

## Platelet-to-Lymphocyte Ratio Predicts In-Hospital Mortality Risk in Elderly Patients with Acute Myocardial Infarction (Postprint)

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### Abstract

**Background** Previous studies have demonstrated that the platelet-to-lymphocyte ratio (PLR) holds significant predictive value for adverse outcomes in cardiovascular disease; however, few studies have investigated the predictive value of PLR for short-term prognosis in elderly patients with acute myocardial infarction (AMI).

**Objective** To determine the predictive ability of PLR for in-hospital mortality risk in elderly AMI patients.

**Methods** We retrospectively collected medical history data from 1,423 elderly inpatients with AMI treated in the Department of Cardiology, the Second Affiliated Hospital of Dalian Medical University from December 2015 to December 2021. The data included gender, age, BMI, blood pressure classification, glycosylated hemoglobin, platelet count, neutrophil count, lymphocyte count, estimated glomerular filtration rate (eGFR), lipid-related indicators, prevalence of heart failure and diabetes, and use of statins and antiplatelet drugs during hospitalization. The primary endpoint was defined as all-cause mortality during hospitalization. Patients were divided into a survival group (n=1,315) and a death group (n=108) based on mortality status. ROC curve analysis was used to determine the predictive ability of PLR for in-hospital mortality risk in elderly AMI patients, and decision curve analysis was employed to evaluate the clinical utility of PLR and its combined indicators.

**Results** The death group exhibited statistically significant differences compared with the survival group in terms of age, BMI, PLR, white blood cell count, neutrophil count, lymphocyte count, red blood cell count, hemoglobin, fasting blood glucose, aspartate aminotransferase (AST), triglycerides (TG), cardiac troponin I (cTnI), eGFR classification, proportion of heart failure, proportion

of antiplatelet drug use, and proportion of lipid-lowering drug use ( $P < 0.05$ ). The area under the ROC curve (AUC) for PLR in predicting in-hospital mortality risk in elderly AMI patients was 0.661 ( $P < 0.001$ ). When PLR was combined with creatine kinase-MB (CK-MB) and cTnI, the AUCs were 0.705 and 0.779, respectively ( $P < 0.001$ ). Decision curve analysis based on the Bootstrap method demonstrated that PLR yielded substantial net benefit within a risk threshold range of 6%–82%, and PLR combined with cTnI produced substantial net benefit within a risk threshold range of 2%–86%, indicating clinical utility.

**Conclusion** PLR can effectively predict in-hospital mortality risk in elderly AMI patients, and this predictive ability is significantly improved when combined with cTnI.

## Full Text

### Platelet-lymphocyte Ratio Predicts In-hospital Mortality in Elderly Patients with Acute Myocardial Infarction

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## Abstract

**Background:** Previous studies have demonstrated the important predictive value of platelet-lymphocyte ratio (PLR) for adverse outcomes in cardiovascular disease, but few have explored its predictive value for short-term prognosis in elderly patients with acute myocardial infarction (AMI).

**Objective:** To determine the predictive ability of PLR for in-hospital mortality risk in elderly AMI patients.

**Methods:** Medical history data were retrospectively collected from 1,423 elderly AMI inpatients treated in the Department of Cardiology of the Second Hospital of Dalian Medical University from December 2015 to December 2021. Data included gender, age, BMI, blood pressure classification, glycated hemoglobin, platelet count, neutrophil count, lymphocyte count, estimated glomerular filtration rate (eGFR), lipid-related indices, heart failure and diabetes status, and use of statins and antiplatelet agents during hospitalization. The primary outcome was defined as all-cause death during hospitalization. Patients were divided into

a non-death group (n=1,315) and a death group (n=108) based on mortality status. ROC curve analysis was used to determine the predictive ability of PLR for in-hospital mortality risk, and decision curve analysis (DCA) was employed to evaluate the clinical application value of PLR and its combined indicators.

**Results:** There were statistically significant differences between the death and non-death groups in age, BMI, PLR, white blood cell count, neutrophil count, lymphocyte count, red blood cell count, hemoglobin, fasting blood glucose, aspartate aminotransferase (AST), triglycerides (TG), troponin I (CTNI), eGFR classification, proportion of heart failure, proportion of antiplatelet drug use, and proportion of lipid-lowering drug use ( $P<0.05$ ). The area under the ROC curve (AUC) of PLR for predicting in-hospital mortality risk in elderly AMI patients was 0.661 ( $P<0.001$ ). When PLR was combined with creatine kinase isoenzyme MB (CK-MB) and CTNI, the AUCs were 0.705 and 0.779, respectively ( $P<0.001$ ). Decision curve analysis based on the Bootstrap method showed that PLR produced substantial net benefit when the risk threshold was between 6% and 82%, and PLR combined with CTNI produced substantial net benefit when the risk threshold was between 2% and 86%, indicating clinical application value.

**Conclusion:** PLR can effectively predict the risk of in-hospital death in elderly AMI patients, and this predictive ability is significantly enhanced when combined with CTNI.

**Keywords:** Myocardial infarction; Platelet to lymphocyte ratio; In-hospital death; Death; Forecasting

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## Introduction

Coronary heart disease (CHD) plays an important role in global disease burden and mortality, with acute myocardial infarction (AMI) being the leading cause of death among CHD patients [1-2]. Although mortality rates have improved with advances in percutaneous coronary intervention technology and stent materials, along with continued emphasis on antiplatelet therapy for secondary prevention in AMI patients, studies have shown that the 12-month mortality rate for AMI patients remains at 10% [3-4]. Data from the European Society of Cardiology (ESC) encompassing 37 countries indicate that the in-hospital mortality rate for AMI patients ranges from 4% to 12% [5]. In China, population aging is becoming increasingly severe, and cardiovascular disease has become the leading cause of death [6]. Compared with younger populations, elderly AMI patients have higher rates of in-hospital mortality. Therefore, identifying a reliable and convenient indicator to predict in-hospital mortality risk in elderly AMI patients is of great significance for improving their prognosis.

The platelet-to-lymphocyte ratio (PLR) was initially applied to evaluate prognosis in malignant tumor patients [7] and has recently gained attention in the

cardiovascular disease field. The entire process of AMI occurrence, development, and plaque rupture is accompanied by inflammatory responses, while CHD risk factors such as hypertension, hyperlipidemia, and diabetes also create a chronic inflammatory state in the body [8-11]. Consequently, inflammatory markers like PLR that reflect the body's inflammatory status have attracted increasing attention from cardiologists. Regardless of platelets' role in systemic inflammatory responses, they are closely associated with endothelial activation [12], and low lymphocyte counts are also associated with poorer cardiovascular outcomes [13]. Platelet and lymphocyte counts can be influenced by various physiological conditions, whereas PLR is relatively more stable. Some studies have used PLR to predict long-term prognosis in CHD patients [14], but few have explored the predictive value of PLR for in-hospital mortality risk in elderly AMI patients. Therefore, this study investigates the ability of PLR to predict short-term prognosis in elderly AMI patients.

## Methods

**Study Population and Data Collection** We retrospectively collected medical history data from 1,423 elderly AMI inpatients treated in the Department of Cardiology at the Second Hospital of Dalian Medical University from December 2015 to December 2021. Data were extracted from the hospital's medical record management system after de-identification of key patient information to protect privacy. This study complies with the ethical requirements of the Declaration of Helsinki and was approved by the Ethics Committee of the Second Hospital of Dalian Medical University (NO.2023-152).

**Inclusion and Exclusion Criteria** **Inclusion criteria:** (1) Age  $\geq 60$  years; (2) Patients meeting diagnostic criteria for AMI, including both STEMI and NSTEMI [15-16].

**Exclusion criteria:** (1) Patients with incomplete medical history data in the electronic record system; (2) Patients with severe diseases (such as advanced malignant tumors) and life expectancy less than six months; (3) Patients with hematological diseases; (4) Patients who had recently received chemotherapy and/or radiotherapy.

**Data Collection** Baseline data were retrospectively collected after patient admission, including gender, age, BMI, blood pressure classification, glycosylated hemoglobin, platelet count, neutrophil count, lymphocyte count, estimated glomerular filtration rate (eGFR), lipid-related indices, heart failure and diabetes status, and use of statins and antiplatelet agents during hospitalization. The primary outcome was defined as all-cause death during hospitalization. Patients were divided into a non-death group (n=1,315) and a death group (n=108) based on mortality status.

**Statistical Analysis** Data were processed using SPSS 22.0 and R 4.2.1 software. Categorical data were expressed as relative numbers and compared between groups using the  $\chi^2$  test. Normally distributed continuous data were expressed as ( $\bar{x}\pm s$ ) and compared using independent t-tests. Non-normally distributed continuous data were expressed as M(P25, P75) and compared using non-parametric tests. Receiver operating characteristic (ROC) curve analysis was used to evaluate the predictive ability of indicators for in-hospital all-cause mortality in AMI patients. The DeLong method was used to compare the areas under the ROC curves (AUCs) constructed by different indicators. Bootstrap method was used to generate decision curves to evaluate the clinical application value of PLR and PLR combined with CTNI.  $P<0.05$  was considered statistically significant.

## Results

**Baseline Patient Characteristics** There were statistically significant differences between the death and non-death groups in age, BMI, PLR, white blood cell count, neutrophil count, lymphocyte count, red blood cell count, hemoglobin, fasting blood glucose, aspartate aminotransferase (AST), triglycerides (TG), troponin I (CTNI), eGFR classification, proportion of heart failure, proportion of antiplatelet drug use, and proportion of lipid-lowering drug use ( $P<0.05$ ). No significant differences were observed between the two groups in gender, blood pressure classification, diabetes proportion, platelet count, glycated hemoglobin (HbA1c), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), remnant cholesterol (RC), or creatine kinase isoenzyme MB (CK-MB) ( $P>0.05$ ).

**Predictive Value of PLR for In-hospital Mortality Risk in Elderly AMI Patients** The AUC of PLR for predicting in-hospital mortality risk in elderly AMI patients was 0.661 ( $P<0.001$ ). To better evaluate the predictive ability of PLR for in-hospital mortality risk, we combined PLR with CK-MB and CTNI based on probability P values from regression models. The AUCs of PLR+CK-MB and PLR+CTNI for predicting in-hospital mortality risk in elderly AMI patients were 0.705 and 0.779, respectively ( $P<0.001$ ). Using the DeLong method to compare AUCs, the AUCs of PLR+CK-MB and PLR+CTNI were greater than that of PLR alone. The AUC of PLR+CTNI was significantly greater than that of PLR+CK-MB ( $P<0.05$ ) [Figure 1: see original paper].

**Comparison of PLR, PLR+CK-MB, and PLR+CTNI Predictive Ability in Different Myocardial Infarction Subgroups** Using the DeLong method, we analyzed the predictive ability of PLR and its combined indicators (PLR+CK-MB, PLR+CTNI) for in-hospital mortality risk in NSTEMI and STEMI patients. The results showed that although the AUCs of PLR and its combined indicators were larger in NSTEMI patients compared to STEMI patients, the overall differences in AUC were not statistically significant ( $P>0.05$ ) [Figure 2: see original paper].

**Decision Curve Analysis Results for PLR and PLR+CTNI** To evaluate the clinical application value of PLR and PLR+CTNI as predictive indicators for estimating in-hospital mortality risk in elderly AMI patients, clinical decision curves were generated using the Bootstrap method (500 resamples). The results indicated that PLR produced substantial net benefit when the risk threshold was between 6% and 82%, and PLR combined with CTNI produced substantial net benefit when the risk threshold was between 2% and 86%, demonstrating clinical application value [Figure 3: see original paper].

## Discussion

This study evaluated the predictive ability of PLR for in-hospital mortality risk in elderly AMI patients, demonstrating strong predictive performance with an AUC of 0.661. The predictive ability could be further enhanced by combining PLR with CK-MB or CTNI. We then used the DeLong method to compare the predictive ability of PLR, PLR+CK-MB, and PLR+CTNI for outcome events in different myocardial infarction subgroups. Although the AUCs were larger in NSTEMI patients, the overall differences were not statistically significant. Additionally, clinical decision analysis curves were generated based on the Bootstrap method to further evaluate the clinical application value of PLR and PLR+CTNI.

As previously mentioned, regardless of platelets' role in general inflammatory responses, they are closely associated with endothelial activation and coordination [12]. Platelets play a critical role in the pathophysiology of acute coronary syndrome, which is the primary reason why antiplatelet agents are highly emphasized before and after percutaneous coronary intervention (PCI). However, platelet counts in human blood are susceptible to various factors and are not stable, whereas PLR improves this situation to some extent [17-18]. PLR was initially applied to evaluate prognosis in malignant tumor patients and later gained attention in the cardiovascular field. PLR also incorporates lymphocyte count, which is considered to have anti-atherosclerotic effects. Therefore, the combined ratio reflects both the intensified inflammatory response and the anti-atherosclerotic process in atherosclerosis formation [19].

Our study results showed that elderly AMI patients who died during hospitalization had higher white blood cell counts, neutrophil counts, and platelet counts than non-survivors, indicating a more intense inflammatory response in these patients, consistent with pathological changes during acute myocardial infarction. Lymphocyte counts were lower in the death group compared to the non-death group, possibly related to suppressed lymphocyte proliferation, differentiation, and redistribution in the stress state following AMI [20]. Lymphocytes are considered to have anti-inflammatory effects, so the combination of increased platelet count and decreased lymphocyte count in AMI patients leads to significantly elevated PLR, reflecting heightened systemic inflammation.

Previous studies have shown that PLR levels are directly correlated with the

degree of coronary atherosclerosis [21]. Azab et al. [14] demonstrated that PLR is an independent predictor of death after discharge in NSTEMI patients, particularly when  $PLR > 176$ , which significantly predicts 4-year all-cause mortality. Thus, PLR has been confirmed as one of the predictors of long-term death in AMI patients. Additionally, PLR is associated with no-reflow during PCI [22], coronary slow flow [23], and some adverse events after angioplasty [24]. Previous research has primarily focused on the relationship between PLR and long-term cardiovascular risk in AMI patients, with few studies examining PLR and short-term prognosis risk. Therefore, this study specifically investigated this issue. Some studies have found that PLR's predictive ability for cardiovascular outcomes is not significant [25], suggesting that PLR should be combined with other indicators for prediction. This is also why we combined PLR with CK-MB and CTNI in our ROC curve analysis. The results showed that the predictive ability was indeed significantly improved after combination, which can be further validated in future studies regarding the clinical application value of PLR combined with other indicators.

This study has several limitations. First, we were unable to observe patients' long-term prognosis, which somewhat limits the evaluation of PLR's predictive value for long-term mortality risk in AMI patients. Second, some critically ill patients died before routine tests could be performed, making it impossible to obtain their baseline clinical data and reducing the sample size.

In conclusion, PLR demonstrates good predictive ability for in-hospital mortality risk in elderly AMI patients, which is significantly improved when combined with CK-MB or CTNI. Although the AUCs of PLR and its combined indicators were higher in NSTEMI patients than in STEMI patients, the overall differences were not statistically significant.

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**Author Contributions**

WANG Yu and CHEN Yan were responsible for conceptualization, overall design, and writing; CHEN Yan, HAN Yuanyuan, LYU Zhibo, XU Qing, CHEN Shengyue, and LU Chuan were responsible for data collection and organization; CHEN Yan and ZHENG Mingxin were responsible for statistical processing, testing, and review; ZHAO Xin was responsible for overall quality control of the manuscript. This article has no conflicts of interest.

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