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Sumatera Medical Journal

Correlation of Platelet-Lymphocyte Ratio (PLR) and Contrast-Induced Nephropathy (CIN) in Patients with ST-Segment Elevation Myocardial Infarction (STEMI) Undergoing Primary Percutaneous Coronary Intervention (PCI)

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Abstract. Acute Coronary Syndrome (ACS) is a series of clinical disorders caused by acute ischemic heart disease. The clinical spectrum of ACS is unstable angina pectoris (UAP), non ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI). Inflammation occurs from the early stages of atheroma formation to plaque rupture and thrombosis. Thrombocytosis and lymphopenia are associated with the degree of systemic inflammation and the platelet lymphocyte ratio (PLR) is a new marker involving both hematological indices. ST segment elevation myocardial infarction is a type of acute myocardial infarction with high mortality. Management of STEMI patients is carried out with reperfusion therapy consisting of primary percutaneous coronary intervention (PCI) and fibrinolytics. Contrast-induced nephropathy is a serious complication of angiograph procedures that results from administration of contrast media.

Keyword: ACS, STEMI, platelet lymphocyte ratio, primary PCI

Received date month year | Revised date month year | Accepted date month year

1. Introduction

Acute myocardial infarction (AMI) is one of the most cardiovascular diseases in hospitalized patients in industrialized countries [1]. According to WHO, myocardial infarction is classified based on symptoms, ECG image abnormalities, and heart enzymes. Myocardial infarction can be divided into non ST segment elevation myocardial infarction (NSTEMI), and ST segment elevation myocardial infarction (STEMI) [2]. STEMI is a condition that results in cardiac myocyte cell death due to prolonged ischemia due to acute coronary occlusion [3]. Coronary

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Journal Homepage: http://smj.usu.ac.id

occlusion occurs due to atherosclerosis, a disease caused by an inflammatory process that involves the interaction of immune mechanisms and several metabolic substances accompanied by accumulation of lipids on the artery walls.

Lymphocytopenia is a condition that is often found in chronic inflammatory conditions due to increased lymphocyte apoptosis. Lymphocyte value can be used as an early sign of physiological stress and systemic inflammation. The increase in the number of megakaryocytes and thrombocytosis are two results due to the inflammatory state, which can lead to a prothrombotic state. Circulating platelets contribute to atheroma plaque formation and triggering further complications. Platelet Lymphocyte Ratio (PLR) is a novel prognostic marker and a marker of systemic inflammation that describes the aggregation and inflammation pathways in coronary heart disease.

The initial management of STEMI is reperfusion therapy, either with percutaneous coronary intervention (PCI) or pharmacology [4]. Primary PCI is an action to drain coronary arteries that are blocked by thrombus, which causes STEMI by using coronary catheters whether followed by stenting or not. One of the complications of the PCI procedure is the incidence of contrast-induced nephropathy. Contrast-induced nephropathy (CIN) is an acute impairment of renal function, assessed by an increase in serum creatinine of more than 25% or 0.5 mg / dL within 48–72 hours after intravenous contrast administration [5].

In previous studies, PLR value have been known to be correlated with CIN. PLR value was found higher in CIN group compared to non CIN group. PLR value is an independent predictor of the incidence of CIN in STEMI patients undergoing primary PCI. Age, Killip Class and NLR values were other independent predictors of the incidence of CIN [6].

The high PLR value may be the result of the inflammatory process CIN. The advantage of PLR values is that the platelet and lymphocyte components reflect coagulation and inflammatory activity, both of which are important mechanisms for inducing contrast-induced nephropathy. PLR values can help identify high-risk candidate patients for CIN [7].

This study was conducted to determine the correlation in the use of PLR values with the incidence of contrast-induced nephropathy in STEMI patients undergoing primary PCI in North Sumatra. The results of this study are expected to provide education and prognosis to patients.

2. Materials and Methods

2.1. Place and Year Work

The present study was carried out from June – December 2020. The experiment was conducted in cardiac centre of H. Adam Malik General Hospital.

2.2. Ethics Statement

The research was approved by The Health Research Ethical Committee of Faculty of Medicine, Universitas Sumatera Utara. Written informed consent was obtained prior to the investigation.

2.3. Subjects

The study included a total of 61 STEMI patients undergoing primary PCI. Each individual was recruited from the H. Adam Malik General hospital, Murni Teguh Memorial hospital and Grand Medistra hospital, North Sumatra, Indonesia from January 2019 to November 2019. Inclusion criteria include STEMI patients undergoing primary PCI;serum creatinine test is carried out at admission and 48 hours after the primary PCI.

2.4. Statistical Analysis

For baseline characteristics, the Kolmogorov-Smirnov test was used to test the normality of distribution. Quantitative variables with a normal distribution were specified as mean (standard deviation), variables with nonnormal distribution were shown as median (interquartile range), and categorical variables were shown as number and percentage values. For continuous variables with a normal distribution, the Student t test was used to compare groups, whereas the Mann-Whitney U test was used when the distribution was not normal. For categorical variables, the x^2 test or the Fisher exact test was used, as appropriate. All statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 26. $P < 0.05$ were considered significant.

3. Results

The study population consisted of 61 patients; 11 (18%) patients developed CIN and 50 (82%) patients with non-CIN. Baseline demographic data and laboratory parameters are shown in Table 1. The patients in the CIN group had a higher prevalence of hypertension and diabetes mellitus than those in the non-CIN group. In the CIN group, creatinine, ureum, HDL, triglyserides, white blood cell, neutrophil, platelet, and PLR were higher, whereas CrCL, LDL, hematocrit, lymphocyte, and hemoglobin were lower compared with the non-CIN group.

Table 1 Baseline Demographic Data and Laboratory Parameters.

Variable	**Contrast-Induced Nephropathy**		**p value**
	CIN (+) (n=11,18%)	**CIN(-) (n=50,82%)**	
Demographic data			
Age (years)	54.64±7.42	56.50±9.15	0.531
Sex (n,%)			
Male	8 (72.7)	46 (92.0)	0.103
Female	3 (27.3)	4 (8.0)	0.103
Hypertension (n,%)	7 (63.6)	25 (50.0)	0.412
Diabetic Melitus (n,%)	4 (36.4)	6 (12.0)	0.07
Smoking (n,%)	8 (72.7)	44 (88.0)	0.343
Congestive Heart Failure (n,%)	5 (45.5)	9 (18.0)	0.106
Anemia (n,%)	4 (36.4)	8 (16.0)	0.203
Laboratorium parameters			
Creatinine pre PCI (mg/dL)	1.089±0.1	1.07±0.29	0.880
Cretinine post PCI (mg/dL)	**1.4±0.14**	**0.99±0.27**	**<0.001**
Ureum pre PCI (mg/dL)	24 (15-37.5)	28.2 (15-56)	0.208
Ureum post PCI (mg/dL)	**43 (34-47)**	**26 (15-55)**	**<0.001**
CrCL pre PCI (mg/dL)	73.86 (42.08-116.34)	75.66 (36.83-326.39)	0.499
CrCL post PCI (mg/dL)	**58.04 (32.87-91.28)**	**83.84 (37.49-273.75)**	**0.001**
Hemoglobin (g/dL)	13.79±2.23	13.96±1.63	0.765
Hematocrit (%)	40.17±5.94	42.26±5.10	0.237
Leucocytes (/µL)	13560 (5410-21000)	13105 (7310-22830)	0.505
Platelet ($x10^3$/µL)	284.27±69.96	275.32±78.13	0.728
Neutrophils ($x10^3$/µL)	**13.93 (3.70-89.40)**	**10.93 (4.90-89.40)**	**0.042**

Lymphocytes (x10^3/µL)	**1.5 (0.73-2.44)**	**1.88 (0.74-10.20)**	**0.013**
Monocytes (x10^3/µL)	0.88 (0.30-11.50)	0.59 (0.25-7.70)	0.91
Eosinophils (x10^3/µL)	0.02 (0.00-0.15)	0.07 (0.00-0.64)	0.061
Basophils (x10^3/µL)	0.04 (0.01-0.10)	0.05 (0.01-0.2)	0.449
PLR	**216.38±69.46**	**146.29±61.62**	**0.001**
HDL (mg/dL)	**44 (30-55)**	**37.5 (26-55)**	**0.027**
LDL (mg/dL)	116 (77-224)	122 (56-227)	0.858
Triglyserides (mg/dL)	122 (35-348)	119 (58-348)	0.750

The angiographic characteristics and medications during hospitalization are presented in Table 2. The prevalence of multivessel disease was significantly lower in the CIN group compared with the non-CIN group. The total used of contrast volume was not significantly different between groups. Both group dominated with administration of high osmolality contrast rather than low osmolality contrast. The rates of treatment with angiotensin-converting enzyme inhibitor/angiotensin receptor blocker and statin were higher in patients who developed CIN.

Table 2 The Angiographic Characteristics and Medications During Hospitalization

	Contrast-Induced Nephropathy		**p-value**
	CIN(+)(n=11,18%)	**CIN (-) (n=50,82%)**	
Angiographic characteristics			
Contrast volume (ml)	100 (80-300)	100 (75-150)	0.229
Contrast osmolality (n,%)			
High	11 (100)	42 (84)	0.330
Low	0 (0)	8 (16)	
Multi vessel disease (n,%)	3 (27.3)	29 (58)	0.13
Medications during hospitalization (n,%)			
ACE-inhibitor	7 (63.6)	27 (54)	0.740

β-Blocker	5 (45.5)	28 (56)	0.525
Diuretic	4 (36.4)	21 (42)	0.503
MRA	2 (18.2)	6 (12)	0.627
Statin	11 (100)	49 (98)	>0.999

An ROC curve analysis was performed to determine the cutoff value of PLR to predict the development of CIN. The area under the curve (AUC) for PLR was 0.795 (95% CI) and a PLR cutoff of 184.75 or higher predicted CIN with a sensitivity of 81.8% and a specificity of 80% (Figure 1)

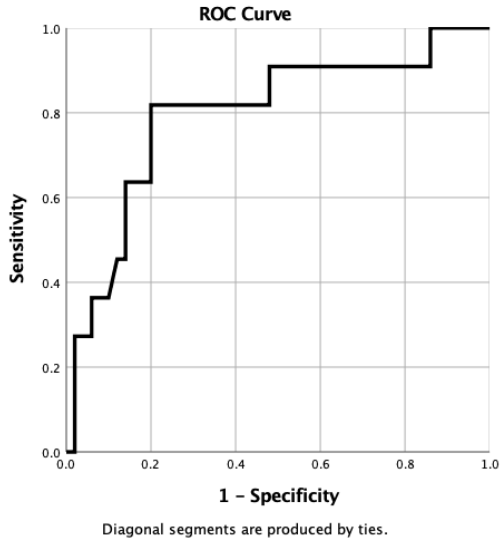

Figure 1. The ROC curve shows the predictive cutoff value of PLR for CIN

Table 3 Bivariate Analysis of PLR-CIN

PLR	**STEMI patients undergoing primary PCI**						**p-value**
	CIN (11)		**Non-CIN (50)**		**Total (61)**		
	F	**%**	**F**	**%**	**F**	%	
Cut-off point							
≤184,75	2	(3,3)	40	(65,6)	42	(68,9)	
>184,75	9	(14,8)	10	(16,4)	19	(31,1)	<0.001
Total	11	(18)	50	(82)	61	(100)	

4. Discussion

Contrast-induced nephropathy represents a significant adverse event of contrast medium administration, leading to worse clinical outcomes despite successful early coronary revascularization. The mechanisms of CIN remain poorly understood, although several mechanisms have been identified, revealing a complex multifactorial physiopathology with a high interindividual variability of the nephrotoxic effect of contrast media. Several factors have been strongly implicated to have some roles in its development of CIN, including intrarenal vasoconstriction, reduced renal blood flow, oxidative stress, inflammation, renal ischemia, reactive oxygen species formation, reduction of nitric oxide production, tubular epithelial, and vascular endothelial injury [8].

A recent study showed that a higher PLR value is related to the presence of coronary artery disease and is correlated with CRP and fibrinogen levels. Both thrombocytosis and lymphocytopenia correlate with the degree of systemic inflammation, and PLR represents a novel marker incorporating both hematologic indices. The advantage of the PLR could be that it reflects the condition of both inflammation and thrombosis pathways, and it may be more valuable than either platelet or lymphocyte counts alone. Since a complete blood count is easily available, the PLR may help clinicians to identify patients at high risk of CIN and decide whether postprocedural hydration is needed [7].

Our analysis showed that , PLR of the CIN group was significantly higher compared to the non-CIN group, (216.38 ± 69.46 vs 146.29 ± 61.62 respectively, p= 0.001) and higher PLR was an independent risk factor for the development of CIN in patients with STEMI undergoing pPCI. This is in accordance with the research of Sun et al. which found PLR value in CIN group was higher compared to non-CIN group (173.8 ± 62. vs 116.2 ± 51.7 respectively, p=0.001) The cut off of PLR for CIN was 184.75 with a sensitivity of 81.8% and a specificity of 80%, with an AUC value of 0.795 (95% CI).Based on demircelik et al study, the cut off of PLR for CIN was 148.3 with a sensitivity of 75.6% and a specificity of 72.2%, with an AUC value of 0.715 (95% CI) [9].

This study has some limitations. The number of study samples is small so the study is could not assess other confounding factors. This study examines laboratory parameters in 3 different centers and using different devices, even though using the same parameter unit. Several novel renal biomarkers, including neutrophil gelatinase-associated lipocalin, cystatin C, urinary Kim-1, and interleukin 18, were not measured.

5. Conclusion

There is a significant correlation between PLR value and the incidence of CIN in STEMI patients undergoing primary PCI.

6. Acknowledgement

The authors would like to express their gratitude to Department of Cardiology, Universitas Sumatera Utara and all the patients who participated in this multicenter study.

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