

# Predictive value of lymphocyte-to-monocyte ratio in patients with contrast-induced nephropathy after percutaneous coronary intervention for acute coronary syndrome

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## ABSTRACT

**Background and Objectives:** Lymphocyte-to-monocyte ratio (LMR) has emerged as a new indirect marker of inflammation, which is associated with adverse outcomes in cardiovascular diseases. The aim of this study was to evaluate whether admission LMR is associated with contrast-induced nephropathy (CIN) in patients who underwent percutaneous coronary intervention for acute coronary syndrome (ACS). **Methods:** A total of 873 patients were assessed. LMR was calculated via dividing lymphocyte count by monocyte count. **Results:** LMR was significantly lower in the with-CIN group. ROC analysis showed that the LMR ratios <2.52 predicted CIN development with sensitivity of 66.3% and specificity of 55.8%. Multivariate analysis showed that eGFR, admission glucose, and LMR were independent predictors of CIN in patients with ACS. **Conclusion:** LMR is an easily accessible marker and could be used as a predictor of CIN in patients with ACS undergoing percutaneous coronary intervention.

**Key words:** lymphocyte-to-monocyte ratio, acute coronary syndrome, contrast-induced nephropathy, percutaneous coronary intervention

## INTRODUCTION

Contrast-induced nephropathy (CIN) is characterized by the development of acute renal impairment following contrast medium exposure during cardiovascular procedures such as coronary angiography, percutaneous coronary intervention (PCI), or transcatheter valve interventions.<sup>[1, 2]</sup> The incidence changes between 5% and 25% after cardiovascular interventions in several studies.<sup>[3, 4]</sup> It has been demonstrated that CIN is associated with worse clinical outcomes and prognosis in these patients.<sup>[5, 6]</sup> The patients with acute coronary syndrome (ACS) tend to develop higher rates of CIN than elective patients.<sup>[3, 4]</sup> CIN can be observed nearly in half of patients with diabetes mellitus or chronic kidney disease

(CKD). Because of the increased incidence of CIN after urgent percutaneous coronary intervention (PCI), easily accessible markers might be useful for detection of the patients who might develop CIN.<sup>[6]</sup> Early identification of CIN affects its progression and clinical outcomes.<sup>[4]</sup>

Various studies have showed that systemic inflammatory response severity associated with poor prognosis in cardiovascular diseases could be measured from peripheral blood-based parameters.<sup>[7, 8]</sup> Lymphocytes and monocytes are the two important cells included in inflammatory response and immune reaction. The lymphocyte-to-monocyte ratio (LMR) is recently developed inflammatory marker and was associated with various cardiovascular diseases.<sup>[7, 9-12]</sup> Although underlying pathophysiology of

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CIN has not been fully understood, it has been found that inflammation plays a central role in acute renal injury and CIN.<sup>[13, 14]</sup> In this study, we aim to investigate the role of admission LMR to predict CIN development in patients with acute coronary syndrome who underwent primary PCI.

## PATIENTS AND METHODS

### *Study population*

We studied consecutive patients with acute coronary syndrome who underwent coronary angiography at our institution between March 2013 and December 2018. Our hospital database was retrospectively analyzed, and the data of 1009 patients were recorded consecutively. For this analysis, patients with emergency surgery, with multivessel PCI in first attempt, and in medical therapy due to diffuse disease after coronary angiography were excluded in an attempt to make the study group more homogeneous. Patients with acute renal failure or end-stage renal failure requiring dialysis on admission, active infection, primary chronic liver disease, known malignant diseases or end-stage other diseases, chronic inflammatory or autoimmune disease history, chronic medical therapy with steroid or nonsteroidal anti-inflammatory drugs, history of recipient of transplanted organs, and contrast medium exposure within the last 2 weeks were also excluded from the study. According to the inclusion and exclusion criteria, 136 patients were excluded, and we conducted our study with the remaining 873 patients. The study protocol was approved by Ethics Committee of the Kocaeli University.

### *Study protocol and definitions*

STEMI was defined as the (1) prolonged typical chest pain (>20 minutes) and (2) the presence of ST elevation at least 1 mm in 2 or more continuous leads with reciprocal ST depression and new-onset left bundle branch block.<sup>[15]</sup> Unstable angina pectoris (UA) and non-ST elevation myocardial infarction (NSTEMI) were described as NSTEMI-ACS according to the presence of ST-segment depression, T-wave inversion, or no electrocardiographic changes in appropriate clinical manifestations including chest pain or angina-equivalent symptoms.<sup>[16]</sup> Thrombolysis in Myocardial Infarction grade 3 coronary flow in the treated culprit vessel with a residual stenosis <20% was considered successful PCI without any major complication. Multivessel disease is defined by the presence of ≥50% diameter stenosis of two or more epicardial coronary arteries.

### *Coronary angiography and medical therapy*

All patients underwent coronary angiography 1–72 hours after admission and PCI with stent implantation was performed to culprit lesion. First medical contact (FMC) was defined as first direct contact by a health

practitioner with the patient. “FMC to wire time” was the time from FMC to the wire crossing of culprit lesion. Coronary angiography was performed using the femoral and radial approach according to operator’s choice. PCI was performed immediately after diagnostic coronary angiography when appropriate in all patients. Intravenous unfractionated heparin was administered 70–100 units/kg to maintain an activated clotting time of 200–250 seconds (>300 seconds when tirofiban was not used) during PCI.

Nonionic, low-osmolar contrast medium (iohexol; Omnipaque 350 mg/mL; GE Healthcare) was used to visualize the coronary arteries. Coronary stenting was performed using standard techniques. The use of tirofiban was left to the discretion of the interventional cardiologist during PCI. CIN was defined as an increase in serum creatinine level of ≥0.5 mg/dL or ≥25% above baseline within 48–72 hours after contrast medium administration.<sup>[17]</sup>

On admission, all patients received aspirin and available ADP receptor blocker. In addition, the decision to use beta-blockers, angiotensin-converting enzyme inhibitor (ACEi) or angiotensin receptor blocker (ARB), statins, diuretics, and nitrates was also left to the discretion of the interventional and clinical cardiologists as directed by international guidelines. About the patients with STEMI, if the patient had been diagnosed for CKD previously, the hydration protocol was started immediately before the procedure. For the other patients with STEMI, the hydration protocol was started just after the procedure if de novo CKD was detected on admission or total contrast volume used for intervention was above 4 mL/kg. The hydration protocol was intravenous isotonic saline (1 mL/kg/h, 0.9% sodium chloride) for 24 hours after intervention. Also, hydration rate was reduced to 0.5 mL/kg/h in cases with LVEF <40% or overt heart failure. Patients with NSTEMI-ACS and CKD were started hydration at least 12 hours before the procedure and continued after intervention for 24 hours. The hydration protocol was same to patients with STEMI.

### *Data collection*

The collected data included demographic information and medical history, such as age, gender, smoking status, body mass index (BMI), prior MI, prior PCI, hypertension, using of statin and ACE or ARB before admission, hyperlipidemia, and diabetes mellitus. Vital signs on admission including systolic blood pressure, diastolic blood pressure, and heart rate were evaluated for the study. Patients’ rhythm was obtained from 12-lead electrocardiography (ECG).

Venous blood samples were drawn immediately after hospital admission before coronary angiography. The

monocyte, lymphocyte, neutrophil, hemoglobin, and other hematological parameters were counted using the automated blood cell counter within 30 minutes after blood sampling. Admission biochemical analyses including creatinine, triglyceride, cholesterol, and glucose levels were also measured via the standard laboratory techniques. These laboratory results were recorded in all patients. The estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formula. The LMR was calculated as the ratio of the lymphocyte count to the monocyte count. The NL ratio was calculated as the ratio of the neutrophil count to the lymphocyte count. The PL ratio was calculated as the ratio of the platelet count to the lymphocyte count. Serum creatinine level measurement was repeated at 48 and 72 hours after contrast medium exposure in all patients. Left ventricular ejection fraction (LVEF) was calculated with modified Simpson method by echocardiography within 24 hours after admission.

### Statistical analysis

The statistical analysis of the study was performed using SPSS 21.0 software (SPSS, Chicago, Illinois, USA). Continuous variables are presented as mean  $\pm$  standard deviation and categorical variables as numbers, percentages, or proportions. The normality of continuous variables' distribution was determined using the Kolmogorov-Smirnov test. Between-group comparisons were performed using the chi-square test for categorical variables, independent-samples *t* test for continuous variables with normal distributions, and the Mann-Whitney *U* test for continuous variables with abnormal distributions. Univariate and multivariate logistic regression analyses were used to determine the independently associated predictors of CIN. The potential candidate predictors were assessed by univariate analysis. Variables that were associated with CIN on univariate analysis were included as covariates in a multivariate logistic regression model. The receiver-operating characteristics (ROC) curve analysis was performed to identify optimal cutoff point of LMR in the predicting of CIN, and the sensitivity and specificity at that point were obtained. All analyses were two-sided and considered significant at a *P* value  $< 0.05$ .

## RESULTS

A total of 873 patients were enrolled after applying inclusion-exclusion criteria in this study, and there were 95 (10.9%) patients in the with-CIN group, and 778 (89.1%) patients in the without-CIN group. Baseline clinical characteristics of study patients with and without CIN are summarized in Table 1. The mean age of with-CIN group ( $66.2 \pm 9.3$ ; 66.3% male) was higher than that of

the without-CIN group ( $58.7 \pm 11.6$ ; 72.8% male), and the difference was statistically significant ( $p < 0.001$ ). There was no statistical difference between with-CIN group and without-CIN group in terms of gender, blood pressure, BMI, and heart rate on admission. The patients in the with-CIN group had significantly a higher prevalence of diabetes mellitus, hypertension, previous MI, previous CABG, and lower LVEF than those in the without-CIN group. No significant differences in the frequency of smoking, hyperlipidemia, previous PCI, and type of rhythm on admission were observed between the groups. Additionally, there was no difference in terms of use of statin and ACEi or ARB therapy on hospital admission between the groups.

Laboratory findings on admission of study patients in with- and without-CIN group are shown in Table 2. In the with-CIN group, basal creatinine ( $1.47 \pm 0.94$  *vs.*  $1.06 \pm 0.71$ ,  $P < 0.001$ ) and serum glucose level ( $162.9 \pm 98.3$  *vs.*  $127.3 \pm 66.3$ ,  $P = 0.004$ ) were higher, whereas eGFR ( $56.1 \pm 27.6$  *vs.*  $81.7 \pm 27.4$ ,  $P < 0.001$ ), hemoglobin ( $12.48 \pm 2.12$  *vs.*  $13.58 \pm 1.88$ ,  $P < 0.001$ ), total cholesterol ( $170.9 \pm 44.5$  *vs.*  $184.4 \pm 41.2$ ,  $P < 0.001$ ), and HDL cholesterol ( $36.4 \pm 10.1$  *vs.*  $38.2 \pm 8.9$ ,  $p = 0.012$ ) were lower. Postprocedural creatinine level at 48–72 hours was significantly higher in the patients with CIN than those without CIN ( $2.64 \pm 1.23$  *vs.*  $1.08 \pm 0.73$ ,  $P < 0.001$ ). No significant differences in the monocyte, lymphocyte, and platelet count were observed between the groups. The neutrophil count [ $0.64$  ( $0.44$ – $0.95$ ) *vs.*  $0.61$  ( $0.44$ – $0.80$ ),  $P = 0.030$ ] and mean platelet volume [ $9.4$  ( $8.4$ – $10.5$ ) *vs.*  $8.7$  ( $7.7$ – $9.9$ ),  $P < 0.001$ ] were significantly higher in the with-CIN group than in the without-CIN group. NLR was nearly significantly higher in the with-CIN group than in the without-CIN group [ $3.99$  ( $2.88$ – $7.52$ ) *vs.*  $3.79$  ( $2.24$ – $6.06$ ),  $P = 0.055$ ]. However, LMR was significantly lower in the with-CIN group than in the without-CIN group [ $2.42$  ( $1.67$ – $3.49$ ) *vs.*  $3.25$  ( $2.40$ – $4.99$ ),  $P < 0.001$ , respectively].

The angiographic and interventional characteristics of the study patients with and without CIN are presented in Table 3. There was no difference in term of type of ACS between the with-CIN group and without-CIN group. There was no difference in terms of FMC to wire time (minutes) in STEMI patients with CIN and without CIN ( $60.8 \pm 29.5$  *vs.*  $55.9 \pm 24.6$ ,  $P = 0.436$ ). FMC to wire time (hours) was higher in NSTEMI-ACS patients with CIN than those without CIN, and it was statistically nearly significant ( $12.9 \pm 5.9$  *vs.*  $14.6 \pm 4.4$ ,  $P = 0.056$ ). Total amount of contrast media ( $171.6 \pm 36.7$  *vs.*  $161.4 \pm 31.9$ ,  $P = 0.118$ ), the frequency of multivessel disease [ $48$  (50.5%) *vs.*  $318$  (40.9%),  $P = 0.072$ ], and the use of tirofiban during PCI [ $20$  (21.1%) *vs.*  $149$  (19.2%),  $P = 0.658$ ] were higher in the with-CIN group, but these differences were not statistically significant. The

**Table 1: Baseline clinical characteristics of the study patients with and without contrast-induced nephropathy**

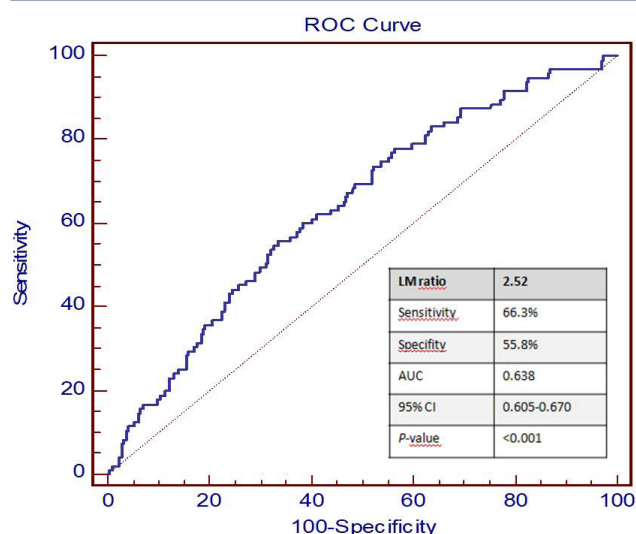
Variables	CIN (+) (n = 95)	CIN (-) (n = 778)	p value
Age (years)	66.2 ± 9.3	58.7 ± 11.6	<0.001
Male, n (%)	63 (66.3%)	566 (72.8%)	0.187
Body mass index (kg/m <sup>2</sup> )	27.5 ± 4.9	27.9 ± 8.4	0.455
Systolic blood pressure, mmHg	125 ± 32	128 ± 24	0.499
Diastolic blood pressure, mmHg	73 ± 18	77 ± 13	0.206
Heart rate on admission, bpm	80 ± 18	78 ± 17	0.101
<b>Comorbidities, n (%)</b>			
Hypertension	43 (45.3%)	274 (35.2%)	0.055
Diabetes mellitus	41 (43.2%)	233 (29.9%)	0.009
Hyperlipidemia	28 (29.5%)	262 (33.7%)	0.412
Smoking	44 (46.3%)	315 (40.5%)	0.276
Previous MI	23 (24.2%)	116 (14.9%)	0.019
Previous PCI	8 (8.4%)	72 (9.3%)	0.790
Previous CABG	12 (12.6%)	50 (6.4%)	0.026
LVEF, %	38.5 ± 16.3	42.9 ± 16.3	0.011
<b>Rhythm, n (%)</b>			
Sinus rhythm	82 (86.3%)	712 (91.5%)	0.134
Atrial fibrillation	8 (6.3%)	49 (8.4%)	
Pacemaker rhythm	5 (5.3%)	17 (2.2%)	
<b>Medical therapy on admission, n (%)</b>			
Statin	17 (17.9%)	149 (19.2%)	0.768
ACEi or ARB	32 (33.7%)	227 (29.2%)	0.364

ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; CABG: coronary artery bypass graft; CIN: contrast-induced nephropathy; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention.

**Table 2: Admission laboratory findings of the study patients with and without contrast-induced nephropathy**

Variables	CIN (+) (n = 95)	CIN (-) (n = 778)	p value
Basal creatinine, mg/dL	1.47 ± 0.94	1.06 ± 0.71	<0.001
Postprocedural creatinine, mg/dL	2.64 ± 1.23	1.08 ± 0.73	<0.001
eGFR, mL/min/1.73 m <sup>2</sup>	56.1 ± 27.6	81.7 ± 27.4	<0.001
Glucose on admission, mg/dL	162.9 ± 98.3	127.3 ± 66.3	0.004
Hemoglobin, g/dL	12.48 ± 2.12	13.58 ± 1.88	<0.001
Total cholesterol, mg/dL	170.9 ± 44.5	184.4 ± 41.2	<0.001
Triglyceride, mg/dL	163.3 ± 106.1	158.9 ± 86.4	0.983
HDL cholesterol, mg/dL	36.4 ± 10.1	38.2 ± 8.9	0.012
LDL cholesterol, mg/dL	130.9 ± 28.1	132.5 ± 29.6	0.708
Monocyte count (/mm <sup>3</sup> ), median (IQR)	0.64 (0.44–0.95)	0.61 (0.44–0.80)	0.161
Lymphocyte count (/mm <sup>3</sup> ), median(IQR)	1.66 (1.21–2.33)	1.86 (1.34–2.43)	0.302
Neutrophil count (/mm <sup>3</sup> ), median (IQR)	7.67 (5.45–11.1)	6.99 (4.92–9.66)	0.030
Platelet count (× 10 <sup>9</sup> /L), median (IQR)	231 (188–281)	237.5 (204–290)	0.211
Mean platelet volume, fL, median (IQR)	9.4 (8.4–10.5)	8.7 (7.7–9.9)	<0.001
Lymphocyte-to-monocyte ratio	2.42 (1.67–3.49)	3.25 (2.40–4.99)	<0.001
Neutrophil-to-lymphocyte ratio	3.99 (2.88–7.52)	3.79 (2.24–6.06)	0.055
Platelet-to-lymphocyte ratio	135.3 (92.1–216.7)	130.1 (96.1–192.7)	0.897

CIN: contrast-induced nephropathy; eGFR: estimated glomerular filtration rate; HDL: high-density lipoprotein; IQR: interquartile range; LDL: low-density lipoprotein.



**Figure 1: The receiver-operating characteristic (ROC) analysis for the lymphocyte-to-monocyte ratio in predicting contrast-induced nephropathy in patients with acute coronary syndrome.**

ratio of culprit vessel of ACS was similar between the two groups. In the with-CIN group, the use of ACEi or ARB therapy during hospitalization [66 (69.5%) *vs.* 662 (85.1%),  $P < 0.001$ ] was lower, whereas the use of diuretic therapy [17 (17.9%) *vs.* 61 (7.8%),  $P = 0.001$ ] was higher compared with the without-CIN group.

Univariate and multivariate logistic regression analysis model of predictors for the postprocedural CIN in study population is presented in Table 4. In univariate analysis, age, previous MI, hypertension, diabetes mellitus, LVEF, admission serum glucose, hemoglobin, eGFR, and LMR were found to be associated with CIN. In the multivariate analysis, eGFR ( $P < 0.001$ , odds ratio [OR] 0.978, 95% CI 0.968–0.988), serum glucose on admission ( $P = 0.030$ , [OR] 1.004, 95% CI 1.000–1.007), and LMR ( $P = 0.012$ , [OR] 0.850, 95% CI 0.749–0.965) were found to be independent predictors of CIN in the study patients (Table 4). The optimal cutoff point of LMR for CIN prediction was found to be 2.52 in the ROC curve analysis (AUC = 0.638, 95% CI 0.605–0.670,  $P < 0.001$ ). The LMR  $< 2.52$  predicted CIN development with sensitivity of 66.3% and specificity of 55.8% (Figure 1).

## DISCUSSION

This study showed that a lower LMR was an independent predictor of CIN in patients with ACS who underwent PCI. In addition, eGFR and admission glucose level were also related with the development of CIN. To the best of our knowledge, this study is the first to show the relationship between LMR and development of CIN in patients with ACS. The present study showed that preprocedural LMR

$< 2.52$  predicted CIN, although its sensitivity and specificity are relatively low (66.3% and 55.8%, respectively).

CIN is an important issue, despite a successful coronary intervention it might be the cause of morbidity and mortality. It affects short- and long-term prognosis of the patients with ACS regardless of whether revascularization was successful.<sup>[18]</sup> Its incidence ranges from 2% to 50% according to the risk level of investigated population.<sup>[19, 20]</sup> The uses of high contrast medium volume, heart failure, age, diabetes, previous renal disease, and hypovolemia are the established risk factors for the development of CIN.<sup>[21, 22]</sup> The underlying mechanism of CIN was not fully understood, but decreased renal blood flow, medullary hypoxia, inflammation, endothelial dysfunction, and direct tubular injury by contrast media might be included in pathogenesis.<sup>[23, 24]</sup> Many factors are involved in pathogenesis of CIN, and the contrast media is found to be in the center of the process.<sup>[25]</sup> Inflammatory reaction and aggravated prothrombotic status occur in the development of CIN, and mediators reflecting these reactions could be a marker of CIN.<sup>[2]</sup> Significant relationship has been found between inflammation and acute renal injury.<sup>[26, 27]</sup>

White blood cell count and subtypes are known as inflammatory markers in cardiovascular diseases, and they are easily obtained with complete blood count.<sup>[28]</sup> Neutrophils, monocytes, and lymphocytes are the main cells of systemic inflammatory reactions in the body. Decreased lymphocyte count and increased monocyte count are associated with cardiovascular prognosis.<sup>[10, 29, 30]</sup> The PLR and NLR were extensively studied in various studies.<sup>[31, 32]</sup> The NLR has been described widely as a predictor of long-term prognosis, mortality, and infarct size in acute coronary syndrome.<sup>[33]</sup> It was also introduced as a potential predictor of CIN development in ACS patients who underwent primary PCI.<sup>[34]</sup> Recently, the LMR has been investigated as a new hematological marker which binds two independent cells of inflammation. Firstly, it has been showed that LMR is associated with prognosis in various cancers.<sup>[35, 36]</sup> LMR is an emerging inflammatory marker, and high monocyte levels and low lymphocyte levels were related with coronary atherosclerosis.<sup>[7]</sup> Murat *et al.* also reported that the low level of LMR is associated with bare metal stenosis in patients with stable coronary artery disease.<sup>[37]</sup>

Lymphocytes are important mediators of immune system, and lymphopenia is considered a surrogate marker of the immune dysregulation.<sup>[38]</sup> Blood monocytes are penetrated into the vascular intima and subintima, differentiate into macrophages in response to several locally produced cytokines, and initiate the inflammatory process. In this context, LMR is considered an indicator of systemic inflammation. The decreased LMR is not directly a

**Table 3: Angiographic and interventional characteristics of the study patients with and without contrast-induced nephropathy**

Variables	CIN (+) (n = 95)	CIN (-) (n = 778)	P value
Type of ACS, n (%)			0.181
STEMI	46 (48.4%)	433 (55.7%)	
NSTE-ACS	49 (51.6%)	345 (44.3%)	
FMC to wire time			
STEMI (minutes)	60.8 ± 29.5	55.9 ± 24.6	0.436
NSTE-ACS (hours)	14.6 ± 4.4	12.9 ± 5.9	0.056
Total amount of contrast volume, mL	171.6 ± 36.7	161.4 ± 31.9	0.118
Multivessel disease, n (%)	48 (50.5%)	318 (40.9%)	0.072
Use of tirofiban during PCI, n (%)	20 (21.1%)	149 (19.2%)	0.658
Culprit vessel, n (%)			0.708
Left main coronary artery	1 (1.1%)	7 (0.9%)	
Left anterior descending artery	34 (35.8%)	338 (43.4%)	
Right coronary artery	33 (34.7%)	240 (30.8%)	
Left circumflex artery	25 (26.3%)	175 (22.5%)	
Bypass graft	2 (2.1%)	18 (2.3%)	
Medical therapy during hospitalization, n (%)			
Statin	86 (90.5%)	696 (89.5%)	0.748
ACEi or ARB	66 (69.5%)	662 (85.1%)	<0.001
Beta-blocker	85 (89.5%)	710 (91.3%)	0.565
Diuretic	17 (17.9%)	61 (7.8%)	0.001
ADP receptor antagonists	94 (98.9%)	773 (99.4%)	0.648
Aspirin	91 (95.8)	752 (96.7%)	0.661
Nitrates	25 (26.3%)	202 (25.9%)	0.941

ACEi: angiotensin-converting enzyme inhibitor; ACS: acute coronary syndrome; ADP: adenosine-diphosphate; ARB: angiotensin receptor blocker; CIN: contrast-induced nephropathy; FMC: first medical contact; LVEF: left ventricular ejection fraction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

**Table 4: Univariate and multivariate logistic regression analysis model of potential predictors for the postprocedural CIN in patients with acute coronary syndrome**

Variable	Univariate analysis odds ratio (95% CI)	P value	Multivariate analysis odds ratio (95% CI)	P value
Age, years	1.060 (1.039–1.082)	<0.001	1.026 (0.999–1.053)	0.055
Previous MI	0.549 (0.330–0.913)	0.021	0.687 (0.370–1.277)	0.235
Hypertension	0.657 (0.428–1.011)	0.056		
Diabetes mellitus	0.529 (0.343–0.817)	0.004	0.888 (0.491–1.605)	0.693
LVEF	0.982 (0.966–0.998)	0.025	0.993 (0.976–1.010)	0.388
eGFR	0.968 (0.960–0.976)	<0.001	0.978 (0.968–0.988)	<0.001
Admission glucose	1.005 (1.003–1.008)	<0.001	1.004 (1.000–1.007)	<b>0.030</b>
Hemoglobin	0.757 (0.679–0.843)	<0.001	0.919 (0.802–1.054)	0.228
LM ratio	0.813 (0.721–0.916)	0.001	0.850 (0.749–0.965)	<b>0.012</b>
NL ratio	1.006 (0.981–1.032)	0.651		

CIN: contrast-induced nephropathy; eGFR: estimated glomerular filtration rate; LM: lymphocyte-to-monocyte; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NL: neutrophil-to-lymphocyte.

component of CIN and reflects an increased inflammatory status, which leads to the development of CIN.<sup>[39]</sup> LMR could be easily obtained from peripheral blood and may be used to predict CIN in patients who underwent urgent coronary angiography. Usage of this marker allows monitoring patients more closely and paying more attention to give more effort for CIN prevention. On the other hand, NLR was not found to be an independent predictor of CIN in the present study. But, it should be remembered that the NLR was nearly significantly higher in the with-

CIN group than in the without-CIN group. In fact, if the number of study patients was slightly higher, NLR could be a predictor of CIN.

In addition to LMR, we found that admission glucose levels and eGFR were also independent predictors of CIN. As expected, chronic kidney disease is the most important intrinsic predisposing factor for CIN. The risk is proportionally increasing every impairment of GFR, and in patients with GFR of 10–15 mL/min, possibility to develop

CIN may exceed 50%.<sup>[21]</sup> Diabetes is also a well-known important risk factor to develop CIN.<sup>[40]</sup> In this study, diabetes mellitus was not an independent factor; however, admission glucose level was an independent predictor of CIN. Parallel to our study, Baydar *et al.* reported that the presence of acute hyperglycemia in NSTEMI-ACS patients undergoing primary PCI was associated with a significant increase in the incidence of CIN.<sup>[41]</sup> They also showed that hyperglycemia was associated with increased CIN risk and associated with in-hospital mortality and morbidity.<sup>[41]</sup> Higher admission glucose level may indicate both worse regulated diabetes and a higher inflammatory stress response via noninsulin mechanisms. These may make admission glucose level more valuable instead of diabetes in the context of CIN in patients with ACS.

In conclusion, we found that LMR is an independent predictor of CIN in patients with ACS who underwent PCI. Our results suggest that LMR may be used as a simple biomarker in the identification of patients with increased risk of CIN.

## LIMITATIONS

This study is an observational, retrospective, and single-center study. We did not measure LMR variation during the clinical follow-up, and other inflammatory markers like C-reactive protein were not measured in the present study. Repeated measurement of serum creatinine levels was not made after 72 hours; hence, we may have missed some patients with CIN. Also, the sensitivity and the specificity of predicted LMR value (<2.52) were relatively low. Therefore, our results should be confirmed with large prospective randomized studies.

## CONCLUSION

Inflammation is an important factor in the development of CIN. Decreased LMR values may represent a pro-oxidant and pro-inflammatory effect on CIN in patients with ACS undergoing PCI. Thus, the LMR value <2.52 predicted the development of CIN in our study with a relatively low sensitivity and specificity. In this context, LMR may be used as a simple biomarker for predicting the CIN in patients with ACS who underwent PCI.

## Conflict of Interest

The authors have no conflicts of interest to declare.

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## REFERENCES

- Selistre Lda S, Souza VC, Dubourg L, Wagner MB, Hoefel Filho JR, Saitovitch D. Contrast-induced nephropathy after computed tomography. *J Bras Nefrol* 2015;37:27-31.
- Sun XP, Li J, Zhu WW, Li DB, Chen H, Li HW, *et al.* Platelet to Lymphocyte Ratio Predicts Contrast-Induced Nephropathy in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. *Angiology* 2018;69:71-8.
- Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, *et al.* A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. *J Am Coll Cardiol* 2004;44:1393-9.
- Kaya A, Kaya Y, Topcu S, Gunaydin ZY, Kurt M, Tanboga IH, *et al.* Neutrophil-to-lymphocyte ratio predicts contrast-induced nephropathy in patients undergoing primary percutaneous coronary intervention. *Angiology* 2014;65:51-6.
- Bartholomew BA, Harjai KJ, Dukkipati S, Boura JA, Yerkey MW, Glazier S, *et al.* Impact of nephropathy after percutaneous coronary intervention and a method for risk stratification. *Am J Cardiol* 2004; 93: 1515-9.
- Demircelik MB, Kurtul A, Ocek H, Cakmak M, Ureyen C, Eryonucu B. Association between Platelet-to-Lymphocyte Ratio and Contrast-Induced Nephropathy in Patients Undergoing Percutaneous Coronary Intervention for Acute Coronary Syndrome. *Cardiorenal Med* 2015;5: 96-104.
- Kurtul A, Yarlioglu M, Celik IE, Duran M, Elcik D, Kilic A, *et al.* Association of lymphocyte-to-monocyte ratio with the no-reflow phenomenon in patients who underwent a primary percutaneous coronary intervention for ST-elevation myocardial infarction. *Coron Artery Dis* 2015;26:706-12.
- Zhang Q, Hu M, Sun J, Ma S. The combination of neutrophil-to-lymphocyte ratio and platelet correlation parameters in predicting the no-reflow phenomenon after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. *Scand Cardiovasc J* 2020; 54:352-57.
- Ommen SR, Gibbons RJ, Hodge DO, Thomson SP. Usefulness of the lymphocyte concentration as a prognostic marker in coronary artery disease. *Am J Cardiol* 1997;79:812-4.
- Nunez J, Nunez E, Bodi V, Sanchis J, Mainar L, Minana G, *et al.* Low lymphocyte count in acute phase of ST-segment elevation myocardial infarction predicts long-term recurrent myocardial infarction. *Coron Artery Dis* 2010; 21:1-7.
- Hu P, Shen H, Wang G, Zhang P, Liu Q, Du J. Prognostic significance of systemic inflammation-based lymphocyte- monocyte ratio in patients with lung cancer: based on a large cohort study. *PLoS one* 2014; 9:e108062.
- Oksuz F, Elcik D, Yarlioglu M, Duran M, Ozturk S, Celik IE, *et al.* The relationship between lymphocyte-to-monocyte ratio and saphenous vein graft patency in patients with coronary artery bypass graft. *Biomarker Med* 2017; 11:867-76.
- Ortega LM, Harmouch I, Nayer A. Contrast-induced nephropathy: pathogenesis and new therapeutic options for prevention. *Am J Ther* 2015;22:469-76.
- Azzalini L, Spagnoli V, Ly HQ. Contrast-Induced Nephropathy: From Pathophysiology to Preventive Strategies. *Can J Cardiol* 2016;32:247-55.
- Ibanez B, James S, Agewall S, Antunes MJ, Bucchiarelli-Ducci C, Bueno H, *et al.* [2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation.]. *Kardiol Pol* 2018;76:229-313.
- Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, *et al.* 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2016;37:267-315.

17. Silvain J, Collet JP, Montalescot G. Contrast-induced nephropathy: the sin of primary percutaneous coronary intervention? *Eur Heart J* 2014;35:1504-6.
18. Fox CS, Muntner P, Chen AY, Alexander KP, Roe MT, Wiviott SD. Short-term outcomes of acute myocardial infarction in patients with acute kidney injury: a report from the national cardiovascular data registry. *Circulation* 2012;125:497-504.
19. Caixeta A, Mehran R. Evidence-based management of patients undergoing PCI: contrast-induced acute kidney injury. *Catheter Cardiovasc Interv* 2010;75 Suppl 1:S15-20.
20. Kurtul A, Yarlioglu M, Duran M, Murat SN. Association of Neutrophil-to-lymphocyte Ratio with Contrast-induced Nephropathy in Patients with Non-ST-elevation Acute Coronary Syndrome Treated with Percutaneous Coronary Intervention. *Heart Lung Circ* 2016;25:683-90.
21. McCullough PA, Wolyn R, Rocher LL, Levin RN, O'Neill WW. Acute renal failure after coronary intervention: incidence, risk factors, and relationship to mortality. *Am J Med* 1997;103:368-75.
22. Wi J, Ko YG, Shin DH, Kim JS, Kim BK, Choi D, *et al.* Prediction of Contrast-Induced Nephropathy With Persistent Renal Dysfunction and Adverse Long-term Outcomes in Patients With Acute Myocardial Infarction Using the Mehran Risk Score. *Clin Cardiol* 2013;36:46-53.
23. Goldenberg I, Matetzky S. Nephropathy induced by contrast media: pathogenesis, risk factors and preventive strategies. *CMAJ* 2005;172:1461-71.
24. Verdoodt A, Honore PM, Jacobs R, De Waele E, Van Gorp V, De Regt J, *et al.* Do statins induce or protect from acute kidney injury and chronic kidney disease: An update review in 2018. *J Trans Int Med* 2018; 6:21-5.
25. Solomon R, Dauerman HL. Contrast-induced acute kidney injury. *Circulation*. 2010;122:2451-5.
26. Akcay A, Nguyen Q, Edelstein CL. Mediators of inflammation in acute kidney injury. *Mediators Inflamm* 2009;2009:137072.
27. Kocas C, Yildiz A, Abaci O, Karaca OS, Firdin N, Dalgic Y, *et al.* Platelet-to-Lymphocyte Ratio Predicts Contrast-Induced Nephropathy in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome. *Angiology* 2015;66:964-8.
28. Pantzaris N-D, Platanaki C, Pierrako C, Karamouzos V, Velissaris D. Neutrophil-to-lymphocyte ratio relation to sepsis severity scores and inflammatory biomarkers in patients with community-acquired pneumonia: A case series. *J Trans Int Med* 2018; 6:43-6.
29. Widmer A, Linka AZ, Attenhofer Jost CH, Buergi B, Brunner-La Rocca HP, Salomon F, *et al.* Mechanical complications after myocardial infarction reliably predicted using C-reactive protein levels and lymphocytopenia. *Cardiology* 2003; 99:25-31.
30. Nacar AB, Erayman A, Kurt M, Buyukcaya E, Karakas MF, Akcay AB, *et al.* The relationship between coronary collateral circulation and neutrophil/lymphocyte ratio in patients with coronary chronic total occlusion. *Medical Principles and Practice*. 2015; 24:65-9.
31. Yilmaz S, Sen F, Unal S, Yayla C, Ozeke O, Aras D, *et al.* Usefulness of the platelet-to-lymphocyte ratio in predicting bare-metal stent restenosis. *Scand Cardiovasc J* 2015; 49: 39-44.
32. Gungor H, Babu AS, Zencir C, Akpek M, Selvi M, Erkan MH, *et al.* Association of preoperative platelet-to-lymphocyte ratio with atrial fibrillation after coronary artery bypass graft surgery. *Med Princ Pract* 2017; 26:164-8.
33. Chen C, Cong BL, Wang M, Abdullah M, Wang XL, Zhang YH, *et al.* Neutrophil to lymphocyte ratio as a predictor of myocardial damage and cardiac dysfunction in acute coronary syndrome patients. *Integr Med Res* 2018;7:192-9.
34. Yuan Y, Qiu H, Hu X, Luo T, Gao X, Zhao X, *et al.* Predictive value of inflammatory factors on contrast-induced acute kidney injury in patients who underwent an emergency percutaneous coronary intervention. *Clin Cardiol* 2017;40:719-25.
35. Stotz M, Pichler M, Absenger G, Szkandera J, Armingier F, Schaberl-Moser R, *et al.* The preoperative lymphocyte to monocyte ratio predicts clinical outcome in patients with stage III colon cancer. *Br J Cancer* 2014;110:435-40.
36. Han LH, Jia YB, Song QX, Wang JB, Wang NN, Cheng YF. Prognostic significance of preoperative lymphocyte-monocyte ratio in patients with resectable esophageal squamous cell carcinoma. *Asian Pac J cancer Prev* 2015;16:2245-50.
37. Murat SN, Yarlioglu M, Celik IE, Kurtul A, Duran M, Kilic A, *et al.* The Relationship Between Lymphocyte-to-Monocyte Ratio and Bare-Metal Stent In-Stent Restenosis in Patients With Stable Coronary Artery Disease. *Clin Appl Thromb Hemost* 2017;23:235-40.
38. Alsayyad MM, Abd Alsamir HS. The prognostic value of lymphocyte-to-monocyte ratio in nephropathy of type 2 diabetes mellitus. *Sci J Al-Azhar Med Faculty, Girls*. 2019;3:181.
39. Kose N, Akin F, Yildirim T, Ergun G, Altun I. The association between the lymphocyte-to-monocyte ratio and coronary artery disease severity in patients with stable coronary artery disease. *Eur Rev Med Pharmacol Sci*. 2019;23:2570-75.
40. Heyman SN, Rosenberger C, Rosen S, Khamaisi M. Why is diabetes mellitus a risk factor for contrast-induced nephropathy? *BioMed Res Int* 2013;2013:123589.
41. Baydar O, Kilic A. Acute hyperglycemia and contrast-induced nephropathy in patients with non-ST elevation myocardial infarction. *Cardiovasc Endocrinol Metab* 2020;9:24-9.

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