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Original Article

# Platelet to lymphocyte ratio is associated with contrast induced nephropathy after primary percutaneous coronary intervention for ST-elevation myocardial infarction section

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**Abstract**

**Aim:** Platelet to lyphocyte ratio is a novel inflammatory marker which is correlated with markers such as C-reactive protein and associated with cardiovascular outcomes in coronary artery disease. Contrast iduced nephropathy is an important complication of pecutaneous coronary intervention. Association between platelet to lymphocyte ratio and contrast induced nephropathy development after primary percutaneous coronary intervention with a diagnosis of ST-elevation myocardial infarction was evaluated in this study.

**Material and Methods:** Data of 3352 consecutive patients who underwent primary percutaneous coronary intervention for ST-elevation myocardial infarction were analysed. Independent predictors of contrast induced nephropathy were investigated with logistic regression analysis.

**Results:** Patients with contrast induced nephropathy had significantly higher platelet to lymphocyte ratio (150.0 vs 119.1, p=0.001). In multivariate logistic regression analysis platelet to lymphocyte ratio (OR 1.100, 95% CI 1.050-1.130, p=0.033) was found as an independent predictor of contrast induced nephropathy.

**Conclusion:** Platelet to lymphocyte ratio may have a role to predict contrast induced nephropathy in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction.

**Keywords:** Contrast Induced Nephropathy; ST-Elevation Myocardial Infarction; Primary Percutaneous Coronary Intervention.

## INTRODUCTION

Primary percutaneous coronary intervention (p-PCI) is the treatment modality of choice for ST-segment elevation myocardial infarction (STEMI). Despite its well-known merits, p-PCI is associated with a higher risk for contrast induced nephropathy (CIN) compared to other cardiovascular invasive procedures since acute coronary syndrome (ACS) predisposes to CIN (1,2).

While general population has a 2% risk of CIN after PCI, risk of patients with diabetes or previous renal impairment may reach 50% (3,4). In addition, acute coronary syndrome increases the risk of CIN almost three fold (1,2). Since, identification of patients with increased risk for CIN which is associated with increased health costs, morbidity and mortality is essential (5).

Platelet-to-lymphocyte ratio (PLR) is a relatively novel inflammatory marker. Previous studies showed that PLR is correlated with C-reactive protein and predicts cardiovascular outcomes in coronary artery disease peripheral artery disease ( 6,7). Moreover, PLR was found as a an independent predictor of prognosis after STEMI and non-ST segment elevation myocardial infarction (7,8).

Two recent small studies showed that PLR might be associated with CIN in patients undergoing PCI for non-ST segment elevation ACS (9,10). In the present study, relationship of PLR with development of CIN after p-PCI for STEMI was evaluated in a large sample size of patients since it has not been investigated so far.

## MATERIAL AND METHODS

### Study population

Between December 2009 and September 2014, 3352

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consecutive STEMI patients who underwent urgent cardiac catheterization were enrolled into the study. Patients with chronic kidney disease and receiving peritoneal or hemodialysis treatment were excluded from the study along with patients with a renal transplant, collagen vascular disease and acute infection. Patients who received contrast agent in last month and aminoglycosides, metformin, non-steroidal anti-inflammatory drugs, acetylcysteine or intravenous loop diuretics 1 week before and after PCI were also excluded from the study. As a result, one hundred and eighty two patients were excluded from the study and remaining 3170 formed the study population. The study protocol was approved by the Institutional Ethics Committee.

**Analysis of patient's data and laboratory analysis**

Medical records were used to obtain data about medical history including cardiovascular risk factors and sociodemographic parameters. Blood samples were taken and 12-lead ECG was obtained from all patients at admission. A transthoracic echocardiographic examination was done 24 to 72 hours after p-PCI. Modified Simpson's method was used to calculate left ventricular ejection fraction. Basic hematologic parameters including platelet and lymphocyte counts were analyzed by using an automatic hematology analyzer (Coulter LH Series, Beckman Coulter, Inc, Hialeah, Florida).

**Definitions**

ST-segment elevation myocardial infarction was defined as symptoms consistent with ischemia and a ST segment elevation ≥1 mm in at least two contiguous electrocardiogram leads. A ST elevation of 1.5 mm for female patients, 2 mm for male patients >40 years old and 2.5 mm for male patients < 40 years old were required for V2 and V3. A new onset left bundle-branch block was also considered as STEMI. A serum creatinine level increase ≥ 0.5 mg/dl or ≥ 25% above baseline within 72 h after contrast administration were defined as CIN. Modification of Diet in Renal Disease (MDRD) equation was used to calculate estimated glomerular filtration rate (11) . Patients without a documented diabetes diagnosis which do not use insulin or oral antidiabetics at admission were accepted as non-diabetic. Patients who are on ongoing antihypertensive treatment or with a systolic blood pressure 140 mmHg or diastolic blood pressure ≥ 90 mmHg were defined as hypertensive. Current tobacco users were defined as smokers. Patients who have a parent or sibling with documented coronary artery disease (CAD) before 60 years of age were defined as having positive family history for coronary artery disease.

**Coronary angiography and PCI**

A chewable 300 mg aspirin, 600 mg clopidogrel and 5,000 units of intravenous heparin were given before coronary angiography, followed by additional heparin boluses if necessary to maintain an activated clotting time of > 300 s (or 200-250s if tirofiban used). All patients were given 100 mg aspirin and 75 mg clopidogrel daily as maintenance antiplatelet therapy. Nonionic, iso-osmolar contrast material was used (iodixanol, Visipaque 320 mg/100 ml; GE Healthcare, Cork, Ireland). After visual angiographic evaluation, primary angioplasty including balloon angioplasty and stent implantation was performed just for IRA. The use of tirofiban was left to the discretion of the operator. Hydration with intravenous isotonic saline (0.9%) at a rate of 1 ml/kg/h for 12 h was started immediately after intervention to all patients.

**Statistical analysis**

SPSS Statistics version 20.0 for Windows ( SPSS Inc, Chicago, IL) was used for statistical analysis. Data were presented as mean and standard deviation, median and interquartile range, or proportions as appropriate. After the evaluation of distribution pattern with The Kolmogorov-Smirnov test, data with normal distribution was compared with Student's t test and data without normal distribution was compared with Mann-Whitney U test . Chi-square test was used to evaluate categorical variables. Optimum cut-off levels of PLR to predict the presence of CIN was determined with receiver-operating characteristics (ROC) curve analysis. Logistic regression analysis was used to examine the association between presence of CIN and other variables. Any variable with a p value < 0.1 in univariate logistic regression analysis was included to the multivariate logistic regression model. A p value < 0.05 was considered as significant.

## RESULTS

Baseline characteristics of the patients were shown in table 1. 719 patients (22.6%) developed CIN. Patients with CIN were significantly older than patients without (59.60 vs. 55.6, p=0.001).

Rates of diabetes mellitus (29.2% vs. 21.7%, p=0.001) and hypertension (45.2% vs. 38.0, p=0.001) were higher in CIN group. Patients with culprit lesion in left anterior descending artery (54.7% vs 46.9%) and post-procedural TIMI flow grade 1 (13.4% vs. 5.9%) were more frequent in CIN group. (Table 2.)

Patients with CIN had significantly higher admission creatinine (0.95 vs. 0.80, p=0.001), peak CK-MB (191 vs.155, p=0.001), WBC count (13.50 vs.12.5, p=0.006), PLR (150.0 vs 119.1, p=0.001) and neutrophil to lymphocyte ratio (NLR) (5.20 vs 4.15, p=0.001) (table 3). In multivariate logistic regression analysis, age (OR 1.023, 95% CI 1.015-1.031, p=0.001), Killip class >1 (OR 1.529, 95% CI 1.050-2.227, p=0.027), PLR (OR 2.100, 95% CI 1.550-2.630, p=0.001) and NLR (OR 1.033, 95% CI 1.010-1.070, p=0.038) were found as independent predictors of CIN (table 4).

**Table 1. Baseline characteristics of study patients**

| Variables | CIN (+) (n=719) | CIN (-) (n=2451) | p value |
|---|---|---|---|
| Age, years | 59.60±12.9 | 55.61±11.4 | 0.001 |
| Male gender, n (%) | 581 (80.8) | 2065 (84.3) | 0.059 |
| Diabetes mellitus, n (%) | 210 (29.2) | 532 (21.7) | 0.001 |
| Hypertension, n (%) | 325 (45.2) | 932 (38.0) | 0.001 |
| Family history of CAD, n (%) | 129 (17.9) | 487 (19.9) | 0.249 |
| Hyperlipidemia, n (%) | 228 (31.7) | 796 (32.5) | 0.699 |
| Smoking, n (%) | 430 (59.8) | 1524 (62.2) | 0.250 |
| Hemodialysis, n (%) | 4 (0.6) | 3 (0.1) | 0.084 |
| Previous CABG, n (%) | 16 (2.2) | 75 (3.1) | 0.239 |
| Previous PCI, n (%) | 74 (10.3) | 200 (8.2) | 0.074 |
| Anterior MI, n (%) | 393 (54.7) | 1138 (46.4) | 0.001 |
| Cardiogenic shock, n (%) | 54 (7.5) | 45 (1.8) | 0.001 |
| Killip class >1, n (%) | 94 (13.1) | 101 (4.1) | 0.001 |
| SBP < 100 mmHg, n (%) | 100 (13.9) | 197 (8.0) | 0.001 |
| HR > 100 min-1, n (%) | 72 (10.0) | 87 (3.5) | 0.001 |
| LVEF, (%) | 45.76±9.5 | 47.70±7.7 | 0.001 |
| Admission anemia, n (%) | 193 (26.8) | 520 (21.2) | 0.001 |

CABG, coronary artery by-pass graft; CAD, coronary artery disease; CIN, contrast induced nephropathy; HR, heart rate; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary interventrion; SBP, systolic blood pressure;

**Table 2. Angiographic and Procedural Characteristics of Patients**

| Variables | CIN (+) (N=719) | CIN (-) (N=2451) | P value |
|---|---|---|---|
| Culprit lesion, n (%) | | | |
| LMCA | 3 (0.3) | 4 (0.2) | 0.009 |
| LAD | 393 (54.7) | 1152 (46.9) | |
| CX | 85 (11.8) | 353 (14.3) | |
| RCA | 235 (32.7) | 928 (37.8) | |
| Graft | 4 (0.6) | 14 (0.6) | |
| No. of diseased vessels, n (%) | | | |
| 1 | 293 (40.8) | 1116 (45.5) | 0.076 |
| 2 | 244 (33.9) | 771 (31.5) | |
| 3 | 182 (25.3) | 564 (23.0) | |
| Preprocedural TIMI flow grade, n (%) | | | |
| 1 | 666 (92.6) | 2186 (89.2) | 0.024 |
| 2 | 34 (4.7) | 178 (7.3) | |
| 3 | 19 (2.6) | 87 (3.5) | |
| Postprocedural TIMI flow grade, n (%) | | | |
| 1 | 96 (13.4) | 144 (5.9) | 0.001 |
| 2 | 40 (5.6) | 119 (4.9) | |
| 3 | 583 (81.1) | 2188 (89.3) | |
| Contrast volume (ml) | 250 (100-750) | 250 (100-850) | 0.058 |
| Tirofiban use, n (%) | 352 (49.0) | 1174 (47.9) | 0.618 |
| Stent length (mm) | 18 (8-56) | 18 (5-66) | 0.058 |
| Stent diameter (mm) | 3 (2.5-4.0) | 3 (2.5-4.5) | 0.065 |

CIN, contrast induced nephropathy; CX, circumflex coronary artery; LAD, left anterior descending artery; LMCA, left main coronary artery, RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction

| Table 3. Laboratory Findings of the Patients | | | |
|---|---|---|---|
| **Variables** | **CIN (+) (N=719)** | **CIN (-) (N=2451)** | **P value** |
| Admission creatinine (mg/dl) | 0.95 (0.5-10.0) | 0.80 (0.5-7.3) | 0.001 |
| Peak creatinine (mg/dl) | 1.3 (0.6-8.1) | 1.0 (0.6-5.5) | 0.001 |
| Peak CK-MB (U/l) | 191 (14-1544) | 155 (7-1827) | 0.001 |
| Total cholesterol (mg/dl) | 188.0±40.0 | 190.0±39.0 | 0.229 |
| LDL-C (mg/dl) | 118.0±31.0 | 119.0±31.0 | 0.447 |
| HDL-C (mg/dl) | 40.5±10.1 | 40.3±8.1 | 0.583 |
| Trigyceride (mg/dl) | 135 (26-1150) | 132 (11-1649) | 0.342 |
| Glucose (mg/dl) | 134 (48-614) | 132 (18-598) | 0.071 |
| WBC (x $10^3$/ml) | 13.50±4.3 | 12.5±3.7 | 0.006 |
| Hemoglobin (g/L) | 13.6±2.9 | 13.8±2.8 | 0.095 |
| MPV (fL) | 8.6±1.0 | 8.6±2.3 | 0.245 |
| HbA1C (%) | 6.54±0.78 | 6.52±0.98 | 0.061 |
| RDW (%) | 13.86±1.5 | 13.77±1.35 | 0.302 |
| PLR | 150 (7.50-806.7) | 119.10 (6.1-620) | 0.001 |
| NLR | 5.20 (0.2-26.8) | 4.15 (0.5-25.7) | 0.001 |

**CK-MB, creatinine kinase myocardial band; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; RDW, red cell distribution width; WBC, white blood cell**

| Table 4. Independent Predictors of CIN | | | | |
|---|---|---|---|---|
| **Variables** | **Univariable** | | **Multivariable** | |
| | **OR ( 95% CI)** | **p value** | **OR ( 95% CI)** | **p value** |
| Age | 1.029 (1.021-1.036) | 0.001 | 1.023 (1.015-1.031) | 0.001 |
| Diabetes | 1.488 (1.234-1.795) | 0.001 | 1.103 (0.900-1.352) | 0.346 |
| Hypertension | 1.344 (1.137-1.590) | 0.001 | 1.130 (0.939-1.358) | 0.195 |
| Killip class > 1 | 3.499 (2.607-4.697) | 0.001 | 1.529 (1.050-2.227) | 0.027 |
| BP < 100 mmHg | 1.848 (1.430-2.389) | 0.001 | 0.954 (0.682-1.335) | 0.785 |
| HR > 100 $min^{-1}$ | 3.024 (2.187-4.181) | 0.001 | 1.096 (0.651-1.848) | 0.730 |
| LVEF | 0.973 (0.964-0.983) | 0.001 | 0.998 (0.987-1.009) | 0.715 |
| Anemia | 1.363 (1.125-1.650) | 0.002 | 1.001 (1.000-1.003) | 0.991 |
| Peak CK-MB | 1.001 (0.911-1.003) | 0.139 | - | - |
| WBC | 1.041 (1.019-1.062) | 0.001 | 1.020 (0.994-1.047) | 0.125 |
| PLR | 2.130 (1.610-2.440) | 0.001 | 2.100 (1.550-2.630) | 0.001 |
| NLR | 1.079 (1.059-1.100) | 0.001 | 1.033 (1.010-1.070) | 0.038 |
| Inotrope use | 3.740 (2.871-4.871) | 0.001 | 1.289 (0.841-1.974) | 0.244 |

**BP, blood pressure; CK-MB, creatinine kinase myocardial band; HR, heart rate; LVEF, left ventricular ejection fraction; NLR, neutrophil to lymphocyte ratio; PLR, platelet to lymphocyte ratio; WBC, white blood cell**

## DISCUSSION

The results of the present study suggested that PLR is an independent predictor of CIN in patients with STEMI who underwent p-PCI. Age, higher Killip class and NLR were other independent predictors of CIN.

One of the most important complications of p-PCI is contrast induced nephropathy. Previous studies revealed that patients with CIN have higher mortality and morbidity including end-stage renal failure and re-infarction (11-13). In patients with STEMI, CIN is associated with poorer short and long term prognosis even in the setting of successful early revascularization (14,15).Older age, hypovolemia, DM, hypertension, heart failure, dyslipidemia, low GFR, anemia and use of higher volume of contrast media are major risk factors for CIN (16).

Exact pathophysiologic mechanism of CIN has not been completely understood. However, inflammation clearly plays a central role in the development of CIN (17). Decrease of the renal blood flow due to myocardial infarction possibly starts the renal injury. Neuro-hormonal activation such as sympathetic nervous system and the renin-angiotensin-aldosterone system occurs as a result and causes renal vasoconstriction and medullary

hypoxia. Direct toxicity of the contrast medium is the other contributor factor (18-20).

Recent studies showed that PLR is an inflammation marker which is correlated with CRP and fibrinogen levels (21,22,6). Inflammation causes both thrombocytosis and lymphopenia and PLR, as a marker combines both, predicts clinical outcomes better than platelet or lymphocyte count alone. Stress induced hypercortisolemia, subsequent release of platelets into the bloodstream and transient lymphopenia causes incrase of PLR in proinflammatory and prothrombotic states (23). Possibly, PLR predicts CIN since it is an indicator of higher inflammatory burden in patients with CIN.

Two recent small studies showed that PLR might be associated with CIN in patients undergoing PCI for non-ST elevation ACS (9,10). The present study supports these two studies and clearly shows the association between PLR and CIN after p-PCI.

There are some limitations in the present study. Its retrospective and single center design is the first one. The second one is that PLR was measured only once and there are not any information about a temporal trend of PLR. Moreover, other well-known inflammation markers such as C reactive protein were not measured and it is another limitation of the study.

## DISCUSSION

In conclusion, PLR is an independent predictor of CIN after p-PCI in this patient group. As a cheap and readily available marker, PLR may have a role in prediction of CIN in STEMI patients undergoing p-PCI.

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