Combined Predictive Value of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio for In-Hospital Mortality Risk in Patients with Acute Myocardial Infarction: A Propensity Score-Matched Retrospective Cohort Study [Postprint]

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Abstract

Background Previous studies have demonstrated that the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) possess significant predictive value for cardiovascular diseases. However, no research has yet explored whether the combination of NLR and PLR can enhance their predictive value for in-hospital mortality risk in patients with acute myocardial infarction (AMI).

Objective To investigate whether a combined predictive model (NLR+PLR) constructed using logistic regression algorithm can enhance the predictive value for in-hospital mortality risk in patients with AMI.

Methods This study is a single-center, retrospective cohort study. A total of 3246 AMI patients with complete medical records who were hospitalized in the Department of Cardiology, the Second Affiliated Hospital of Dalian Medical University from December 2015 to December 2021 were included. The outcome was defined as all-cause death during hospitalization.

Results (1) Based on propensity score matching (PSM), patients who died during hospitalization were matched at a 1:1 ratio. All deceased patients were successfully matched, resulting in 115 pairs. There was no statistically significant difference in the 20 covariates included in the matching between patients who died during hospitalization (N=115) and those who did not (N=115) ($P > 0.05$). (2) The ability of NLR+PLR (NLR combined with PLR) to predict in-hospital mortality risk (AUC=0.754) was superior to that of NLR alone (AUC=0.731)

and PLR alone (AUC=0.577), with statistically significant differences in the area under the ROC curve (P = 0.037 and P < 0.001, respectively). (3) The optimal cutoff value for NLR+PLR was 0.5491 (Youden' s index = 0.4087, sensitivity = 85.22%, specificity = 55.65%). Cox regression analysis showed that patients with NLR + PLR > 0.549 had a higher mortality risk (HR2.936; 95%CI 1.963–4.392; P < 0.001) than those with NLR + PLR ≤ 0.549. (4) The predictive ability of NLR + PLR for in-hospital mortality risk in patients with ST-segment elevation myocardial infarction (STEMI) (AUC = 0.797) was higher than that for patients with non-ST-segment elevation myocardial infarction (NSTEMI) (AUC = 0.739).

Conclusion In this retrospective cohort study, we adjusted for multiple risk factors affecting in-hospital mortality in AMI patients through propensity score matching. Our findings indicate that, compared with NLR or PLR alone, the combination of NLR and PLR can better predict the risk of in-hospital death in AMI patients, particularly demonstrating superior efficacy in STEMI patients.

Full Text

Combined Predictive Value of Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio for In-Hospital Mortality Risk in Acute Myocardial Infarction Patients: A Propensity Score-Matched Retrospective Cohort Study

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Abstract

Background: Studies have demonstrated that neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) hold important predictive value for cardiovascular diseases. However, no research has investigated whether combining NLR and PLR can enhance their predictive value for in-hospital mortality in patients with acute myocardial infarction (AMI).

Objective: To investigate whether a combined predictive model (NLR + PLR) constructed using logistic regression algorithm can improve the prediction of in-hospital mortality risk in AMI patients.

Methods: This single-center retrospective cohort study included 3,246 AMI patients with complete medical records admitted to the Department of Cardiology at the Second Affiliated Hospital of Dalian Medical University between December 2015 and December 2021. The outcome was defined as all-cause mortality during hospitalization.

Results: (1) Using propensity score matching (PSM) at a 1:1 ratio, all deceased patients were successfully matched, yielding 115 matched pairs. No statistically significant differences existed between the deceased (N=115) and non-deceased (N=115) groups across the 20 covariates included in the matching (P>0.05). (2) NLR + PLR (combined NLR and PLR) demonstrated superior predictive ability for in-hospital mortality risk (AUC=0.754) compared to NLR alone (AUC=0.731) and PLR alone (AUC=0.577), with statistically significant differences in area under the ROC curve (P=0.037 and P<0.001, respectively). (3) The optimal cutoff value for NLR + PLR was 0.5491 (Youden index=0.4087, sensitivity=85.22%, specificity=55.65%). Cox regression analysis revealed that patients with NLR + PLR>0.549 had higher mortality risk (HR=2.936; 95%CI 1.963-4.392; P<0.001) than those with NLR + PLR$ $0.549. (4) NLR + PLR showed greater predictive ability for in-hospital mortality risk in ST-segment elevation myocardial infarction (STEMI) patients (AUC=0.797) than in non-ST-segment elevation myocardial infarction (NSTEMI) patients (AUC=0.739).

Conclusions: In this retrospective cohort study, we adjusted for multiple risk factors affecting in-hospital mortality in AMI patients through propensity score matching. Our findings suggest that NLR combined with PLR can better predict in-hospital mortality risk in AMI patients compared to either marker alone, particularly in STEMI patients.

Keywords: Combined predictive value; Acute myocardial infarction; Propensity score matching; Neutrophil to lymphocyte ratio; Platelet to lymphocyte ratio

Introduction

Acute myocardial infarction (AMI) represents the most critical emergency event in cardiovascular disease. Although percutaneous coronary intervention (PCI) techniques and stent materials have advanced considerably, resulting in generally optimistic prognoses for most AMI patients after admission, some patients still experience adverse outcomes following emergency intervention. Previous research has characterized AMI by plaque instability and vulnerability, with acute events triggered by unstable plaque rupture considered the leading cause of death in coronary artery disease patients [1]. Pathological features of vulnerable plaques include thin-cap fibroatheroma (TCFA $ $65 m), large lipid pools, vascular inflammation (macrophage/monocyte infiltration), intimal erosion with plaque rupture and hemorrhage, and platelet aggregation [2,3].

Inflammatory response is inseparable from coronary plaque rupture. Most AMI patients present with risk factors such as hypertension and hypercholesterolemia that enhance systemic inflammatory responses [4-10], thereby destabilizing coronary plaques and substantially increasing the risk of acute coronary events. Consequently, there is an urgent need to identify novel inflammatory markers that accurately reflect the current inflammatory status of AMI patients to better assess their risk of acute coronary events.

NLR and PLR have attracted considerable attention in recent years. While platelets, neutrophils, and lymphocytes are individually unstable and susceptible to physiological conditions, their ratios (PLR and NLR) are more reliable and can reflect systemic inflammatory status [11,12]. Multiple studies have demonstrated associations between NLR and PLR with risk stratification and poor prognosis in acute coronary syndrome (ACS) patients [13-15]. However, few studies have investigated the short-term prognostic value of combined NLR and PLR as a joint predictive indicator in AMI patients. Therefore, this study aimed to evaluate risk factors for in-hospital mortality in AMI patients based on propensity score matching and explore the value of combined NLR and PLR in short-term prognosis.

Methods

Data Collection

This study included 3,246 AMI patients with complete medical records admitted to our hospital' s Department of Cardiology between December 2015 and December 2021. Data were extracted from the hospital' s medical record management system after de-identifying patient names, admission numbers, and other identifying information. The primary outcome was defined as all-cause mortality during hospitalization. After PSM, 115 matched pairs were generated. Detailed baseline characteristics before and after matching are presented in Table 1 . This retrospective observational cohort study complied with the ethical principles of the Declaration of Helsinki after de-identification of personal information without patient intervention.

Inclusion Criteria: Patients meeting diagnostic criteria for acute coronary syndrome, including both STEMI and NSTEMI.

Exclusion Criteria: (1) Incomplete medical record data in the electronic system; (2) Patients with severe diseases (e.g., advanced malignancies) with life expectancy less than six months; (3) Patients with hematological disorders; (4) Patients who recently received chemotherapy and/or radiotherapy.

Propensity Score Matching

We calculated propensity scores for all patients included in the analysis, incorporating 20 covariates into the propensity score calculation. A 1:1 matching

method based on these scores was used to pair deceased and non-deceased patients. The caliper value was set at 0.03. Multiple methods were employed to assess baseline differences between the matched groups. The 20 covariates included sex, age, BMI, ACS type, employment status, education level, diabetes, serum sodium, serum potassium, total cholesterol, triglyceride levels, apolipoprotein ratio, serum albumin, glycated hemoglobin, blood pressure classification, heart failure, estimated glomerular filtration rate, and in-hospital use of statins, aspirin, and angiotensin-converting enzyme inhibitors (ACEI).

Statistical Analysis

Data were processed using SPSS 23.0, MedCalc 15.0, and R 4.2.1. Categorical variables were described as frequencies or percentages. Continuous variables were expressed as mean ± standard deviation if normally distributed; otherwise, as median with interquartile range [median (25th percentile, 75th percentile)]. Group comparisons for continuous variables used t-tests or ANOVA for normal distributions and nonparametric tests otherwise. Categorical variable comparisons employed Fisher' s exact test or chi-square test. Logistic regression analysis determined hazard ratios (HR) for blood cell variables. Receiver operating characteristic (ROC) curve analysis identified cutoff values and compared predictive abilities across different indicators. A combined predictive model was constructed using logistic regression, with its predictive value assessed by calculating the area under the ROC curve. The DeLong method compared areas under different ROC curves. Missing data not exceeding 20% were imputed using multiple imputation.

Baseline characteristic balance was evaluated using absolute standardized mean difference (SMD), with <10% considered nonsignificant [16-18]. Kernel density plots illustrated propensity score distribution changes before and after matching. The Kaplan-Meier method estimated cumulative risk of endpoint events between deceased and non-deceased groups. $P<0.05$ was considered statistically significant.

Results

Baseline Characteristics Before and After Matching

Before matching, baseline data differed significantly between AMI patients who died during hospitalization and those who survived. We calculated propensity scores for 20 major covariates affecting in-hospital mortality and applied 1:1 matching to eliminate intergroup differences. Results showed significant pre-matching differences in sex, age, BMI, employment status, cardiac and renal function, serum electrolyte levels, and therapeutic medications, which were eliminated after matching. Even for covariates without pre-matching differences (education level, blood pressure classification, and AMI type), the distribution

proportions became more balanced between groups after matching, as shown in Table 1 .

Covariate Balance Assessment After Propensity Score Matching

After propensity score matching, 115 matched pairs were created. The caliper value was set at 0.03. We used kernel density plots and standardized mean difference (SMD) to demonstrate differences in the 20 covariates between deceased and non-deceased groups before and after matching, as shown in Figure 1 [Figure 1: see original paper] and Figure 2 [Figure 2: see original paper].

Figure 1 displays propensity score distributions for deceased versus non-deceased AMI patients. In the overall population, deceased patients had substantially higher propensity scores, while in the matched population, propensity scores were nearly identically distributed.

Figure 2 presents absolute standardized differences. Given baseline variable differences between deceased and non-deceased groups, propensity score methods were used to balance baseline characteristics. Importantly, after matching, most intergroup standardized differences were <10%. Variables included: sex (0=female, 1=male), AMI type (1=NSTEMI, 2=STEMI), occupation (0=retired, 1=employed), education (0=compulsory, 1=secondary, 2=university), diabetes mellitus (0=no, 1=yes), triglycerides (TG), low-density lipoprotein cholesterol (LDLC), apolipoprotein A/B ratio (AB ratio), albumin (ALB), glycated hemoglobin (HbA1C), hypertension classification (0=normal, 1=stage 1, 2=stage 2, 3=stage 3), heart failure (HF) (0=no, 1=yes), estimated glomerular filtration rate (eGFR) categories (0=>60, 1=30-60, 2=<30), ACEI use, aspirin use, and statin use (0=no, 1=yes).

Predictive Value of NLR + PLR, NLR, and PLR for In-Hospital Mortality in AMI Patients

ROC curve analysis revealed an AUC of 0.754 for NLR + PLR, 0.731 for NLR alone, and 0.577 for PLR alone. Optimal cutoff values were determined using the Youden index from ROC results. At the threshold of 0.5491, NLR + PLR achieved optimal sensitivity (55.70%) and specificity (85.22%), as shown in Table 2 and Figure 3 [Figure 3: see original paper]. AUC comparisons among NLR + PLR, NLR, and PLR demonstrated significant differences, as presented in Table 3 .

High NLR + PLR as a Significant Predictor of Cumulative In-Hospital Mortality Risk in AMI Patients

Univariate Cox regression showed that patients with NLR + PLR>0.5491 had higher mortality risk (HR=2.936; 95%CI 1.963–4.392; P<0.001). Similarly, patients with NLR>6.495 had higher mortality risk (HR=2.216; 95%CI 1.510–3.254; P<0.001), and patients with PLR>178.9855 had higher cumulative mor-

tality risk (HR=1.638; 95%CI 1.106-2.426; P=0.013), as illustrated in Figure 4 [Figure 4: see original paper].

Superior Predictive Ability of NLR + PLR in STEMI Versus NSTEMI Patients

To better evaluate the predictive value of NLR + PLR for in-hospital mortality risk across MI subtypes, we stratified patients into NSTEMI and STEMI groups. ROC analysis showed that NLR + PLR achieved an AUC of 0.797 in STEMI patients (specificity=85.42%, sensitivity=68.29%), superior to NLR or PLR alone. In NSTEMI patients, NLR + PLR yielded an AUC of 0.739 (specificity=82.09%, sensitivity=54.05%), with no statistically significant difference between NLR + PLR and NLR alone (P=0.275). These findings indicate that NLR + PLR demonstrates superior predictive ability for in-hospital mortality risk in STEMI patients compared to NSTEMI patients, as shown in Table 4 and Figure 5 [Figure 5: see original paper].

Discussion

In this retrospective study of 3,246 AMI patients, we evaluated the predictive value of combined NLR and PLR for in-hospital mortality risk using propensity score matching. We found that NLR + PLR demonstrated superior predictive ability for in-hospital mortality risk in AMI patients compared to either marker alone. Furthermore, NLR + PLR showed better performance in predicting in-hospital mortality risk in STEMI patients than in NSTEMI patients, with no significant predictive advantage over NLR alone in NSTEMI patients (AUC_{NLR}+PLR 0.739 vs. AUC_{NLR} 0.720, P=0.274). Finally, using the NLR + PLR cutoff value (NLR + PLR>0.5491) to reclassify patients, we found that AMI patients in the high NLR + PLR group had 2.93 times higher in-hospital mortality risk than those in the low NLR + PLR group.

NLR and PLR have garnered increasing attention in cardiovascular disease research due to their low measurement cost and convenient calculation. Although neutrophils, lymphocytes, and platelets are readily available from routine blood tests, they are susceptible to various physiological conditions, whereas NLR and PLR are relatively stable [19], contributing to their research interest. Atherosclerosis development is inseparable from inflammatory activation and sustained responses. Metabolic stimuli and inflammatory reactions cause significant neutrophil proliferation during coronary atherosclerotic plaque formation. Excessive neutrophil production promotes atherosclerosis progression, and neutrophil apoptotic fragments participate in lipid pool formation, promoting thin-cap fibroatheroma development [20]. Consequently, neutrophils are closely associated with atherosclerosis development and AMI occurrence. Lymphocytes participate in inflammatory regulation and decrease in count during AMI due to redistribution. Moreover, higher neutrophil counts and lower lymphocyte

counts indicate greater inflammatory and stress levels with more severe myocardial injury [21,22]. In our study, deceased patients had higher neutrophil counts and significantly lower lymphocyte counts than survivors, suggesting stronger inflammatory and stress responses in fatal AMI cases.

Although previous studies have validated NLR' s value in predicting in-hospital mortality in AMI patients [13], such events are often multifactorial, involving age, sex, blood pressure, and hepatic/renal function, which can affect NLR' s predictive value. Our study balanced multiple confounding factors—including sex, age, BMI, hepatic/renal function, in-hospital medications, and lipid levels—between deceased and non-deceased AMI patients using propensity score matching. After matching, no differences remained in these indicators. Even for blood pressure stratification variables without significant pre-matching differences, post-matching distributions became more balanced across blood pressure categories. Following propensity score matching, NLR and PLR remained significant predictors of in-hospital mortality risk, though PLR was significantly weaker than NLR, consistent with previous findings [14,23]. We therefore hypothesized that combined NLR + PLR might outperform either marker alone in predicting in-hospital mortality risk. Our results confirmed that NLR + PLR is more powerful than NLR or PLR alone for predicting in-hospital mortality risk in AMI patients, with high NLR + PLR representing a risk factor for in-hospital death. Using propensity score matching, we achieved balanced baseline data between matched groups, validated through multiple methods including histograms, kernel density plots, and chi-square tests. This provides evidence for NLR + PLR as a predictive indicator for in-hospital mortality risk in AMI patients.

This study also incorporated education level and retirement status data. Nearly 90% of our cohort was retired with limited economic income, often facing greater life and psychological stress. Previous research indicates that low socioeconomic status, life stress, and pressure increase vascular inflammatory responses and cardiovascular event risk through the following mechanism: lower socioeconomic status → increased amygdala metabolic activity → increased leukopoietic activity → arterial inflammation → cardiovascular events [24,25].

This study has several limitations. First, we could not observe long-term prognosis, limiting assessment of NLR + PLR' s predictive value for long-term mortality risk in AMI patients. Second, some critically ill patients died before routine testing, preventing acquisition of their clinical baseline data and reducing our sample size.

In conclusion, NLR + PLR demonstrates good predictive ability for in-hospital mortality risk in AMI patients, particularly showing superior performance in STEMI patients.

Author Contributions

CHEN Yan, LÜ Zhibo, XU Qing, CHEN Shengyue, and HAN Yuanyuan were responsible for data collection and organization. CHEN Yan and CHEN Shengyue contributed to study conception, statistical analysis, and manuscript writing. ZHAO Xin provided overall quality control for the manuscript.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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