000
ALB (g/L)	38.4(36.2–41.1)	36.6(34.1–39.3)	37.9(34.7–40.3)	38.0(35.1–40.4)	0.300
PH	7.40(7.38–7.43)	7.41(73.8–7.43)	7.41(7.38–7.42)	7.40(7.38–7.43)	0.601
$PaCO_2$ (mmHg)	41.7(37.3–46.5)[a]	41.0(35.9–45.3)[a]	36.4(31.8–40.3)[b]	35.8(31.9–39.9)[b]	<0.001
Lac (mmol/L)	1.5(1.2–2.0)[a]	1.6(1.3–2.0)[a]	1.3(1.0–1.8)[b]	1.5(1.2–1.8)[b]	<0.001
PFR (mmHg)	377.2(329.7–416.8)	354.1(312.1–427.8)	354.7(308.3–410.1)	357.4(314.9–408.0)	0.265
Treatment, n (%)					
Antibiotic	108(99.1)	175(100.0)	214(99.1)	336(98.5)	0.450
Expectorant	108(99.1)	173(98.8)	212(98.1)	334(97.9)	0.796
Inhaled corticosteroids	86(78.9)	148(84.6)	185(85.6)	296(85.9)	0.245
Systemic corticosteroids	23(21.1)	42(24.0)	33(15.3)	54(15.8)	0.068

Note: Different letters indicate significant differences among groups.

Abbreviations: NLR, neutrophil-lymphocyte ratio; HR, heart rate; RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood count; NEU, neutrophil; LYM, lymphocyte; EOS, eosinophil; PLT, platelet; HB, hemoglobin; PLR, platelet-lymphocyte ratio; ALB, albumin; PFR, PaO_2/FiO_2.

Table 2 NLR Stability and Clinical Outcomes in AECOPD Patients

	Persistent High Group (n=109)	Decreased Group (n=175)	Increased Group (n=216)	Persistent Low Group (n=341)	*P*
Hospital mortality	1(0.9)[a,b]	8(4.6)[a]	2(0.9)[a,b]	1(0.3)[b]	0.001
Transfer to ICU	14(12.8)[a]	18(10.3)[a]	2(0.9)[b]	5(1.5)[b]	<0.001
IMV	9(8.3)[a]	8(4.6)[a,b]	2(0.9)[b,c]	2(0.6)[c]	<0.001
LOS>14 days	72(66.1)[a]	112(64.0)[a]	28(13.0)[b]	39(11.4)[b]	<0.001
Adverse hospital outcomes	79(72.5)[a]	120(68.6)[a]	30(13.9)[b]	42(12.3)[b]	<0.001
Hospital cost	23021 (15,772–31502)[a]	21282 (16,133–30409)[a]	14086 (10,949–17666)[b]	14082 (11,153–17619)[b]	<0.001

Note: Different letters indicate significant differences among groups.
Abbreviations: NLR, neutrophil-lymphocyte ratio; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; ICU, intensive care unit; IMV, intensive mechanical ventilation; LOS, length of hospital stay.

(15.7%), and 12 (3.5%), respectively, as shown in Figure 5a. The Cox regression analysis shows that compared to the persistent high group, only the differences in the persistent low group (HR: 0.13; 95% CI: 0.10–0.24) and the decreased group (HR: 0.40; 95% CI: 0.22–0.73) are statistically significant for the risk of death, while the increased group (HR: 0.63; 95% CI: 0.37–1.04) does not show a statistically significant difference, as shown in Figure 5b.

Differential Mortality Risks After Discharge Among Subgroups

The subgroup analysis reveals that the persistent low group consistently demonstrates a significantly lower mortality risk after discharge across various subgroups compared to the persistent high group. In contrast, the decreased group had significantly lower risk specifically among younger patients (HR: 0.41; 95% CI: 0.20–0.85), non-smokers (HR: 0.43; 95% CI: 0.22–0.84), those not using systemic corticosteroids (HR: 0.41; 95% CI: 0.21–0.75) or with Charlson comorbidity index ≤ 3 (HR: 0.41; 95% CI: 0.22–0.79), as shown in Supplementary Table 3.

Discussion

This has been the first large, retrospective observational study evaluating the stability of NLR during AECOPD and its relationship to clinical outcomes. The results showed that more than 40% of patients did not maintain stable NLR levels

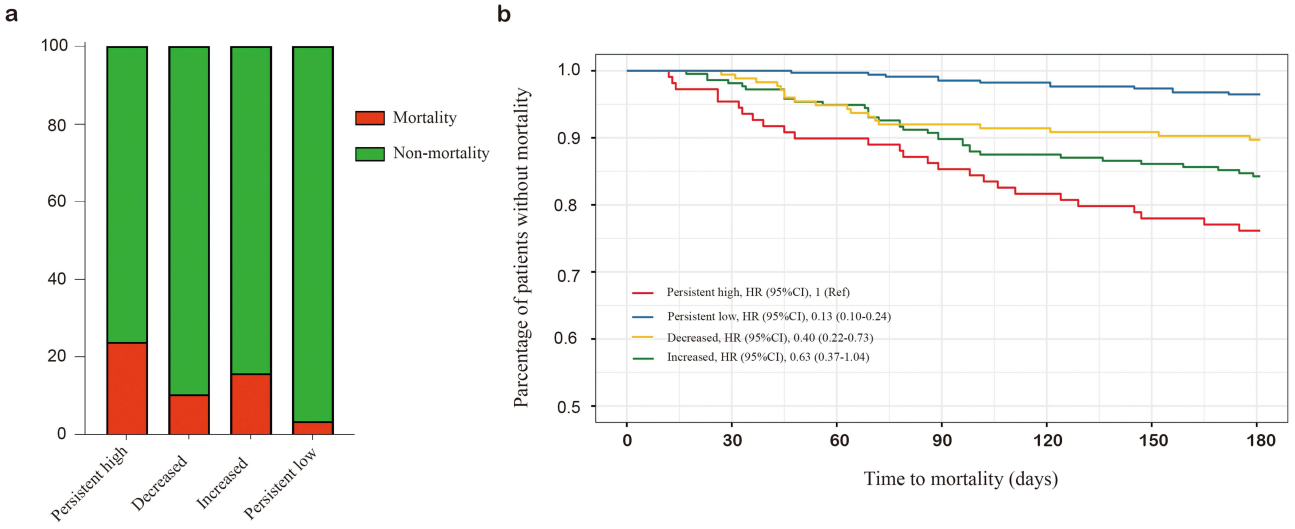

Figure 5 Survival analyses according to NLR group using Cox proportional hazards mode.
Note: (**a**) Distribution of mortality and non-mortality rates among patients with different NLR groups. (**b**) Kaplan-Meier survival curves show the time of death within 6 months after discharge for the different NLR groups.
Abbreviations: NLR, neutrophil-lymphocyte ratio; HR, hazard ratio; CI, confidence interval.

above or below 3.8 during hospitalization but instead showed increasing or decreasing trends. Compared to the persistent high group, those in the persistent low group had better clinical outcomes, including lower ICU transfer rates, lower IMV, shorter LOS, and lower total costs. Additionally, the risk of death after discharge was significantly lower in the persistent low group and decreased group, while there were no significant differences in the increased group.

AECOPD is defined as an acute worsening of symptoms such as cough, sputum production, and dyspnea compared to the patient's baseline, and is closely associated with rapid decline in lung function, increased frequency of rehospitalization, and elevated disease-related mortality.[11] The etiology of AECOPD is complex and multifactorial, involving infectious agents such as viruses and bacteria, as well as non-infectious factors such as meteorological effects and air pollution. However, the underlying cellular and molecular mechanisms remain unclear.[4] Excessive inflammatory responses and immune dysfunction play a critical role in the development and progression of COPD. Studies have shown that 70% of COPD patients have elevated levels of at least one inflammatory marker.[12] Moreover, the clinical symptoms, pulmonary function parameters, disease progression, and incidence of comorbidities in COPD patients are closely associated with the persistent elevation of these inflammatory markers.[13–15] Serum CRP, interleukin-6, interleukin-8, fibrinogen, and TNF-alpha have been extensively studied as inflammatory biomarkers in AECOPD.[15] However, more easily obtainable and interpretable inflammatory markers, such as the NLR derived from routine blood tests, have gained widespread use in the prognostic assessment of various diseases, including cardiovascular diseases,[16] infectious diseases,[17] malignancies,[18] and chronic kidney diseases.[19]

The chronic inflammatory state in COPD not only leads to neutrophil chemotaxis but also increases the production and release of inflammatory mediators. Neutrophil activation promotes the release of enzymes such as neutrophil elastase, matrix metalloproteinase-8, and myeloperoxidase, ultimately resulting in irreversible airway damage and remodeling.[20] Lymphocytes, including T lymphocytes, B lymphocytes, and NK cells, indirectly reflect the immune status of the body and play a regulatory role in the inflammatory response.[21]

In our study, after adjusting for factors such as age, smoking status, use of systemic corticosteroids, and Charlson comorbidity index, NLR was identified as an independent risk factor for adverse hospital outcomes during hospitalization. Our findings also indicate that NLR is a stronger predictor of adverse hospital outcomes.[22] Although some studies suggest that platelets play a crucial role in regulating inflammation and immune responses, with platelet P-selectin expression and subsequent platelet-leukocyte aggregate formation enhancing leukocyte pro-inflammatory functions,[23] the role of PLR in predicting patient outcomes remains controversial.[24,25] The predictive ability of PLR for AECOPD outcomes warrants further investigation.

Our determined NLR threshold level aligns with previous studies on NLR's role in predicting outcomes of AECOPD.[26] However, few studies have reported on the stability of NLR during AECOPD. In our study, using a threshold of 3.8, we categorized patients into four groups. We observed that 46.5% of patients exhibited fluctuating NLR levels during hospitalization. The persistent high group and the decreased group displayed similar clinical characteristics during their hospital stays, such as older age, higher frequency of exacerbations in the year prior to admission, faster respiratory rates, elevated levels of WBC, neutrophil, and $PaCO_2$, lower eosinophil counts, and poorer hospital outcomes. These findings are consistent with previous studies that classified patients based on a single NLR measurement post-admission.[27,28]

In addition to NLR, eosinophil counts among different patient groups also validate our findings. Previous studies have demonstrated a negative correlation between blood eosinophil counts and NLR.[29] Higher eosinophil levels are associated with shorter hospital stays, and similar findings have been observed in the analysis of hospital costs.[30,31] In our study, the persistent high group and the decreased group exhibited lower eosinophil counts, aligning with their poorer clinical outcomes. This reinforces the potential utility of NLR as an adjunct marker in assessing inflammation and predicting prognosis in AECOPD patients.

We observed that using a single NLR threshold to categorize patients did not effectively predict post-discharge outcomes. We analyzed mortality after discharge using a four-group method. Compared to the persistent high group, both the decreased and persistent low groups had better outcomes, while the increased group showed no statistical difference. This indicates that only patients with high NLR at discharge have a higher mortality risk, while those with high admission NLR but decreased discharge NLR do not. Previous studies may have overlooked this by including decreased

NLR patients in the persistent high NLR group, limiting the detection of significant associations.[32] The subgroup analysis showed that the decreased group had significantly lower mortality risk among younger patients, non-smokers, those not using systemic corticosteroids, or those with Charlson comorbidity index ≤ 3. This suggests NLR's potential as a prognostic marker in AECOPD management, with the persistent low group showing broader benefits and the decreased group showing advantages in specific subgroups.

The study's limitations include its single-center, retrospective design, which may not reflect broader populations. Additionally, the lack of follow-up on the frequency of acute exacerbations post-discharge limits the understanding of long-term outcomes. Future research should incorporate at least 12 months of follow-up to monitor exacerbation frequency. Furthermore, the elevated NLR at the hospital admission because of moderate-to-severe AECOPD may strongly depend on the etiology of AECOPD and the NLR at discharge both from the etiology of AECOPD and its response to the intervention set. NLR should be considered a simple and valuable prognostic biomarker, but limited to acute (first NLR) and short-term (last NLR) adverse events. The prognostic role of elevated NLR in stable COPD patients, as a marker of low-grade systemic inflammation, requires further definition in large, prospective, longitudinal studies with extended follow-up.[33]

Conclusion

AECOPD patients who have persistent low NLR group face a low risk of adverse hospital outcomes and mortality after 6-month after discharge. The stability of NLR may serve as a novel biomarker for identifying AECOPD patients at increased risk of poor hospital outcomes.

Abbreviation

AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; NLR, neutrophil-lymphocyte ratio; IMV, invasive mechanical ventilation; LOS, length of hospital stay; ICU, intensive care unit; IQR, interquartile ranges; SD, standard deviation; ROC, receiver operating characteristic; OR, odds ratio; CI, confidence interval; HR, hazard ratio; RR, respiratory rate; WBC, white blood cell; Lac, lactate; CRP, C-reactive protein; PLR, platelet-lymphocyte ratio.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable requests.

Ethical Approval

The study was approved by the Ethics Committee of Hebei Yanda Hospital.

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.

Funding

There is no funding to report.

Disclosure

The authors have no competing interests to declare.

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