



Platelet-to-lymphocyte ratio relates to poor prognosis in elderly patients with acute myocardial infarction

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Abstract

Background The platelet to lymphocyte ratio (PLR) is a novel biomarker to predict the prognosis of acute myocardial infarction (AMI) patients.

Aim The study aimed to evaluate the in-hospital outcomes of elderly patients with AMI and assessed the prognostic value of PLR on in-hospital adverse events.

Methods A total of 1,001 patients were divided into an older group ($n = 560$) and a younger group ($n = 441$) based on age ≥ 60 years and successfully underwent primary percutaneous coronary intervention (PCI) within 12 h after presentation. Total white blood cells (WBCs), neutrophils, lymphocytes, and platelets counts were measured at admission.

Results The incidence of heart rupture, acute heart failure, total adverse events, and death resulting from all events were significantly higher in patients ≥ 60 years than in younger patients, whereas the incidence of postoperative angina and reinfarction were similar between groups. Regarding blood counts, total white blood cells, neutrophils, lymphocytes, and platelets were lower in the older group than in the younger group. The platelet-to-lymphocyte ratio (PLR) was significantly higher in the older group. In receiver operating characteristic curve analysis, high PLR > 147 predicted adverse events (specificity 72% and sensitivity 63%). In multiple logistic regression analysis, age, hypertension, and PLR were identified as independent predictors of adverse events.

Conclusions The in-hospital outcomes of elderly patients with acute myocardial infarction were poor. PLR was an independent risk factor for in-hospital adverse events, which suggested that strong inflammation and prothrombotic status may contribute to the poor prognoses of elderly patients.

Keywords Age · In-hospital outcomes · Prognostic factors · Platelet-to-lymphocyte ratio · Acute myocardial infarction

Introduction

Acute myocardial infarction (AMI) is the most critical cardiovascular disease with high mortality and morbidity rates. It is a thrombotic and inflammatory process usually caused by an occluded coronary artery [1]. Several biomarkers of inflammation and thrombocytosis have been associated with AMI, such as lymphocyte and platelet counts [2, 3]. Lymphocytes represent a quiescent and controlled immune response with less myocardial damage [4]; lymphocyte counts decrease due to increased apoptosis. A low blood lymphocyte count has been shown to be related to

worse cardiovascular consequences in patients with coronary artery diseases (CAD) or chronic heart failure [4–6]. Platelets play critical roles in the development of atherosclerosis and acute coronary syndromes [7]. Activated platelets accelerate atherosclerosis formation, progression, and destabilization of atherosclerotic plaques, which promote the development of atherothrombotic disease or eventually result in cardiovascular disease (CVD) events [8]. The platelet-to-lymphocyte ratio (PLR) offers insight into the aggregation and inflammation pathways and may be more useful than either platelet or lymphocyte count alone in predicting coronary atherosclerotic burden [9]. Several studies identified a relationship between the PLR and prognoses of AMI patients [10–12]. As a novel inflammatory marker, PLR has been demonstrated to be significantly and independently associated with the occurrence of in-hospital major adverse cardiovascular events [13]. Furthermore, age is an important

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risk factor for poor prognoses in patients with coronary artery diseases (CADs) [14]. The mortality of AMI increases with age. Few studies have investigated the importance of PLR on outcomes in elderly patients. The study aimed to evaluate the in-hospital outcomes of elderly patients with AMI who had undergone primary percutaneous coronary intervention (PCI). We assessed the prognostic value of PLR on in-hospital adverse events.

Methods

Patients

From January 2012 to February 2016, patients with ST elevation myocardial infarction (STEMI) consecutively admitted to Tangshan Gongren Hospital were selected. These patients successfully received primary percutaneous coronary intervention within 12 h from the onset of chest pain. Written informed consent was obtained from all participants. This study was conducted in accordance with the Declaration of Helsinki and with approval from the Ethics Committee of the Tangshan Gongren Hospital. Patients were divided into an older group and a younger group based on age ≥ 60 years. AMI was defined based on the criteria formulated by the American College of Cardiology and the European Society of Cardiology: an increase in troponin $I > 1$ ng/mL with a new ST elevation was measured from the *J* point in ≥ 2 contiguous leads with at least 0.2 mV in leads V1, V2, and V3, or at least 0.1 mV in the remaining leads during the first 12 h after the onset of symptoms. The exclusion standards are treated with fibrinolytic agents; a history of coronary revascularization either coronary artery bypass graft or PCI; any disease affecting platelet and lymphocyte count (e.g., hematological diseases, malignancy, severe renal or liver diseases, infections or systemic inflammatory conditions and autoimmune diseases).

Clinical data

Baseline characteristics of patients with STEMI were recorded, such as age, gender, history of hypertension, history of hyperlipidemia, history of diabetes mellitus, smoking, and BMI. Arterial hypertension was defined as having a history of antihypertensive drugs or having a systolic blood pressure ≥ 140 mmHg and/or a diastolic blood pressure ≥ 90 mmHg in at least 2 measurements. Diabetes mellitus was defined as a fasting plasma glucose ≥ 126 mg/dL at any measurement or having a glycated hemoglobin fraction of $\geq 6.5\%$ or a history of antidiabetic drug. Hyperlipidemia was defined as total cholesterol ≥ 200 mg/dl or low-density lipoprotein cholesterol ≥ 130 mg/dl or triglycerides ≥ 150 mg/dl. Body mass index (BMI) was calculated

as the ratio of weight (in kilogram) to height squared (in square meters). Patients were considered overweight if their BMI was between 25 and 29 and obese if the body mass index was ≥ 30 kg/m². Smoking was defined as current and regular use of cigarettes. Blood samples were collected on admission to measure complete blood counts with an auto-analyzer, which included the total white blood cells (WBCs), neutrophils, lymphocytes, and platelets. PLR was measured by dividing platelet counts by lymphocyte counts.

Coronary angiography

Primary percutaneous coronary intervention procedures were performed by an experienced team at a high-volume center with a 24-h intensive care service. All patients received coronary angiography and conventional multi-position projection to determine the number of diseased coronary arteries and infarcted arteries for PCI. Patients were treated with 300 mg aspirin and 300 mg clopidogrel or 180 mg ticagrelor preoperatively and a subcutaneous injection of low molecular weight heparin postoperatively, as well as a IIb/IIIa receptor antagonist, aspirin, clopidogrel/ ticagrelor, angiotensin-converting enzyme inhibitors/angiotensin receptor blocker, β -receptor blockers and nitrate esters, according to the guidelines. A successful procedure was defined as infarcted artery stenosis $< 30\%$ associated with a Thrombolysis in Myocardial Infarction (TIMI) grade of 2 or 3.

Follow-up and outcomes

Adverse events included angina pectoris (with new ischemic electrocardiographic ST-T changes), re-infarction (coronary angiography confirmed in-stent acute and subacute thrombotic occlusion), acute heart failure (HF), and heart rupture (free wall rupture and ventricular septal rupture) in-hospital. Acute heart failure should be diagnosed with evidence of typical signs and symptoms of HF (dyspnea, edema, rales, third heart sound, jugular turgor, and lung congestion on chest X-rays). In patients who had more than one event, only the first event was counted. Deaths resulting from any event were counted.

Statistical analysis

Continuous variables were reported as the mean \pm standard deviation (SD), and categorical variables were expressed as the number of patients and percentages. Comparisons of parametric values between the 2 groups were performed using independent samples *t*-test. Categorical variables were compared using the chi-squared test. Receiver operation characteristic (ROC) curves were used to derive sensitivity and specificity of PLR to predict the presence of in-hospital adverse events. Logistic regression analysis was applied to

screen the association of different baseline variables between groups with in-hospital adverse events. Statistical analysis was carried out using the SPSS 21.0 for Windows software package. $P < 0.05$ was considered to indicate a significant difference.

Results

From January 2012 to February 2016, 1,001 patients with AMI were admitted to Tangshan Gongren Hospital and successfully received primary PCI. Among the 1001 patients, there were 560 patients (400 male, 260 female; mean age 67.3 ± 5.6 years) in the older group and 441 patients (405 male, 36 female; mean age 49.7 ± 7.2 years) in the younger group. Baseline clinical characteristics are listed in Table 1. There were more female patients in the older group (28.6% vs. 8.2%, $P = 0.00$) and more hypertensive patients in the younger group (50.1% vs. 43.8%, $P = 0.04$). Other risk

factors, including hyperlipidemia, diabetes, and smoking, were similar in the two groups. BMI was lower in the older group (24.6 ± 2.7 vs. 26.1 ± 3.4 , $P = 0.00$). For the other variables, WBC, neutrophil, lymphocyte, and platelet counts were lower. The platelet-to-lymphocyte ratio (PLR) was higher in the older group (190 ± 107 vs. 165 ± 79 , $P = 0.00$). Finally, the 3-vessel incidence rate was more frequent in the older group (29.5% vs. 15.7%, $P = 0.00$).

The adverse events of the two groups are listed in Table 2. The incidences of acute heart failure (10.0% vs. 2.3%, $P = 0.00$) and heart rupture (3.6% vs. 0.0%, $P = 0.00$) were higher in the older group than the younger group; the incidences of postoperative angina and reinfarction were similar between groups. In addition, the total adverse events rate (23.2% vs. 11.3%, $P = 0.00$) was higher in the older group than the younger group. In addition, mortality (8.0% vs. 1.1%, $P = 0.00$) was higher in the older group than the younger group.

ROC curve analysis showed that the optimal cutoff level for the PLR predicted AE was 147 with a sensitivity of 72% and a specificity of 63% [ROC area under the curve (AUC) 0.670, 95% CI 0.589–0.751, $P = 0.001$; Fig. 1].

The association of different variables with in-hospital adverse events was assessed using logistic regression analysis (Table 3). Multivariate logistic regression model for in-hospital AE consisted of age, gender, hypertension, diabetes, smoking, BMI, leukocyte and platelet subtypes, and number of diseased arteries. Only age, hypertension, and PLR were identified as independent predictors of adverse events in the hospital.

Discussion

Aging increases the risk of cardiovascular disease, which is the leading cause of death in elderly people. Age is also an important risk factor for poor prognoses in patients with CAD [14]. Elderly patients frequently have complications from hypertension, hyperlipidemia, and diabetes, which are independently associated with cardiovascular events and deaths in patients with CAD [15, 16]. In addition, cardiovascular disease often progresses asymptotically in elderly people, which results in diagnostic delays and ultimately reduces life expectancy. Patients aged 65 years and older comprise the majority of patients who die; nearly 40%

Table 1 Baseline characteristics of groups (Younger and Older)

Variables	Younger ($n = 441$)	Older ($n = 560$)	t/χ^2	P
Age(years)	49.7 ± 7.2	67.3 ± 5.6	42.6	0.00
Risk factors				
Male n (%)	405 (91.8)	400 (71.4)	65.2	0.00
Diabetes n (%)	95 (24.3)	140 (25.0)	1.6	0.21
Hypertension n (%)	221 (50.1)	245 (43.8)	4.0	0.04
Hyperlipidemia n (%)	45 (10.2)	40 (7.1)	3.0	0.09
Smoking	94 (21.3)	95 (17.0)	3.0	0.09
BMI (kg/m^2)	26.1 ± 3.4	24.6 ± 2.7	7.0	0.00
Laboratory finding				
WBC ($10^9/\text{L}$)	11.1 ± 3.3	10.6 ± 3.1	2.7	0.01
Neutrophil ($10^9/\text{L}$)	8.9 ± 3.4	8.7 ± 2.9	1.2	0.21
Lymphocyte ($10^9/\text{L}$)	1.6 ± 0.5	1.4 ± 0.7	5.2	0.00
Platelet ($10^9/\text{L}$)	230 ± 59	218 ± 71	2.8	0.01
PLR	165 ± 79	190 ± 107	4.4	0.00
Coronary angiographic finding				
1- vessel n (%)	196 (36.9)	175 (31.3)	18.4	0.00
2- vessel n (%)	175 (40.0)	220 (39.3)	0.02	0.90
3- vessel n (%)	69 (15.7)	165 (29.5)	25.9	0.00

Table 2 Comparison of adverse events between groups

	Angina	Reinfarction	HF	Heart rupture	Total incidence	Death
Younger n (%)	15 (3.4)	20 (4.5)	10 (2.3)	0 (0.0)	50 (11.3)	5 (1.1)
Older n (%)	34 (6.1)	20 (3.6)	56 (10.0)	20 (3.6)	130 (23.2)	45 (8.0)
χ^2	3.8	0.6	24.0	16.1	23.6	24.8
P	0.06	0.44	0.00	0.00	0.00	0.00

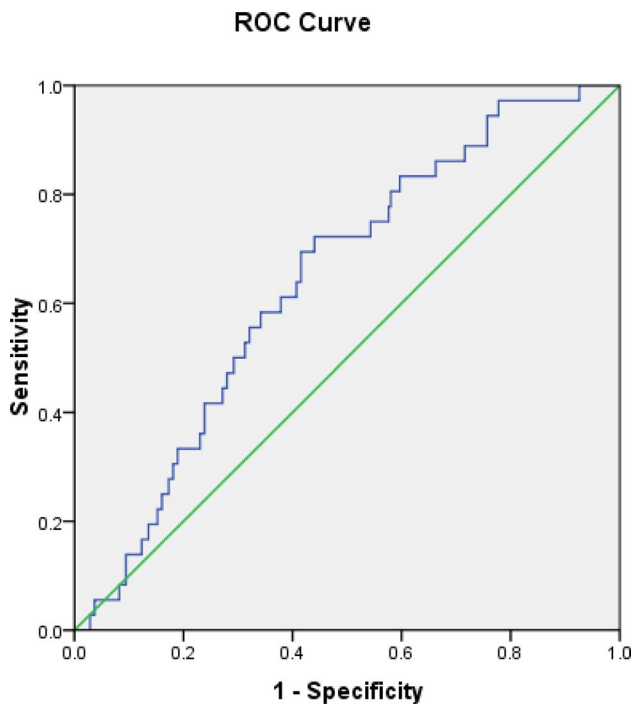


Fig. 1 ROC curves analysis presenting the relationship between PLR and in-hospital adverse events. PLR > 147 predicted in-hospital adverse events with a specificity of 72% and a sensitivity of 63% (area under curve 0.670, 95% CI 0.589–0.751; $P=0.001$). ROC receiver operating characteristic, PLR platelet to lymphocyte ratio, CI confidence interval

Table 3 Independent predictors of in-hospital adverse events

	<i>B</i>	SE	Sig	Exp(B)
Age (≥ 60 year)	0.838	0.186	0.000	2.312
Hypertension	0.621	0.179	0.001	1.860
High PLR	0.857	0.188	0.000	2.356
Constant	– 1.646	0.389	0.000	0.193

of those are admitted to hospitals due to AMI [17]. Nearly 83% of patients who die of ischemic heart disease are older than 65 years [15]. The incidence rates of any-causes-of-death and cardiovascular death increased with age in CAD patients [18]. Rubinstein R et al. reported the outcome rates of the acute coronary syndrome in women ≥ 80 years were significantly higher compared with those < 80 years [19]. Consistent with previous studies, the present study showed that the incidences of acute heart failure, heart rupture, and the total adverse events were higher in the older group than the younger group. Deaths resulting from any event were also more frequent in the older group.

Platelets are an important medium for the initiation of thrombosis and correlate with the occurrence and development of coronary artery thrombosis [20]. Platelets play

vital roles in the pathogenesis of atherosclerosis and in the occurrence of acute thrombotic coronary events [21]. Elevated platelet counts have been shown to have close correlations with acute-phase reactants and proinflammatory substances [22–24]. Higher platelet counts may also reflect the aggravated release of inflammatory mediators, increased thrombocyte activation leading to destructive inflammatory responses, and prothrombotic status. Paul et al. showed that patients with acute STEMI and higher platelet counts had poor in-hospital outcomes [25]. A higher baseline platelet count in patients with AMI has also been associated with poor outcomes within the first year after primary PCI [26]. Lymphocytes represent a quiescent and controlling inflammatory pathway in suppressed immune response [27]. Lymphocyte apoptosis has been observed in atherosclerotic lesions involved in plaque growth, lipid core development, plaque rupture and thrombosis [28]. Lymphocytopenia has been detected in critical inflammatory states and is associated with cardiovascular disease events [28–30]. Thus, the combination of increased platelet counts and low levels of lymphocytes may provide more information than either platelet count or lymphocyte count alone. The PLR value reflects the activity of inflammatory and thrombotic processes. A higher PLR may indicate enhanced thrombocyte activation and a prothrombotic state [31]. Recent studies have demonstrated the prognostic importance of PLR in short-term clinical outcomes (up to 6 months) in STEMI [32, 33]. The association between the PLR and long-term prognoses was also demonstrated in AMI populations [34, 35]. Azab et al. [34] showed that higher PLR values are associated with increased long-term mortality in patients admitted with non-ST-segment elevation myocardial infarction (NSTEMI). Cicek et al. demonstrated that the combination of the neutrophil-to-lymphocyte ratio (NLR) and PLR had short- and long-term prognostic significance in this population [36]. Consistent with previous studies, the present study showed PLR was an independent predictor of in-hospital adverse events in elderly AMI patients undergoing primary PCI. The risk of adverse events in patients with high PLR was approximately 2.4-folds higher than those without high PLR. Furthermore, the PLR of older patients was significantly higher than that of younger patients, which suggested an aggravated inflammation and prothrombotic status may contribute to the poor prognoses of elderly patients.

Limitations

Limitations of the study need to be acknowledged. First, some high-risk elderly patients had not been included in the study. Second, the results of a single-center study may be influenced by patient selection bias. Furthermore, the assessments of other inflammatory markers, such as CRP,

interleukin-6, and thromboxane A2, may help strengthen the study.

Conclusion

The in-hospital outcomes of elderly patients with acute myocardial infarction were poor. Higher PLR was associated with higher rates of adverse events in elderly patients with AMI, e.g., acute heart failure, heart rupture, and death. PLR was an independent risk factor for in-hospital adverse events, which suggested strong inflammation and prothrombotic status may contribute to the poor prognoses of elderly patients. Thus, PLR may be an effective marker for identifying patients requiring more aggressive therapeutic strategies to control adverse events.

Compliance with ethical standards

Conflict of interest The authors declare no funding sources or conflicts of interest.

Statement of human and animal rights The study was approved by the Ethics Committee of the Tangshan Gongren Hospital and conducted in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Consents of participants from both groups were received.

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