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Original Research Article

# PATIENTS UNDERGOING PRIMARY CORONARY INTERVENTION FOR ACUTE MYOCARDIAL INFARCTION WITHOUT ST SEGMENT ELEVATION SHOWED A CORRELATION BETWEEN THE PLATELET LYMPHOCYTE RATIO AND ANGIOGRAPHIC NO-REFLOW

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**Conflict of interest: Nil**

**Abstract**

**Aim:** The purpose of this study was to determine the role of ultrasound (US) as a predictor of **Objective:** In ST-segment elevation myocardial infarction (STEMI), the occurrence of coronary no-reflow is linked to a poor clinical prognosis. An unregulated systemic inflammatory response is significant, even if its pathogenesis is not entirely understood. In patients with acute STEMI who had primary percutaneous coronary intervention (PPCI), we sought to investigate the association between platelet-lymphocyte ratio (PLR) and no-reflow.

**Method:** The study comprised 100 STEMI patients who were also receiving PPCI at Sheikh Bhikhari Medical College, Hazaribagh within 2 years (May 2019 to May 2021) of enrollment. To measure the left ventricular (LV) ejection fraction (EF) and wall motion score index, a transthoracic echocardiographic examination was conducted. Before PPCI, blood samples were checked for platelet and lymphocyte counts. In myocardial infarction grade ≤II, no-reflow was characterised as coronary blood flow thrombolysis.

**Results:** Following PPCI, no-reflow was seen in 57 (28%) of the STEMI patients. PLR was substantially greater in the no-reflow group compared to the normal reflow group (213±93 vs. 101.5±51.2, respectively, P<0.0002) and in hypertension patients compared to normotensive patients (144.6±91.5 vs. 109.0±47.0, respectively, P0.002). PLR (β: 0.484, 95% CI: 0.005-0.002, P<0.001) and LV EF (β: 0.271, 95% CI: 0.008-0.033, P<0.002) were identified as independent predictors of no-reflow following PPCI by logistic regression analysis.

**Conclusion:** In STEMI patients, the no-reflow phenomenon during PPCI is predicted by a rise in PLR prior to the procedure.

**Keywords:** ST-segment elevation myocardial infarction, primary percutaneous coronary intervention, and platelet/lymphocyte ratio

## INTRODUCTION

The first line of treatment for acute ST-segment elevation myocardial infarction (STEMI) is primary percutaneous coronary intervention (PPCI) and stent placement [Figure 1; 1]. However, earlier research demonstrated a significant incidence of coronary slow/no-reflow in 1-40% of patients, which may be related to a halt in myocardial perfusion restoration, causing patients to continue to have severe impairment [1]. Based on TIMI flow grade, myocardial blush grade, ST resolution, myocardial contrast echocardiography, and cardiac magnetic resonance imaging that evaluated microcirculatory dysfunction, no reflow is documented in major registries [2].

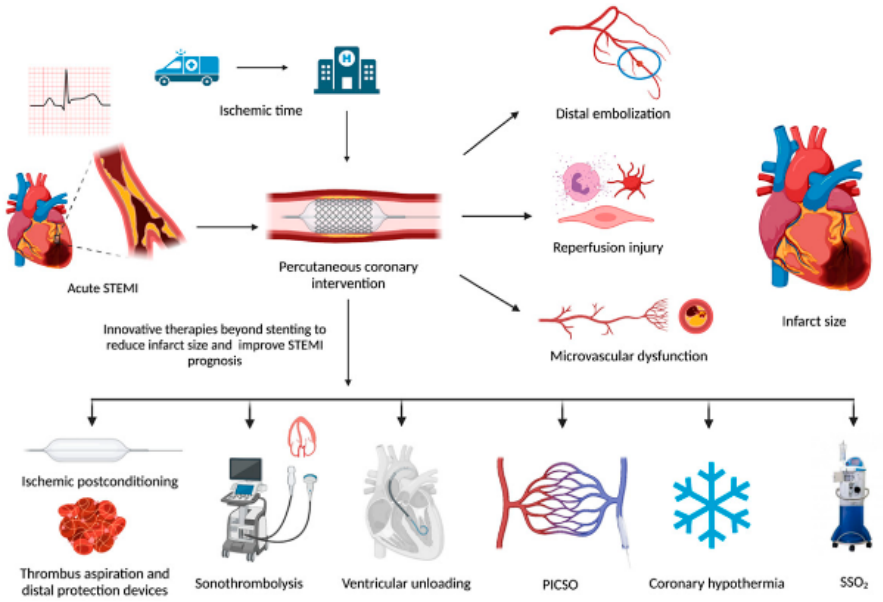


**Figure 1: Treatment related to STEMI**

Distal microembolization of thrombus fragments, swelling of endothelial cells brought on by ischemia-reperfusion damage, and microvascular spasm are a few theories put forth to explain the aetiology of no-reflow [3]. The results of numerous investigations looking into the determinants of the slow/no-reflow phenomena indicated that thrombus burden, reperfusion time, and inflammatory variables are involved [4]. Increased platelet activation is linked to serious negative cardiovascular effects, and it plays a crucial role in the development and progression of atherosclerosis [5]. On the other side, it has been demonstrated that patients with coronary artery disease who have a low blood lymphocyte count have worse cardiovascular outcomes.

The purpose of this study was to investigate the connection between post-intervention TIMI flow in STEMI patients who had undergone PPCI and the platelet/lymphocyte ratio (PLR).

## METHODS:

***Study Design:*** This was a cross-sectional study carried out at Sheikh Bhikhari Medical College, Hazaribagh within 2 years (May 2019 to May 2021) of enrollment of patients.

***Methodology:*** The risk profiles of all patients were examined, including those for smoking, hypertension, diabetes, dyslipidemia, and family history. Electrocardiography (ECG) with 11 leads, conventional echocardiogram, and the wall motion score index (WMSI) were all used to assess the function of the left ventricle (LV).

Platelet, lymphocyte, haemoglobin (HB), serum creatinine, and cardiac biomarkers including troponin and creatine kinase

myocardial band (CK-MB) were all routinely tested in the lab. Following patient assessment and ECG recording, venous blood samples were taken from antecubital veins. Following blood sample, whole blood was analysed. In ethylene diamine tetraacetic acid containers, whole blood was obtained. At the time of diagnosis, all patients got 500 mg of clopidogrel and 200 mg of aspirin prior to PPCI. They also received an intravenous bolus of unfractionated heparin, ranging from 40 to 70 U/kg, to help them reach an activated clotting time of 200 to 250 s during the operation.

The risk profiles of all patients were examined, including those for smoking, hypertension, diabetes, dyslipidemia, and family history. Wall motion score index (WMSI), conventional echocardiogram (ECG) with 11 leads, and assessment of left ventricular (LV) function using ejection fraction (EF%) were all carried out.

Using quantitative cardiovascular angiographic software, the TIMI flow grade was assessed by two separate, skilled interventional cardiologists. TIMI 0 was defined as no antegrade filling of the culprit vessel, TIMI I as sluggish filling and evacuation of the culprit vessel, TIMI II as normal filling with sluggish evacuation, and TIMI III as normal filling with normal evacuation.

A TIMI flow grade of II during PCI without signs of dissection, persistent stenosis, distal embolism, or vasospasm was considered angiographic slow/no-reflow. Based on the post-intervention infarct-related artery flow, the research participants were split into two groups: Patients having a post-intervention TIMI flow grade of III were enrolled in the normal reflow group, whereas those with grades 0, 1, and II were placed in the no-reflow group.

***Sample Size:*** 127 patients were originally enrolled in this study, and 27 patients were excluded, based on exclusion criteria. So, 100 patients were enrolled in this research.

***Exclusion criteria:*** Prior acute coronary syndrome, non-STEMI, unstable angina, STEMI duration more than 11 h, cardiogenic shock, treatment with thrombolytic therapy in the previous 25 h, estimated glomerular filtration rate <50 mL/min/1.72 $m^2$ or renal dialysis, active systemic inflammatory diseases, or active treatment for specific conditions (including allergy, asthma, autoimmune diseases, glomerulonephritis, hepatitis, inflammatory bowel disease, and known malignancy***).***

***Statistical analysis:*** Data were gathered, coded, updated, and input into the SPSS statistical software package. For continuous data, the mean ±standard deviation was shown; for categorical data, the number (%) was used. Analysis using logistic regression was conducted to determine the coronary flow risk variables. The allowable margin of error was set at 5%, while the confidence interval was set at 95%. Statistics were judged significant at $P<0.04$.

**RESULTS:**

**Table 1** displays the demographic and clinical characteristics of the study groups according to TIMI flow.

**Table 1: Baseline traits of Patients**

| Characteristics | TIMI 0-II (%) | TIMI III (%) | *P*-value |
|---|---|---|---|
| Male (%) | 84.4% | 78.1% | 0.1 |
| Female (%) | 15.4% | 21.7% | |
| Obese (%) | 15.4% | 18.2% | 0.83 |
| Diabetic (%) | 44.7% | 43.6% | 0.91 |
| HTN (%) | 53.3% | 51% | 0.86 |
| Dyslipidemia (%) | 12.0% | 23.8% | 0.22 |
| Smokers (%) | 63.7% | 56% | 0.21 |

| | | | |
|---|---|---|---|
| + ve family history (%) | 6.7% | 16.8% | 0.10 |
| Troponin (ng/mL) | 8.1±2 | 5.0±2.3 | 0.06 |
| CK-MB (IU/L) | 194±34 | 103±23 | 0.03 |
| Ejection fraction (%) | 41±5 | 55±3 | 0.02 |
| Platelet (×$10^3$/µL) | 344±113 | 227±83 | 0.0002 |
| Lymphocyte (×$10^3$/µL) | 1.72±0.4 | 2.1±0.8 | 0.01 |
| Platelet/lymphocyte ratio | 199.3±51 | 101±52 | 0.002 |
| Infarction site | | | |
| Anterior (%) | 35.6% | 64.1% | 0.06 |
| Lateral (%) | 51% | 51% | |
| Inferior (%) | 17.3% | 82.6% | |
| Left anterior descending (%) | 35.6% | 64.1% | 0.3 |
| Left circumflex (%) | 14.2% | 85.6% | |
| Obtuse marginal 1 (%) | 33.2% | 66.6% | |
| Obtuse marginal 3 (%) | 1% | 99% | |
| Right coronary artery (%) | 19.1% | 80.7% | |

There were 100 patients participated in the research, with a mean age of 52.8±11.0, a body mass index of 27.5±2.4, 60 (81%) of them being men, 48 (58%) of them smoking, 87 (43%) of them having diabetes, 91 (50%) of them having hypertension, 34 (17.4%) of them being obese, and 40 (20.4%) of them having dyslipidemia. 27 patients (13%), 83 (61.4%), 74 (37.4%), and 3 (2%), respectively, had anterior STEMI, inferior STEMI, and lateral STEMI. There were no risk factors in 11 (5%) patients, one in 20 (25%) patients, two in 41 (34.4%) patients, three in 39 (25.3%) patients, and four in 15 (7%) patients. The mean troponin was 7.73.1, the mean CK-MB was 103±66, the mean PLR was 14.21±11, the mean EF was 46.4%±7.6%, and the mean WMSI was 1.1±0.2.

In 73 patients (61.4%) who had percutaneous coronary intervention (PCI) to the left anterior descending using 67 (71%) drug-eluting stents (DESs), PPCI to the offending artery was carried out. 20 patients (10.4%) underwent PCI to the left circumflex with 20 (10.4%) DESs, 2 patients (1.4%) underwent PCI to the OM1, 1 patient (0.4%) underwent PCI to the OM3, and 51 (21%) patients underwent PCI to the RCA with 51 (21%) DESs.

TIMI flow was used to grade the coronary flow, which revealed that 3 (2%) patients had TIMI 0, 12 (6.4%) had TIMI I, 40 (21%) had TIMI II, and 42 (70.4%) had TIMI III. After successful PCI, we looked at the connections between platelet, lymphocyte, and PLR and risk variables (clinical and angiographic results). The platelet count was considerably greater in the no-reflow group compared to the usual reflow group (344±113 against 227±83, P<0.0002, respectively) and in hypertension patients compared to non-hypertensive patients (271.4±110 versus 237.1±87.7, P<0.016, respectively).

With 17.2±4% versus 24±8%, P<0.0002, the lymphocyte count was considerably lower in the no-reflow group than the reflow group. PLR was substantially higher in the no-reflow group compared to the normal reflow group (23.6±7 against 9.0±5.2, P<0.002, respectively) and in hypertension patients compared to non-hypertensive patients (14.4±9.1 versus 10.8±4.6, P<0.001, respectively). The platelet, lymphocyte, and PLR levels were examined in connection to the patients' clinical and angiographic results using the Pearson correlation coefficient. Platelet counts demonstrated a direct association to TIMI flow (P<0.001) and CK-MB (P<0.003) from all clinical and angiographic data, respectively. The total

lymphocyte count had a direct correlation with HB (P<0.002) and an inverse relationship with TIMI flow (P=0.001). PLR ratio shown a clear connection with CK-MB and TIMI flow (P<0.005 and P<0.0002, respectively).

To determine the independent determinants of TIMI flow in STEMI patients following PPCI, multivariate logistic regression analysis was used. PLR and EF% were independent predictors of TIMI flow in STEMI patients following PPCI (PLR β: 0.484, 95% CI: 0.005-0.002, P<0.001) and (EF% β: 3.406, 95% CI: 0.008-0.033, P<0.003).

## DISCUSSION:

PLR was a reliable indicator of no reflow in STEMI patients receiving PPCI in the current trial. PLR had a stronger relationship with CK-MB, a measure of cardiac enzyme levels, and was greater in hypertension individuals. When compared to patients with delayed or no flow, STEMI patients who had recovered normal coronary flow (TIMI III) had significantly lower platelet counts and PLR but greater lymphocytic counts. The PLR has been suggested as a substitute pro-thrombotic and inflammatory marker in several investigations that have linked the noreflow phenomena to elevated inflammatory activity [6, 7]. Our research supports the association between PLR and the prevalence of no-reflow as a post-procedural issue after PPCI.

No-reflow's aetiology appears to be complex, despite the fact that the pathophysiology of the condition has not yet been fully understood. These factors include distal embolisation of the culprit lesion, endothelial damage, reactive oxygen species production, microvascular leukocytes, platelet plugging, complex interactions between neutrophils and platelets induced by the inflammatory process, and reperfusion injury from neutrophil aggregation [8,9].

PLR originally attracted interest in cancer patients as a prognostic marker [10,11], and then it attracted increasing interest in terms of its value as a prognostic marker in cardiovascular medicine. Platelet activation, a crucial stage of the inflammatory response in cardiovascular events such as CAD, is the mechanism of platelet participation that has been hypothesised [12].

Numerous inflammatory mediators are generated during inflammation, such as interleukin [IL]-1, IL-3, and IL-6, which encourage megakaryocytes to multiply and raise platelet levels in the circulation [13]. By secreting cytokines and coagulation factors, activated platelets aid in the development of an inflammatory milieu that is conducive to atherosclerosis [13]. The regulatory and dormant mechanism of inflammation, on the other hand, is provided by lymphocytes [14,15]. Along with early therapy with pharmacological and/or interventional strategies, early risk stratification to identify individuals at high risk of angiographic no-reflow is crucial for its prevention.

High PLR (>150) doubles the risk of in-hospital, all-cause, and cardiovascular mortality, according to a recent analysis of eight pooled cohorts with a total of 6627 patients who had acute coronary syndrome (pooled relative risk, 2.15; 95% CI, 1.73-2.67, 1.95, and 1.30-2.91, respectively) [16]. PLR and cardiovascular incidents have been linked, according to earlier studies.

Another research [16] established the prognostic utility of PLR in patients with stable CAD having PCI and stent implantation. Higher PLR independently predicted 4-year death in non-STEMI patients. An investigation into the predictive usefulness of PLR and neutrophil-lymphocyte ratio (NLR) in patients without STEMI following elective PCI with drug-eluting stents [17] revealed that PLR and NLR, both individually and together, predicted long-term significant adverse cardiovascular events. Similar to this, 520 individuals with acute STEMI were the subject of a study [18] that discovered a decreased risk of no-reflow (22% of patients). These patients were older than the

ones whose coronary flow had returned to normal. PLR's prediction of the angiographic no-reflow on the admission of 126 had a 73% sensitivity and 71% specificity. Furthermore, no-reflow after PPCI was independently predicted by PLR and stent length.

When combined with previously published data, the current study highlights the importance of inflammatory markers in the pathophysiology of coronary circulation and the no-reflow phenomena and suggests a potential role for the theory of inflammation. However, further research is needed to pinpoint the precise role that PLR plays in the pathophysiology of this condition.

## LIMITATION:

Our research has certain drawbacks. First, there was insufficient patient follow-up and a limited sample size to investigate the frequency of adverse cardiac events and the connection between these cardiac events and PLR. Second, additional inflammatory biomarkers including thromboxane A2 and endothelin 1 were not assessed. Third, there was a large variation in the incidence of no-reflow during PCI, from 1 to 40%. While few other studies also show significant no-reflow rates, most sizable modern research do not. The use of a standardized definition of no-reflow and the clinical and procedural features may be the cause of this discrepancy. Despite epicardial coronary patency, no-reflow is typically understood to be a transient, angiographically visible flow impairment. However, other studies have used more expansive definitions, such as failure to achieve TIMI III flow at the end of the procedure or decreased myocardial flow following PCI as demonstrated by perfusion imaging. In light of this, it is unclear if PLR would have the same prognostic data if the no-reflow rate were lower. Finally, PLR has a limited clinical applicability because it is not often assessed prior to PPCI.

## CONCLUSION:

In STEMI patients undergoing PPCI, high PLR and reduced EF are reliable, independent predictors of no-reflow. PLR evaluation may be considered when addressing patient prognosis and acting as a helpful indicator in the risk stratification model.

## FUNDING:

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