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Platelet to lymphocyte ratio as a prognostic marker in primary percutaneous coronary intervention

Abdulaziz Khaleef J Alanazi, Yusif Eid Awad Al-Rashidi, Abdulmajeed Mutayliq K Aljameeli, Omar Jaber Mathan Alruwaili, Mtaib Obaid S Alanazi, Fahad Obaid S Alanazi

Clinical laboratory

Abstract

We investigated the predictive significance of the platelet-to-lymphocyte ratio (PLR) in patients undergoing primary percutaneous coronary intervention (pPCI) for acute myocardial infarction (AMI). The study included 440 patients who underwent pPCI and were categorized into two groups based on their PLR levels: low PLR (<137) and high PLR (≥137). Thrombolysis In Myocardial Infarction (TIMI) flow grades and Syntax scores (SXS) were computed from initial angiograms. Data on in-hospital mortality rates and cardiac adverse events were collected from medical records. Patients with high PLR exhibited more instances of no-reflow, higher SXS values, and elevated mortality rates ($p < 0.001$, $p < 0.001$, and $p = 0.008$, respectively). Receiver operating characteristic curve analysis revealed that high PLR predicted the occurrence of no-reflow (specificity 71% and sensitivity 85%), SXS ≥ 22 (specificity 52% and sensitivity 61%), and adverse events during hospitalization (specificity 67% and sensitivity 63%). Multivariate regression analysis identified PLR as an independent risk factor for no-reflow, SXS ≥ 22, and in-hospital adverse events. Additionally, we explored the associations between mean platelet volume, red cell distribution width, neutrophil-to-lymphocyte ratio, and the occurrence of no-reflow, SXS, and in-hospital adverse events.

Introduction

Acute myocardial infarction (AMI) is characterized by a thrombotic and inflammatory process typically caused by a blocked coronary artery. Platelets play a pivotal role in this atherothrombotic mechanism, and an elevated platelet count has been associated with larger infarct sizes and poorer short- and long-term outcomes in AMI patients. Conversely, lymphocyte count inversely correlates with inflammation, and a low lymphocyte count is indicative of a worse prognosis in coronary artery disease (CAD) patients. (Wang et al., 2013)

Initially identified as an inflammatory marker in oncological contexts, the platelet-to-lymphocyte ratio (PLR) has been extensively studied and shown to predict poor outcomes in various malignancies. Recently, PLR has also been evaluated in relation to CAD. Despite indications from some studies suggesting that a high PLR may serve as a poor prognostic indicator in AMI, the existing data are insufficient for conclusive statements. (Koseoglu et al., 2014)

Therefore, our study aimed to assess the prognostic significance of PLR in AMI. Specifically, we investigated the correlation between PLR levels and outcomes such as no-reflow, Syntax score (SXS), and in-hospital mortality in patients with ST elevation myocardial infarction (STEMI) who underwent primary percutaneous coronary intervention (pPCI). (Kurtul et al., 2014)

Methodology

In our retrospective study, we enrolled patients who were admitted to our emergency department with ST elevation myocardial infarction (STEMI) and subsequently underwent primary percutaneous coronary

intervention (pPCI). STEMI diagnosis was established based on typical chest pain or symptoms suggestive of acute myocardial infarction (AMI) with ST segment elevation of at least 1 mm in at least 2 contiguous leads on electrocardiogram. All patients underwent pPCI, and none received thrombolytic therapy. Before the intervention, patients received aspirin and clopidogrel loading doses (300 mg and 600 mg, respectively), along with unfractionated heparin targeting an activated clotting time of 200 seconds.

Most procedures used femoral access unless bilateral femoral arteries were occluded, in which case brachial or radial access was chosen. Thrombus aspiration was performed for lesions with significant thrombus burden, and tirofiban infusion was administered if thrombus persisted or if no-reflow occurred post-stenting. Bare metal stents were exclusively used, and post-discharge antiplatelet therapy included clopidogrel 75 mg/day for at least one year and lifelong aspirin 100 mg/day.

Exclusion criteria encompassed prior myocardial infarction, coronary surgery, and conditions affecting platelet or lymphocyte counts (e.g., hematological disorders, malignancies, severe renal or liver disease, infections, systemic inflammatory or autoimmune disorders). Data collected included baseline characteristics, echocardiographic findings, hematological and angiographic data, and in-hospital outcomes such as mortality, arrhythmias, stroke, re-infarction, and cardiogenic shock.

Hematological parameters were measured upon initial presentation in the emergency department using EDTA tubes for blood samples. Platelet and lymphocyte counts, along with other parameters like hemoglobin, mean corpuscular volume (MCV), red cell distribution width (RDW), mean platelet volume (MPV), total white cell count (WBC), and neutrophil count, were determined using a hematology analyzer.

The angiographic data were evaluated retrospectively by two experienced interventional cardiologists, and the Syntax score (SXS) was calculated from the initial angiography to assess the extent of atherosclerosis. No-reflow was defined as the absence of Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 post-stent placement in the infarct-related artery (IRA).

Statistical analyses

Statistical analyses were conducted using SPSS V 16.0. Parametric and nonparametric values were compared using appropriate tests, and multivariate logistic regression analysis was employed to identify independent predictors of no-reflow, Syntax score (SXS), and in-hospital adverse events. Receiver operating characteristic (ROC) analyses determined the cut-off value of PLR for predicting these outcomes, with a significance level set at $p < 0.05$. The study adhered to the Declaration of Helsinki and obtained approval from the institutional ethics committee.

Results

In our study involving 440 patients with ST elevation myocardial infarction (STEMI) who underwent primary percutaneous coronary intervention (pPCI), we observed certain trends and associations. The average age of the patients was 57 years, with 66% being men. Notably, 40% of the patients had anterior localization of the infarction, and there was a 12.5% incidence of no-reflow post-pPCI. The mean Syntax score (SXS) was 17.2, and the mean ejection fraction (EF) was 42.3%. The in-hospital mortality rate was 4.5%.

Patients were categorized based on their platelet to lymphocyte ratio (PLR), with 66% falling into the high PLR group (PLR > 137). Comparing the two PLR groups revealed that the high PLR group had more diabetic and older patients, while the low PLR group had a higher proportion of hyperlipidemic patients. Hematological parameters such as hemoglobin, mean corpuscular volume (MCV), mean platelet volume (MPV), and red cell distribution width (RDW) were similar between the groups. However, the high PLR group showed higher white blood cell (WBC), neutrophil, and platelet counts, as well as a higher neutrophil to lymphocyte ratio (NLR) and lower lymphocyte count.

Patients with high PLR exhibited a higher rate of no-reflow, lower EF, and higher SXS compared to those with low PLR. They also experienced more pulmonary edema, cardiac arrhythmias, re-infarction, and mortality during their hospital stay.

Further analysis using receiver operating characteristic (ROC) curves showed that a PLR > 137 predicted the development of no-reflow, high SXS, and in-hospital adverse events with varying specificities and sensitivities.

When comparing patients with and without no-reflow, those with no-reflow had higher RDW, WBC, platelet and neutrophil counts, PLR, and NLR. They also had lower EF, higher SXS, mortality rates, and more adverse events.

Multivariate regression analysis identified high PLR as an independent risk factor for no-reflow, high SXS, and in-hospital adverse events, along with other factors such as EF, NLR, smoking, age, diabetes, and EF. These findings underscore the prognostic significance of PLR in assessing outcomes post-STEMI and pPCI.

Table I. Comparison of clinical, angiographic and hematological parameters, no-reflow rate, SXS and in-hospital outcomes of patients with low and high PLR

Parameter	Low PLR (51-37)	High PLR (41-37)	p-value
Age, years	56.2 ± 6.6	58.6 ± 9.5	0.04
Diabetes, n (%)	38 (13)	55 (34)	0.036
Family history, n (%)	32 (11)	21 (13)	0.56
Smoking, n (%)	81 (28)	55 (34)	0.195
Hypertension, n (%)	118 (41)	79 (49)	0.466
Male, n (%)	190 (67)	104 (65)	0.68
Hyperlipidaemia, n (%)	145 (51)	59 (37)	0.03
Door to balloon time, minutes	45 ± 27	42 ± 23	0.38
Chest pain to hospital time, hours	3.6 ± 1.8	3.5 ± 2.1	0.42
Anterior localization, n (%)	113 (40)	63 (39)	0.82
Non-anterior localization, n (%)	168 (59)	96 (60)	0.75
IRA-LAD, n (%)	113 (40)	63 (39)	0.82
IRA-CX, n (%)	32 (11)	22 (14)	0.32
IRA-RCA, n (%)	81 (28)	41 (25)	0.44
No-reflow, n (%)	8 (2)	47 (29)	50.001
Syntax score	15.9 ± 8.6	19.4 ± 8.9	50.001
Ejection fraction, %	39 ± 5	43 ± 7	0.013
In-hospital pulmonary edema, n (%)	11 (4)	18 (11)	0.004
Inotropic drug administration, n (%)	17 (6)	17 (10)	0.01
Using of intra-aortic balloon pump, n (%)	4 (1.4)	5 (3)	0.001
In-hospital arrhythmia*, n (%)	6 (2)	13 (8)	0.002
In-hospital adverse events**, n (%)	17 (6)	30 (18)	0.001
In-hospital stroke, n (%)	2 (0.7)	1 (0.6)	0.5
In-hospital re-infarction, n (%)	6 (2)	8 (5)	0.001
In-hospital mortality, n (%)	7 (2)	13 (8)	0.008
WBC ——— 103/mm3	11.1 ± 2.6	12.6 ± 4.4	0.001
Neutrophil ——— 103/mm3	7.8 ± 2.8	10.9 ± 6.3	50.001
Lymphocyte ——— 103/mm3	2.3 ± 0.6	1.4 ± 1.1	50.001
NLR	3.8 ± 1.7	9.0 ± 6.3	50.001
Hemoglobin, g/dl	13.9 ± 1.5	13.2 ± 1.9	0.2
MCV, fL	87 ± 5	86 ± 8	0.48
RDW, %	13.6 ± 1.0	13.7 ± 1.7	0.4
Platelet ——— 103/mm3	266 ± 60	246 ± 71	0.022
MPV, fL	9.1 ± 1.6	9.5 ± 1.5	0.2
Fasting glucose (mg/dl)	111 ± 88	132 ± 76	0.04
High-density lipoprotein cholesterol (mg/dl)	36 ± 17	38 ± 11	0.22

Low-density lipoprotein cholesterol (mg/dl)	122 ± 44	118 ± 78	0.1
Triglycerides (mg/dl)	132 ± 54	152 ± 73	0.05
AST, U/L	76 ± 28	84 ± 25	0.4
ALT, U/L	42 ± 14	47 ± 15	0.6
Creatinine (mg/dl)	0.9 ± 0.4	1.0 ± 0.3	0.3
In-hospital medical treatment			
ASA, n (%)	278 (99)	155 (97)	0.69
Clopidogrel, n (%)	277 (98)	157 (98)	0.8
Beta-blocker, n (%)	248 (88)	135 (84)	0.4
Angiotensin-converting enzyme inhibitor, n (%)	212 (75)	126 (79)	0.1
Calcium channel blocker, n (%)	98 (34)	57 (35)	0.7
Angiotensin receptor blocker, n (%)	58 (20)	23 (14)	0.5
Statins, n (%)	265 (94)	141 (88)	0.3

Discussion

Our study delved into the prognostic value of platelet to lymphocyte ratio (PLR) in patients undergoing primary percutaneous coronary intervention (pPCI) for ST elevation myocardial infarction (STEMI). While previous research has explored the prognostic significance of parameters like red cell distribution width (RDW), mean platelet volume (MPV), and neutrophil to lymphocyte ratio (NLR) in acute myocardial infarction (AMI), studies on the relationship between PLR and coronary artery disease (CAD) remain limited. Thus, our objective was to investigate whether PLR could serve as a predictor for outcomes such as no-reflow, extent of coronary atherosclerosis, and in-hospital mortality in STEMI patients undergoing pPCI. (Bhat et al., 2013)

Platelets play a crucial role in the pathogenesis of AMI, impacting leukocytes and endothelial cells and triggering inflammatory processes that contribute to atherosclerotic plaque development and thrombosis. Elevated platelet count and volume indicate increased platelet activation, leading to microvascular plugging, thrombus formation, and vasoconstriction, all of which contribute to the no-reflow phenomenon and adverse outcomes post-AMI. (Choi et al., 2014)

Lymphocytes are integral to chronic inflammation in atherosclerosis and play roles in transmigration of cells and tissue homeostasis. Reduced lymphocyte count, often seen in response to stress, is associated with higher mortality rates in AMI. PLR emerges as a potential indicator of thrombotic and inflammatory status, offering insights into short- and long-term prognosis in AMI patients. (Liu et al., 2014)

No-reflow, a phenomenon indicating insufficient distal flow despite successful IRA opening, signifies a poorer prognosis in AMI patients. Our study revealed a significant association between high PLR and the development of no-reflow, with PLR > 137 predicting no-reflow with notable specificity and sensitivity. (Azab et al., 2012)

Furthermore, our analysis included the Syntax score (SXS), a tool assessing CAD extent and complexity. Patients with high PLR exhibited higher SXS scores, indicating a more severe CAD profile. This association between PLR and SXS suggests PLR's potential as a prognostic marker for CAD severity, a novel finding in our study. (Gurbel et al., 2009)

Additionally, patients with high PLR experienced higher in-hospital mortality rates, lower EF, and more frequent adverse events such as pulmonary edema and arrhythmias. While the specificity and sensitivity of PLR in predicting adverse events were relatively lower than for no-reflow, this may be attributed to the limited number of patients with adverse events in our study. (Verdoia et al., 2014)

Previous studies have also highlighted the prognostic value of PLR in different cardiac conditions, further supporting its potential as a prognostic indicator. However, our study had limitations, including its retrospective nature, single-center design, and a relatively small sample size, which may have influenced the outcomes observed. (Iyú et al., 2010)

In conclusion, our study underscores the potential of PLR as a predictive marker for no-reflow, CAD severity, and in-hospital mortality in STEMI patients undergoing pPCI. Despite its limitations, PLR offers a simple and cost-effective means of assessing prognostic outcomes in AMI patients, warranting further investigation in larger, prospective studies.

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