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Article

The Role of Neutrophil-to-Lymphocyte Ratio in Predicting All-Cause Mortality and Survival Rates in Patients With Cor Pulmonale

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Abstract

Aims/Background: Cor pulmonale is characterised by right ventricular hypertrophy and dysfunction due to chronic lung disease or pulmonary vascular disease. Mortality in patients with pulmonary heart disease is influenced by a variety of factors; therefore, elucidating prognostic factors is essential to improve patient management and therapeutic strategies. The neutrophil-to-lymphocyte ratio (NLR), a marker of systemic inflammation, has been implicated in cardiovascular and pulmonary diseases. This study aims to evaluate the prognostic value of NLR in assessing all-cause mortality and survival in patients with cor pulmonale. **Methods**: We conducted a retrospective analysis of data from 6681 patients in the Medical Information Mart for Intensive Care IV database, classifying them into low and high NLR groups based on the median NLR value of 8.26. Clinical indicators, including albumin levels, kidney function, and haematological results, were compared between groups. Multivariate models were used to assess the relationship between NLR and mortality risk. Subgroup analyses were conducted to validate findings across different populations. **Results**: The high-NLR group exhibited significantly lower albumin levels, poorer kidney function, and unfavourable haematological parameters. Patients aged $\geq$65 years and those with high-risk medical histories were more prevalent in the high-NLR group. Model analysis demonstrated that elevated NLR was independently associated with increased risk of adverse outcomes, with hazard ratios of 1.58, 1.37, and 1.22 across three adjusted models. A strong correlation was observed between NLR and all-cause mortality, with a nonlinear relationship indicating a complex impact on mortality risk. Subgroup analyses confirmed the consistency of these findings across various patient subgroups. **Conclusion**: NLR is a significant prognostic marker for all-cause mortality in patients with cor pulmonale. Routine assessment of NLR may aid clinicians in risk assessments to enhance prognosis and management strategies. Further research is needed to explore the clinical utility of NLR in this population.

Keywords: cor pulmonale; neutrophil-to-lymphocyte ratio; mortality; survival rates

1. Introduction

Cor pulmonale, a condition characterised by pulmonary hypertension leading to right ventricular enlargement and failure, remains a significant clinical challenge due to its complex etiology and variable progression [1,2]. It is often secondary to chronic lung diseases, such as chronic obstructive pulmonary disease (COPD) and interstitial lung disease, which further complicate its management and prognosis [3]. Although advances have been made in understanding the pathophysiology of cor pulmonale, predicting patient outcomes remains difficult, underscoring the need for reliable prognostic indicators [4,5,6].

Current research has focused on various biomarkers and clinical parameters to enhance risk stratification and guide therapeutic decisions [7,8]. Traditional markers, such as echocardiographic measurements and pulmonary function tests, provide valuable insights but often fall short in predicting long-term outcomes [9,10]. In this context, the neutrophil-to-lymphocyte ratio (NLR)—a systemic inflammation marker—has emerged as a promising prognostic biomarker, given the pivotal role of inflammation in cardiovascular and pulmonary diseases [11,12,13]. Recent studies have shown that elevated NLR levels are associated with increased mortality and adverse clinical outcomes in various cardiovascular conditions [14,15]. Moreover, NLR is increasingly recognised for its diagnostic and prognostic relevance in lung diseases. For example, Chen et al. [16] demonstrated that NLR independently predicts long-term all-cause and cardiovascular mortality risk among patients with COPD. Similarly, Köse et al. [17] reported a positive prognostic value of NLR in patients with low-risk pulmonary embolism. However, the prognostic value of NLR in cor pulmonale has not been fully elucidated. By examining the association between NLR and clinical outcomes, we aim to determine its utility in predicting all-cause mortality and survival, with the potential to improve clinical management and patient prognosis.

2. Methods

2.1 Source of Data

This study utilised data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database (https://mimic.mit.edu), which comprises de-identified

clinical data from patients admitted to Beth Israel Deaconess Medical Center. The database includes detailed information such as demographics, laboratory results, and clinical outcomes, providing a robust analysis [18,19]. Ethical approval and informed consent were waived by Nanjing Lishui People's Hospital, as all data were obtained from publicly accessible databases. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

2.2 Study Population

Inclusion criteria: (1) patients diagnosed with cor pulmonale, as identified using International Classification of Diseases (ICD) codes; and (2) age >18 years. Exclusion criteria: patients without available neutrophil and lymphocyte count data. The primary outcome was all-cause mortality, defined as in-hospital death or death during the follow-up period. Patient survival status and survival time were ascertained from the hospital records. From 2008 to 2019, a total of 6681 patients met the inclusion criteria. Participants were divided into low and high NLR groups based on the median NLR value of 8.26.

2.3 Data Collection

The primary study variable was the NLR, defined as the ratio of the absolute neutrophil count to the absolute lymphocyte count in peripheral blood. Demographic data (age, insurance, marital status, gender), clinical history (hospital stay duration, myocardial infarct, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, rheumatic disease, diabetes, renal disease, malignant cancer, severe liver disease, ventilation status), and laboratory results were extracted from the database. Key laboratory variables included haematological variables (basophils absolute, eosinophils absolute, lymphocytes absolute, monocytes absolute, neutrophils absolute, hematocrit, hemoglobin, mean corpuscular hemoglobin [MCH], mean corpuscular hemoglobin concentration [MCHC], mean corpusular volume [MCV], platelet, red blood cell [RBC], red blood cell volume distribution width [RDW], white blood cell [WBC], albumin, globulin, total protein, aniongap, bicarbonate, blood urea nitrogen [BUN], chloride, creatinine, glucose, sodium, potassium, C-reactive protein [CRP], alanine aminotransferase [ALT], alkaline phosphatase [ALP], aspartate aminotransferase [AST], amylase, bilirubin total, bilirubin direct, bilirubin indirect, creatine kinase [CK], creatine kinase isoenzymes [CK-MB], gamma-glutamyl transpeptidase [GGT], lactate dehydrogenase [LDH], lactate, serum creatinine [SCr] baseline), blood gas analysis variables (saturation of peripheral oxygen [SpO_2], bicarbonate, sodium, potassium, creatinine, blood glucose), as well as hourly patient fluid removal, ventilation duration, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), body temperature, urine output 24-hour, glasgow coma scale (GCS). Clinical severity indicators: acute physiology score III (APS III).

2.4 Statistical Analysis

Continuous variables are expressed as mean ± standard deviation (SD) or as median (interquartile range), while categorical variables are presented as proportions. The Kolmogorov-Smirnov test was used to assess the normality of continuous parameters. If normally distributed, continuous variables were analysed using the *t*-test or one-way analysis of variance (ANOVA); if not normally distributed, the Mann-Whitney U test or Kruskal-Wallis test was applied. Categorical variables were analysed using the chi-square test or Fisher's exact test, as appropriate. To minimise bias, variables with more than 20% missing values were excluded from analysis. For variables with less than 20% missing data, multiple imputation using chained equations (MICE) was performed.

Comparative analysis of clinical indicators between the low and high NLR groups was conducted. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated to assess the impact of NLR on all-cause mortality using Cox proportional hazards models. Three models were developed to adjust for potential confounders: Model 1 (unadjusted, crude), Model 2 (adjusted for age, insurance, marital status, hospital stay duration, basophils absolute, eosinophils absolute, monocytes absolute, hematocrit, hemoglobin, MCH, MCHC, MCV, platelet, RBC, RDW, WBC, SCr baseline, and gender), Model 3 (further adjusted for age, insurance, marital status, hospital stay duration, basophils absolute, eosinophils absolute, lymphocytes absolute, monocytes absolute, hematocrit, hemoglobin, MCH, MCHC, MCV, platelet, RBC, RDW, WBC, SCr baseline, gender, myocardial infarct, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, rheumatic disease, diabetes, renal disease, malignant cancer, severe liver disease, albumin, globulin, total protein, aniongap, bicarbonate, BUN, chloride, creatinine, glucose, sodium, potassium, CRP, ALT, ALP, AST, amylase, bilirubin total, bilirubin direct, bilirubin indirect, CK, CK-MB, GGT, LDH, lactate, heart rate, SBP, DBP, MBP, temperature, SpO_2, urinary output 24 h, GCS, hourly patient fluid removal, ventilation status, ventilation duration, and calcium).

The non-linear relationship between NLR levels and all-cause mortality was assessed using restricted cubic spline (RCS) analysis with knots set at 4. Kaplan-Meier survival curves were plotted and compared using the log-rank test. Subgroup analyses were performed to explore the consistency of NLR's prognostic value across different demographic and clinical categories. Statistical significance was determined with a *p*-value threshold of <0.05.

All statistical analyses were conducted using SPSS (version 26.0; IBM Corp., Armonk, NY, USA) and R (version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria), ensuring rigorous data handling and interpretation.

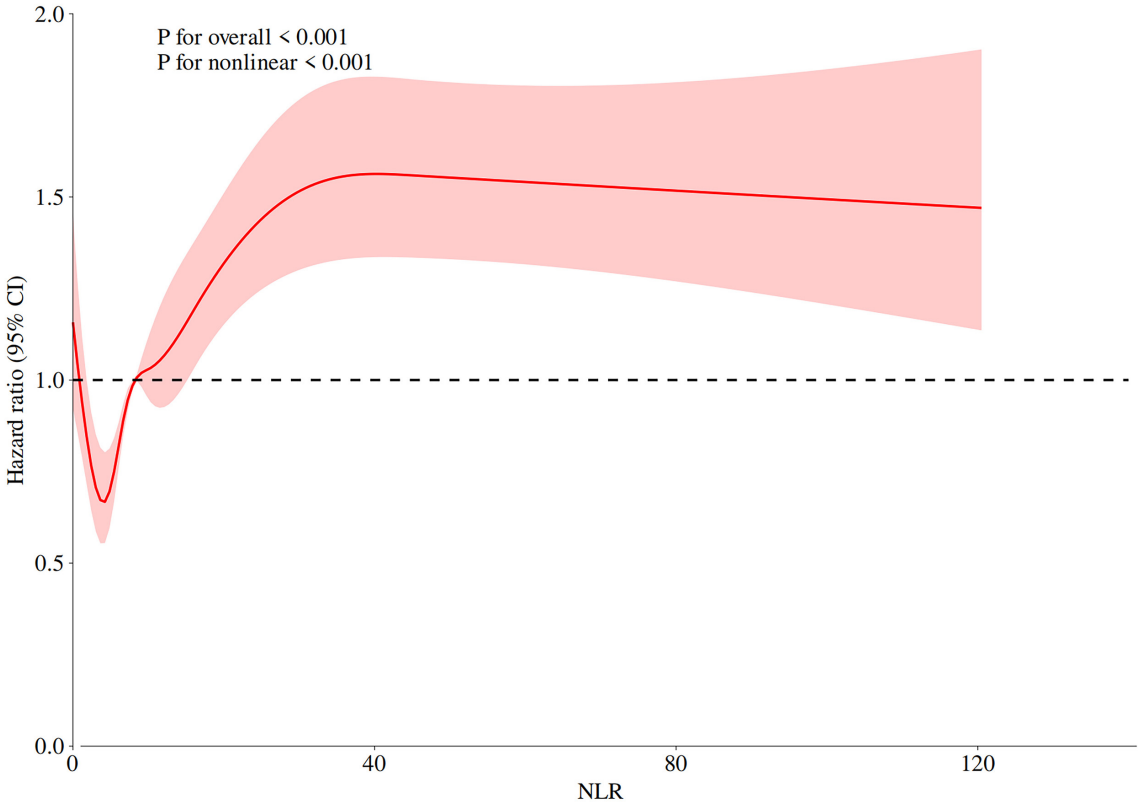

Fig. 1. Significance analysis of neutrophil-to-lymphocyte ratio (NLR) in evaluating all-cause mortality in cor pulmonale.

3. Results

3.1 Study Baseline Data

A total of 6681 patients were included in the study, with patients divided into a low NLR group (n = 3340) and a high NLR group (n = 3341) based on the median NLR value. There were 964 deaths in the high NLR group and 619 deaths in the low NLR group. Median survival time was 82.89 days in the low NLR group and 50.53 days in the high NLR group. Significant differences were observed between the two groups in albumin levels, multiple biochemical markers (including ALT, AST, and creatinine), and haematological indices (such as lymphocyte levels, platelets, and white blood cell counts) (most *p*-values < 0.001). Additionally, demographic analysis of variables such as age, insurance type, and medical history revealed a significant increase in patients aged $\geq$65 and those with high-risk histories (e.g., congestive heart failure, kidney disease) in the high NLR group (Table 1).

3.2 Model Analysis of NLR as a Prognostic Indicator

Across all models, patients in the high NLR group showed a significantly increased risk compared with those in the low NLR group (HR >1, $p < 0.001$). Specifically, the hazard ratios were 1.58 in Model 1, 1.37 in Model 2, and 1.22 in Model 3. As the models were adjusted, the risk decreased but remained significant. All three models, after adjusting for various variables, highlighted the importance of NLR as a prognostic indicator (Table 2). The results suggest that high NLR could be an effective risk predictor and highlight the need for further research into its application for clinical prognostic evaluation.

3.3 Significance Analysis of NLR in Evaluating All-Cause Mortality in Cor Pulmonale

The distribution of NLR values in the study population ranged from approximately 0 to 40, reflecting substantial inter-patient heterogeneity. Overall, as the NLR rises, the HR rises sharply and then remains flat, suggesting a significant association between elevated NLR levels and increased risk. The curve also shows that patients with very low NLR values had HRs below 1.0 compared with the reference value (NLR = 8.26), suggesting a relatively lower mortality risk at extremely low NLR levels. The study demonstrated a highly significant overall correlation between NLR and all-cause mortality in patients with cor pulmonale, with a *p*-value < 0.001. Furthermore, the *p*-value for the nonlinear relationship was also <0.001, suggesting that the relationship between all-cause mortality and NLR at different levels of NLR is nonlinear, possibly indicating that changes in NLR do not have a linear impact on mortality. These results emphasise the importance of the NLR in assessing all-cause mortality in patients with cor pulmonale. The significant *p*-values and nonlinear relationship suggest that clinicians should carefully monitor NLR changes and their potential impact on patient prognosis during risk assessment (Fig. 1).

Table 1. Demographic characteristics of the two groups.

Variables	Total (n = 6681)	Low NLR group (n = 3340)	High NLR group (n = 3341)	Statistic	*p*
Age, n (%)				$\chi^2 = 34.73$	<0.001
<65	3156 (47.24)	1698 (50.84)	1458 (43.64)		
≥65	3525 (52.76)	1642 (49.16)	1883 (56.36)		
Insurance, n (%)				$\chi^2 = 27.09$	<0.001
Medicaid	525 (7.86)	304 (9.10)	221 (6.61)		
Medicare	3044 (45.56)	1431 (42.84)	1613 (48.28)		
Other	3112 (46.58)	1605 (48.05)	1507 (45.11)		
Marital status, n (%)				$\chi^2 = 5.62$	0.132
Divorced	577 (8.64)	293 (8.77)	284 (8.50)		
Married	3190 (47.75)	1582 (47.37)	1608 (48.13)		
Single	2140 (32.03)	1103 (33.02)	1037 (31.04)		
Widowed	774 (11.59)	362 (10.84)	412 (12.33)		
Gender, n (%)				$\chi^2 = 0.02$	0.893
Female	2823 (42.25)	1414 (42.34)	1409 (42.17)		
Male	3858 (57.75)	1926 (57.66)	1932 (57.83)		
Hospital stay duration, [day, median (interquartile range)]	16.37 (9.73–27.59)	15.87 (9.48–27.75)	16.83 (9.89–27.36)	Z = 1.23	0.219
Basophils absolute, [$\times 10^9$/L, median (interquartile range)]	0.02 (0–0.04)	0.02 (0–0.04)	0.01 (0–0.04)	Z = 9.56	<0.001
Eosinophils absolute, [$\times 10^9$/L, median (interquartile range)]	0.05 (0–0.17)	0.1 (0.02–0.22)	0.02 (0–0.14)	Z = 18.59	<0.001
Lymphocytes absolute, [$\times 10^9$/L, median (interquartile range)]	0.89 (0.53–1.40)	1.42 (0.94–2.09)	0.72 (0.45–1.09)	Z = 38.97	<0.001
Monocytes absolute, [$\times 10^9$/L, median (interquartile range)]	0.58 (0.32–0.95)	0.52 (0.29–0.85)	0.61 (0.33–1.01)	Z = 7.95	0.047
Neutrophils absolute, [$\times 10^9$/L, median (interquartile range)]	10.08 (6.17–14.87)	6.17 (3.62–9.15)	12.33 (8.57–17.20)	Z = 42.62	<0.001
Hematocrit, [%, median (interquartile range)]	30.40 (26.30–35.30)	30.20 (26.00–35.10)	30.50 (26.40–35.40)	Z = 1.94	0.052
Hemoglobin, [g/dL, median (interquartile range)]	9.90 (8.50–11.50)	9.90 (8.50–11.50)	9.90 (8.50–11.50)	Z = 0.67	0.498
MCH, [pg, median (interquartile range)]	30.00 (28.30–31.70)	30.20 (28.40–31.80)	30.00 (28.20–31.60)	Z = 2.80	0.005
MCHC, [g/dL, median (interquartile range)]	32.70 (31.50–33.80)	32.80 (31.70–33.90)	32.60 (31.50–33.70)	Z = 4.80	<0.001
MCV, [fL, median (interquartile range)]	92.0 (87.0–96.0)	91.0 (87.0–96.0)	92.0 (87.0–96.0)	Z = 0.35	0.726
Platelet, [$\times 10^9$/L, median (interquartile range)]	182.0 (115.0–263.0)	168.0 (104.0–240.75)	189.0 (121.0–273.0)	Z = 8.64	<0.001
RBC, [$\times 10^{12}$/L, median (interquartile range)]	3.34 (2.85–3.91)	3.33 (2.81–3.89)	3.34 (2.88–3.91)	Z = 1.53	0.125
RDW, [%, median (interquartile range)]	15.50 (14.10–17.50)	15.30 (13.90–17.20)	15.60 (14.20–17.50)	Z = 4.81	<0.001
WBC, [$\times 10^9$/L, median (interquartile range)]	11.20 (7.50–16.20)	8.80 (5.80–17.20)	12.60 (8.60–17.60)	Z = 24.02	<0.001
SCr baseline, [mg/dL, median (interquartile range)]	0.78 (0.50–1.02)	0.70 (0.50–1.00)	0.80 (0.50–1.0)	Z = 4.58	<0.001
Albumin, [g/dL, median (interquartile range)]	2.90 (2.50–3.40)	3.0 (2.60–3.50)	2.80 (2.40–3.30)	Z = 11.42	<0.001
Globulin, [g/dL, mean ± SD]	2.51 ± 0.87	2.54 ± 0.89	2.48 ± 0.86	$t = 2.87$	0.004
Total protein, [g/dL, median (interquartile range)]	5.50 (4.90–6.10)	5.70 (5.0–6.30)	5.40 (4.80–6.10)	Z = 8.03	<0.001
Anion gap, [mEq/L, median (interquartile range)]	15.0 (12.0–18.0)	14.0 (12.0–17.0)	15.0 (12.0–18.0)	Z = 9.94	<0.001

Table 1. Continued.

Variables	Total (n = 6681)	Low NLR group (n = 3340)	High NLR group (n = 3341)	Statistic	*p*
Bicarbonate, [mmol/L, median (interquartile range)]	23.0 (20.0–26.0)	24.0 (21.0–27.0)	23.0 (19.0–26.0)	Z = 7.42	<0.001
BUN, [mg/dL, median (interquartile range)]	25.0 (16.0–43.0)	22.0 (14.0–35.0)	27.0 (17.0–46.0)	Z = 12.85	<0.001
Chloride, [mmol/L, median (interquartile range)]	103.0 (98.0–107.0)	103.0 (99.0–107.0)	102.0 (98.0–107.0)	Z = 3.63	<0.001
Creatinine, [mg/dL, median (interquartile range)]	1.20 (0.80–2.0)	1.0 (0.70–1.67)	1.20 (0.80–2.10)	Z = 9.24	<0.001
Glucose, [mg/dL, median (interquartile range)]	126.0 (102.0–164.0)	122.0 (100.0–158.0)	128.0 (103.0–166.0)	Z = 3.65	<0.001
Sodium, [mmol/L, mean ± SD]	137.94 ± 5.52	138.20 ± 5.44	137.67 ± 5.60	t = 3.96	<0.001
Potassium, [mmol/L, mean ± SD]	4.19 ± 0.74	4.15 ± 0.72	4.22 ± 0.76	t = –3.97	<0.001
CRP, [mg/L, median (interquartile range)]	82.80 (34.80–161.70)	70.80 (23.90–146.90)	90.60 (38.30–171.40)	Z = 8.86	<0.001
ALT, [U/L, median (interquartile range)]	28.0 (16.0–61.0)	26.0 (15.0–51.0)	29.0 (16.5–67.0)	Z = 5.54	<0.001
ALP, [U/L, median (interquartile range)]	91.0 (64.0–144.0)	85.0 (62.0–127.0)	95.0 (66.0–152.0)	Z = 7.69	<0.001
AST, [U/L, median (interquartile range)]	40.0 (23.0–89.0)	37.0 (22.0–75.0)	42.0 (24.0–66.0)	Z = 5.27	<0.001
Amylase, [U/L, median (interquartile range)]	54.0 (33.0–103.0)	52.0 (33.0–89.75)	56.0 (34.0–110.0)	Z = 4.54	<0.001
Bilirubin total, [mg/dL, median (interquartile range)]	0.7 (0.4–1.5)	0.6 (0.4–1.3)	0.7 (0.4–1.7)	Z = 4.44	<0.001
Bilirubin direct, [mg/dL, median (interquartile range)]	1.1 (0.4–2.5)	0.9 (0.3–2.2)	1.2 (0.4–2.7)	Z = 6.85	<0.001
Bilirubin indirect, [mg/dL, median (interquartile range)]	0.7 (0.3–1.4)	0.7 (0.3–1.3)	0.7 (0.3–1.4)	Z = 0.98	0.364
CK, [U/L, median (interquartile range)]	95.0 (39.0–314.0)	92.0 (38.0–304.0)	96.0 (40.0–316.0)	Z = 0.87	0.381
CK-MB, [U/L, median (interquartile range)]	3.0 (2.0–7.0)	3.0 (2.0–7.0)	4.0 (2.0–8.0)	Z = 3.97	<0.001
GGT, [U/L, median (interquartile range)]	165.0 (66.0–396.0)	155.0 (66.0–382.0)	166.0 (66.0–400.0)	Z = 1.72	0.085
LDH, [U/L, median (interquartile range)]	291.0 (214.0–436.0)	272.0 (205.0–401.0)	303.0 (220.0–460.0)	Z = 7.63	<0.001
Lactate, [mmol/L, median (interquartile range)]	1.7 (1.2–2.7)	1.6 (1.1–2.5)	1.8 (1.2–2.8)	Z = 6.97	<0.001
APS III, [point, median (interquartile range)]	63.0 (46.0–85.0)	57.0 (41.0–79.0)	66.0 (49.0–88.0)	Z = 12.18	<0.001
Heart rate, [beats/min, median (interquartile range)]	95.0 (82.0–111.0)	93.0 (80.0–109.0)	96.0 (83.0–111.0)	Z = 3.81	<0.001
SBP, [mmHg, mean ± SD]	120.20 ± 24.40	121.06 ± 24.01	119.35 ± 24.77	t = 2.87	0.004
DBP, [mmHg, median (interquartile range)]	66.0 (55.0–78.0)	66.0 (56.0–78.0)	65.0 (55.0–78.0)	Z = 1.70	0.088
MBP, [mmHg, median (interquartile range)]	81.0 (69.0–93.0)	81.0 (71.0–93.0)	80.0 (69.0–93.0)	Z = 2.00	0.045
Temperature, [°C, mean ± SD]	36.80 ± 0.92	36.78 ± 0.91	36.81 ± 0.93	t = –1.48	0.139
SpO_2, [%, mean ± SD]	96.84 ± 3.87	97.03 ± 3.74	96.66 ± 4.00	t = 3.87	<0.001
Urinary output 24 h, [mL, median (interquartile range)]	125.0 (50.0–275.0)	150.0 (60.0–300.0)	125.0 (50.0–250.0)	Z = 5.16	<0.001
GCS, [point, median (interquartile range)]	15.0 (15.0–15.0)	15.0 (15.0–15.0)	15.0 (15.0–15.0)	Z = 1.13	0.257
Hourly patient fluid removal, [mL, median (interquartile range)]	100.0 (0–280.0)	100.0 (0–280.0)	100.0 (0–270.0)	Z = 0.91	0.362
Ventilation duration, [days, median (interquartile range)]	11.0 (5.0–25.25)	10.13 (5.0–23.87)	11.0 (5.0–27.0)	Z = 2.20	0.027
Calcium, [mmol/L, median (interquartile range)]	1.10 (1.04–1.16)	1.11 (1.05–1.16)	1.10 (1.03–1.16)	Z = 4.83	<0.001
NLR, median (interquartile range)	10.95 (6.17–18.76)	4.44 (2.81–6.17)	15.36 (10.94–24.43)	Z = 70.78	<0.001
Myocardial infarct, n (%)				χ^2 = 0.33	0.565
No	5348 (80.05)	2683 (80.33)	2665 (79.77)		
Yes	1333 (19.95)	657 (19.67)	676 (20.23)		

Table 1. Continued.

Variables	Total (n = 6681)	Low NLR group (n = 3340)	High NLR group (n = 3341)	Statistic	*p*
Congestive heart failure, n (%)				$\chi^2 = 20.02$	<0.001
No	4135 (61.89)	2156 (64.55)	1979 (59.23)		
Yes	2546 (38.11)	1184 (35.45)	1362 (40.77)		
Cerebrovascular disease, n (%)				$\chi^2 = 5.11$	0.024
No	5813 (87.01)	2875 (86.08)	2938 (87.94)		
Yes	868 (12.99)	465 (13.92)	403 (12.06)		
Chronic pulmonary disease, n (%)				$\chi^2 = 6.53$	0.011
No	4750 (71.10)	2422 (72.51)	2328 (69.68)		
Yes	1931 (28.90)	918 (27.49)	1013 (30.32)		
Rheumatic disease, n (%)				$\chi^2 = 19.57$	<0.001
No	6405 (95.87)	3238 (96.95)	3167 (94.79)		
Yes	276 (4.13)	102 (3.05)	174 (5.21)		
Diabetes, n (%)				$\chi^2 = 0.18$	0.667
No	5010 (74.99)	2497 (74.76)	2513 (75.21)		
Yes	1671 (25.01)	843 (25.24)	828 (24.79)		
Renal disease, n (%)				$\chi^2 = 33.27$	<0.001
No	4780 (71.55)	2496 (74.73)	2284 (68.36)		
Yes	1901 (28.45)	844 (25.27)	1057 (31.64)		
Malignant cancer, n (%)				$\chi^2 = 0.53$	0.467
No	5277 (78.99)	2626 (78.62)	2651 (79.35)		
Yes	1404 (21.01)	714 (21.38)	690 (20.65)		
Severe liver disease, n (%)				$\chi^2 = 0.86$	0.355
No	5856 (87.65)	2940 (88.02)	2916 (87.28)		
Yes	825 (12.35)	400 (11.98)	425 (12.72)		
Ventilation status, n (%)				$\chi^2 = 13.55$	0.009
High-flow oxygen therapy	253 (3.79)	116 (3.47)	137 (4.10)		
Invasive ventilation	2160 (32.33)	1101 (32.96)	1059 (31.70)		
Non-invasive ventilation	185 (2.77)	78 (2.34)	107 (3.20)		
Oxygen therapy	3982 (59.60)	2007 (60.09)	1975 (59.11)		
Tracheostomy	101 (1.51)	38 (1.14)	63 (1.89)		

MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RBC, red blood cell; BUN, blood urea nitrogen; RDW, red blood cell volume distribution width; WBC, white blood cell; SCr, serum creatinine; CRP, C-reactive protein; ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; CK, creatine kinase; CK-MB, creatine kinase isoenzymes; GGT, gamma-glutamyl transpeptidase; LDH, lactate dehydrogenase; APS III, acute physiology score III; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; SpO_2, saturation of peripheral oxygen; GCS, glasgow coma scale; NLR, neutrophil-to-lymphocyte ratio; SD, standard deviation.

Table 2. Model analysis of NLR as a prognostic indicator.

Variables	Model 1		Model 2		Model 3	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
NLR median						
Low	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
High	1.58 (1.42–1.74)	<0.001	1.37 (1.24–1.52)	<0.001	1.22 (1.09–1.35)	<0.001

HR, hazard ratio; CI, confidence interval.

Model 1: unadjusted, crude;

Model 2: adjust for age, insurance, marital status, hospital stay duration, basophils absolute, eosinophils absolute, monocytes absolute, hematocrit, hemoglobin, MCH, MCHC, MCV, platelet, RBC, RDW, WBC, SCr baseline, gender;

Model 3: further adjust for age, insurance, marital status, hospital stay duration, basophils absolute, eosinophils absolute, monocytes absolute, hematocrit, hemoglobin, MCH, MCHC, MCV, platelet, RBC, RDW, WBC, SCr baseline, gender, myocardial infarct, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, rheumatic disease, diabetes, renal disease, malignantcancer, severe liver disease, albumin, globulin, total protein, aniongap, bicarbonate, BUN, chloride, creatinine, glucose, sodium, potassium, CRP, ALT, ALP, AST, amylase, bilirubin total, bilirubin direct, bilirubin indirect, CK, CK-MB, GGT, LDH, lactate, heart rate, SBP, DBP, MBP, temperature, SpO_2, urinary output 24 h, GCS, hourly patient fluid removal, ventilation status, ventilation duration, calcium.

3.4 Changes in NLR Levels are Significantly Correlated With Patient Survival Rates

Changes in NLR levels are significantly correlated with patient survival rates. Survival analysis comparing the low NLR group (L) and high NLR group (H) revealed that patients in the high NLR group had a hazard ratio (HR) of 1.58 (95% confidence interval [CI]: 1.42–1.74; $p < 0.001$), demonstrating a significantly increased risk of mortality compared to the low NLR group. These results highlight the importance of NLR in predicting patient survival rates and suggest that clinicians should consider NLR levels when assessing patient prognosis (Fig. 2).

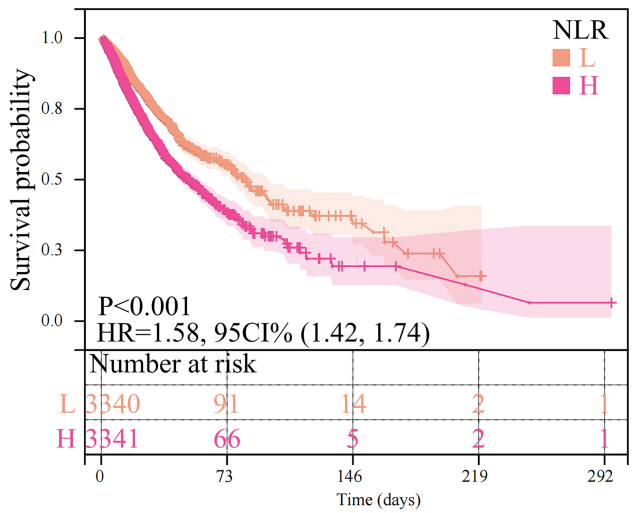

Fig. 2. Changes in NLR levels are significantly correlated with patient survival rates. H, high NLR group; L, low NLR group.

3.5 Subgroup Analysis

Subgroup analyses were conducted based on age, gender, insurance status, marital status, and comorbid conditions. Across all subgroups, patients in the high NLR group had a significantly higher risk of mortality compared with those in the low NLR group, consistent with the overall findings (Fig. 3). No significant interactions between subgroups were observed ($p > 0.05$), indicating that the prognostic value of NLR was robust across different patient populations.

4. Discussion

This study highlights the significant prognostic value of the NLR in patients with cor pulmonale, utilising data from the comprehensive MIMIC-IV database. Our findings indicate that a high NLR is associated with increased all-cause mortality, reinforcing its potential as a reliable biomarker for risk stratification.

The association between elevated NLR and adverse outcomes may be attributed to the role of systemic inflammation in cor pulmonale. Inflammatory states result in increased neutrophil counts and a relative decrease in lymphocytes, thereby increasing the NLR. Increased neutrophils release a large number of inflammatory mediators, such as interleukin-1 and tumour necrosis factor-α, which further exacerbate the inflammatory response, damaging cardiomyocytes and affecting cardiac function. At the same time, inflammation promotes platelet aggregation, increasing the risk of thrombosis and affecting blood circulation to the lungs and heart. In addition, persistent inflammation and stress can lead to metabolic disorders and impaired immune function, increasing vulnerability to infections and other complications, thereby increasing the risk of death [20,21,22]. Thus, NLR, as a marker of inflammation, pro-

Variables	n (%)	High	Low	HR (95%CI)	P	P for interaction
		No. of events/ No. of total				
All patients	6681 (100.00)	964/3341	619/3340	0.63 (0.57 ~ 0.70)	<0.001	
Age						0.802
<65	3156 (47.24)	351/1458	255/1698	0.64 (0.55 ~ 0.75)	<0.001	
⩾65	3525 (52.76)	613/1883	364/1642	0.66 (0.58 ~ 0.75)	<0.001	
Gender						0.181
Fmale	2823 (42.25)	417/1409	300/1414	0.68 (0.59 ~ 0.79)	<0.001	
Male	3858 (57.75)	547/1932	319/1926	0.60 (0.52 ~ 0.68)	<0.001	
Insurance						0.604
Medicaid	525 (7.86)	52/221	50/304	0.71 (0.48 ~ 1.05)	0.089	
Medicare	3044 (45.56)	508/1613	296/1431	0.68 (0.59 ~ 0.78)	<0.001	
Other	3112 (46.58)	404/1507	273/1605	0.61 (0.53 ~ 0.71)	<0.001	
Marital Status						0.175
DIVORCED	577 (8.64)	84/284	54/293	0.59 (0.42 ~ 0.84)	0.003	
MARRIED	3190 (47.75)	469/1608	298/1582	0.62 (0.54 ~ 0.72)	<0.001	
SINGLE	2140 (32.03)	282/1037	177/1103	0.59 (0.49 ~ 0.72)	<0.001	
WIDOWED	774 (11.59)	129/412	90/362	0.85 (0.65 ~ 1.12)	0.242	
Congestive Heart Failure						0.531
No	4135 (61.89)	561/1979	389/2156	0.65 (0.57 ~ 0.74)	<0.001	
Yes	2546 (38.11)	403/1362	230/1184	0.61 (0.51 ~ 0.71)	<0.001	
Cerebrovascular Disease						0.869
No	5813 (87.01)	827/2938	514/2875	0.64 (0.57 ~ 0.71)	<0.001	
Yes	868 (12.99)	137/403	105/465	0.60 (0.46 ~ 0.78)	<0.001	
Chronic Pulmonary Disease						0.442
No	4750 (71.10)	691/2328	449/2422	0.62 (0.55 ~ 0.70)	<0.001	
Yes	1931 (28.90)	273/1013	170/918	0.68 (0.56 ~ 0.82)	<0.001	
Rheumatic Disease						0.257
No	6405 (95.87)	919/3167	597/3238	0.63 (0.57 ~ 0.69)	<0.001	
Yes	276 (4.13)	45/174	22/102	0.88 (0.53 ~ 1.46)	0.609	
Diabetes						0.389
No	5010 (74.99)	722/2513	459/2497	0.62 (0.55 ~ 0.70)	<0.001	
Yes	1671 (25.01)	242/828	160/843	0.68 (0.56 ~ 0.83)	<0.001	
Renal Disease						0.791
No	4780 (71.55)	627/2284	448/2496	0.64 (0.57 ~ 0.73)	<0.001	
Yes	1901 (28.45)	337/1057	171/844	0.63 (0.52 ~ 0.75)	<0.001	
Malignant Cancer						0.055
No	5277 (78.99)	710/2651	389/2626	0.58 (0.51 ~ 0.66)	<0.001	
Yes	1404 (21.01)	254/690	230/714	0.72 (0.60 ~ 0.86)	<0.001	
Severe Liver Disease						0.524
No	5856 (87.65)	792/2916	510/2940	0.62 (0.56 ~ 0.70)	<0.001	
Yes	825 (12.35)	172/425	109/400	0.69 (0.54 ~ 0.87)	0.002	

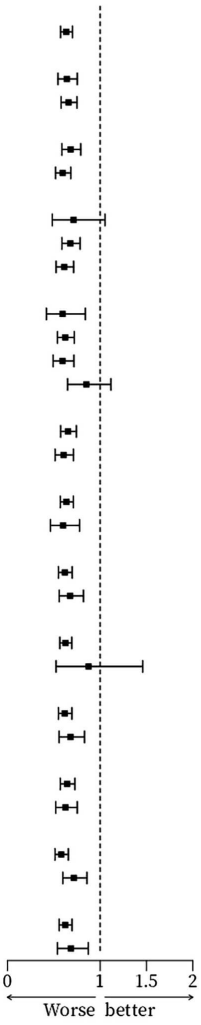

Fig. 3. Subgroup analysis.

vides valuable insights into disease severity and progression.

Previous studies have suggested that NLR may be a useful indicator of disease severity in patients with pulmonary hypertension [23,24]. Our analysis demonstrated consistent results across various models, even after adjusting for confounding variables such as age, gender, and comorbidities. This robustness underscores the independent prognostic significance of NLR. Furthermore, subgroup analyses confirmed that the relationship between high NLR and increased mortality risk persists across different demographic and clinical categories, underscoring its broad applicability. Consistent with our findings, Wu et al. [25] reported that elevated NLR was independently associated with increased all-cause mortality in patients with heart failure.

The nonlinear relationship between NLR levels and mortality highlights the complexity of its clinical impact, indicating that changes in NLR may not uniformly affect outcomes. This finding suggests that clinicians should consider NLR as part of a comprehensive assessment, integrating it with other clinical parameters to enhance prognostic accuracy. A study showed that the New Early Warning Score (NEWS) in combination with the NLR is a better predictor of 30-day mortality in elderly patients with pneumonia [26].

Beyond cor pulmonale, NLR has demonstrated prognostic utility in various diseases. In cardiovascular diseases such as myocardial infarction and heart failure, elevated NLR has been linked to worse outcomes due to its reflection of underlying inflammatory states [27,28,29,30]. Similarly, in oncology, high NLR is associated with poorer prognosis in several cancers, including colorectal and lung cancer, likely reflecting tumour-related inflammation and immune response dysregulation. In infectious diseases such as sepsis, NLR serves as a marker of systemic inflammation and correlates with disease severity and mortality [20,31].

Despite these insights, the study has limitations. Its retrospective design may introduce selection bias, and reliance on a single-center database limits external validity and generalizability. Additionally, only all-cause mortality was analysed, with no examination of long-term prognostic

outcomes, which may introduce bias. Future prospective studies are warranted to validate these findings and explore the mechanisms underlying the NLR-mortality relationship in cor pulmonale.

5. Conclusion

This study supports the integration of the NLR into clinical practice as a valuable tool for prognostic assessment in patients with cor pulmonale. By enhancing risk stratification, NLR may facilitate the tailoring of management strategies and ultimately improve patient outcomes.

Key Points

• The association between elevated NLR and adverse clinical features and comorbidities may be attributed to systemic inflammation.

• NLR may serve as a robust and promising prognostic indicator in cor pulmonale.

• A nonlinear relationship is present between varying NLR levels and all-cause mortality in cor pulmonale.

• In clinical practice, NLR should be monitored dynamically and assessed alongside other clinical indicators to improve prognosis.

Availability of Data and Materials

This study utilised data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database (https://mimic.mit.edu). All data included in this study are available from the corresponding author upon reasonable request.

Author Contributions

JJL designed the research study and wrote the first draft. XLL performed the research. JJL and XLL analysed the data. Both authors contributed to revising the manuscript critically for important intellectual content. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Ethical approval and informed consent were waived by Nanjing Lishui People's Hospital as all data were obtained from publicly accessible databases. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

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Conflicts of Interest

The authors declare no conflicts of interest.

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