RESEARCH

23(96), March - April, 2019

ISSN 2321–7359 EISSN 2321–7367

Medical Science

Association of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios with coronary artery disease severity

Javad Ramezani[1], Hamidreza Bagherian Kalat[2], Amir Masoud Hashemian[3]✉, Neema John Mehramiz[4], Mahdi Foroughian[5]

Introduction: **Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are two measurable parameters through complete blood count (CBC), whose role has recently been considered as inflammatory markers with potential in predicting cardiovascular events. The purpose of this study was to determine the association of NLR and PLR with coronary angiographic findings in patients with acute coronary syndrome (ACS).** ***Methods:*** **This cross-sectional study was conducted on hospitalized patients diagnosed with ACS who underwent angiography. The patients were divided into two groups according to coronary circulation status in the angiography: 1) spontaneous reperfusion group (SRG) consisting of patients with normal coronary circulation and TIMI flow grade of 3; 2) non-SRG group including patients with some degree of impaired coronary circulation and TIMI flow grade of ≤2. Then clinical, laboratory, echocardiographic and angiographic findings were compared. The ROC curve was used to calculate a suitable cut-off point from PLR and NLR to predict the severity of coronary artery involvement and to differentiate SRG from non-SRG. Independent sample t-test, Chi-Square, and logistic regression were applied for statistical analysis.** ***Results:*** **The study consisted of 360 patients (224 males and 136 females) with a mean age of 60.7 ± 12.3 years. According to the angiography, 134 (37.2%) patients were assigned to the SRG group and 226 (62.8%) patients to the non-SRG group. Comparison of laboratory findings in the two groups of SRG and non-SRG showed that white blood cell count, platelet count, neutrophil count, troponin I level, NLR and PLR were significantly higher in the abnormal group. The best cut-off point of PLR and NLR in the non-SRG prediction was 103 and 3.3 in the ACS patients, respectively. The area under the ROC curve, sensitivity and specificity of obtained cut-off points were determined to be 66.6, 73.1%, and 54.5% for the PLR (95% CI=61.5-71.4), and 68.3, 46.9%, and 82.0% for NLR (95% CI=63.2-73.1), respectively.** ***Conclusion:*** **In the ACS patients, the coronary atherosclerosis is associated with inflammatory markers, and PLR and NLR can be used to evaluate the severity of coronary artery involvement.**

INTRODUCTION

Inflammatory phenomena play an essential role in the pathogenesis and acute rupture of atherosclerotic plaques, and as a result of cardiovascular disease (1, 2, 22). Platelets develop atherosclerotic plaques by activating, accumulating and releasing proinflammatory chemokines and cytokines. The increase in platelets exacerbates the unpleasant cardiovascular consequences (3, 4).In addition to platelets, white blood cells are significantly able to generate the plaques, so that increasing neutrophils and reducing lymphocytes can elevate the mortality rate of cardiovascular disease (5, 6).

Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are two parameters that can be measured via complete blood count (CBC), whose functions have attracted recently further attention as inflammatory markers capable of predicting cardiovascular events (7, 8). Recent studies have shown that increased levels of PLR and NLR in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI), also known as coronary angioplasty, have been associated with an increased risk of adverse cardiovascular events (2). Additionally, increased PLR in non-ST elevation-ACS has been shown to be reduced by the left ventricular ejection fraction (LVEF) and is also associated with increased risk of nephropathy induced by contrast agent after angiography (9, 10). Although the relationship between white blood cells and their subsets has been further investigated in association with the severity of coronary artery disease (CAD), the relationship between PLR and CAD intensity has been considered less (11, 12). In addition, the findings of the majority of previous studies have also focused on East Asia or Western patients, but the environmental and

[1]Javad Ramezani, MD: Department of Cardiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [2]Hamidreza Bagherian Kalat, MD: Equally First Author, Department of Emergency Medicine, Mashhad University of Medical sciences, Mashhad, Iran; [3]Amir Masoud Hashemian, MD: Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical sciences, Mashhad, Iran; [4]Neema John Mehramiz: University of Arizona, College of Medicine, Tucson, AZ, USA; [5]Mahdi Foroughian, MD: Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical sciences, Mashhad, Iran;

✉*Corresponding Author:*

Amir Masoud Hashemian, MD: Department of Emergency Medicine, Faculty of Medicine, Mashhad University of Medical sciences, Mashhad, Iran; Tel: 05138525312; 989124244517; Email: hashemianAM@mums.ac.ir

Table 1 Baseline characteristics in patients with acute coronary syndrome based on angiographic findings

Variables, n (%)	Spontaneous reperfusion (n=134)	Non- spontaneous reperfusion (n=226)	P-value
	n (%)	n (%)	
Male sex	75 (56.0)	149 (65.9)	P=0.06
Age (year)*	59.4±12.4	61.6±12.3	P=0.104
Smoking	25 (18.7)	46 (20.4)	P=0.696
Blood pressure	58 (43.3)	120 (53.1)	P= 0.072
Diabetes	34 (25.4)	72 (31.9)	P= 0.192
Ischemic heart disease	75 (56.4)	136 (60.1)	P= 0.482
Coronary artery bypass surgery	2 (1.5)	26 (11.6)	P<0.001
Aspirin	53 (39.6)	72 (31.9)	P= 0.138
Beta blocker	44 (32.8)	57 (25.3)	P= 0.126
Statin	37 (27.8)	52 (23)	P= 0.308
Plavix	21 (15.7)	26 (11.5)	P= 0.257
Left ventricle ejection fraction, (%) *	47.1±10.8	43.3±10.2	P=0.001

* Mean ± standard deviation

genetic differences can develop differences in platelet count and white blood cell count among studied populations (2, 13). Therefore, it seems necessary to perform these studies in different races, including Iranian race, in order to investigate the feasibility of using these indices in examining the severity and prognosis of these patients. The aim of this study was to evaluate the diagnostic accuracy of pre-procedural NLR and PLR in predicting the severity of coronary artery involvement during angiography.

MATERIALS AND METHODS

Study design and setting

This analytical cross-sectional study was conducted on suspected patients with acute coronary syndromes admitted to Imam Reza Hospital of Mashhad, Iran, during June 2016 to August 2017. Inclusion criteria were confirmation of ACS diagnosis (based on history taking, electrocardiography (ECG), and cardiac enzymes) and undergoing the coronary angiography. People with known hematologic or cancerous diseases or under treatment, or inflammatory and infectious diseases were excluded. The guidelines recommended by the 2015 ECS were observed to diagnose the ACS (14, 22). The patients with unstable angina (UA), non-STEMI, and STEMI were enrolled in the study. Moreover, the chest pain, as an indicative of USAP with or without ischemic electrocardiographic findings, was utilized to diagnose the UA. The non-STEMI was diagnosed when characteristic angina pectoris took over 20 minutes with/without associated ST-segment depression of ≥0.1 mV and/or T-wave inversion in two contiguous leads in the ECG and also elevated troponin T level more than the diagnostic cut-off point. The diagnosis of STEMI was performed in accordance with the angina pectoris of more than 20 minutes, associated with ST-segment elevation of ≥1 mm in minimal two contiguous limb leads or ≥2 mm in minimal two contiguous chest leads.

Data collection

Initially, the background information of each patient, including previous history of the disease, drug use, laboratory findings and ECG, and echocardiography, were recorded on admission. Venous blood samples were taken from all patients to measure admission CBC and cardiac biomarkers. The ratio of absolute neutrophil count to absolute lymphocyte count was considered as NLR, as well as the ratio of absolute platelet count to absolute lymphocyte count was calculated as PLR.

After prescribing, the patients underwent coronary angiography. The angiographic findings were the number of involved arteries, the type of involved arteries, the involvement site of arteries and the severity of the arterial involvement on the basis of mild (stenosis less than 50%), moderate (stenosis between 50% and 70%) and severe (stenosis of more than 70%). In order to evaluate the severity of CAD, the patients were divided into two groups according to coronary circulation status in the angiography: 1) spontaneous reperfusion group (SRG) consisting of patients with normal coronary circulation and TIMI flow grade of 3; 2) non-SRG group including patients with some degree of impaired coronary circulation and TIMI flow grade of ≤2. The sample size was determined using the formula for estimating mean in a community and also the comparison of the means in the two independent groups, taking into account the 95% confidence interval and the test power of 80%. The minimum sample size was 98 patients in each group.

Ethical considerations

This research was proposed on 02/22/2017 at the Ethics Committee of the Mashhad University of Medical Sciences entitled "association between TB to Lymphocyte ratio with findings of coronary angiography in patients admitted in emergency department of Imam Reza with Acute Coronary Syndrome" as research project with the number of 950087 and ethical approved code of fm.REC.1395.601.IR.MUMS. All the patients completed the patient consent form and accepted the study.

Statistical analysis

The data were described using frequency distribution, charts, mean and standard deviation. The distribution of quantitative variables was evaluated using Kolmogorov-Smirnov test. Independent-sample t-test and one-way ANOVA were used to compare the quantitative variables with normal distribution. Mann-Whitney and Kruskal-Wallis tests were applied for quantitative variables with non-normal distribution. Frequency distribution of qualitative variables was measured in two groups by Chi-square test. The ROC curve was used to calculate a suitable cut-off point from PLR and NLR to predict the severity of coronary artery involvement and to differentiate SRG from non-SRG.

RESULTS

Background characteristics

The study consisted of 360 patients (224 males and 136 females) with a mean age of 60.7 ± 12.3 years. According to the angiography, 134 (37.2%) patients were assigned to the SRG group and 226 (62.8%)

Table 2 Laboratory and angiographic characteristics of patients with acute coronary syndrome based on angiographic findings

Variables, mean ± SD		Spontaneous reperfusion (n=134)	Non- spontaneous reperfusion (n=226)	Intergroup test (1)
Blood sugar, mg/dL		153.9±84.9	173.9±105.8	P=0.045
Creatinine, mg/dL		1.1±0.3	1.2±0.3	P=0.256
White blood cell count		8.4±2.5	9.5±3.0	P<0.001
Hemoglobin, g/dL		14.0±1.9	13.9±2.1	P=0.728
Platelet count		234.0±63.8	250.6±68.1	P=0.022
Lymphocyte count		29.1±9.5	22.5±9.8	P<0.001
Neutrophil count		63.2±10.9	69.5±12.0	P<0.001
International Normalized Ratio (INR)		1.2±0.6	1.2±0.4	P=0.251
Troponin I, ng/dL		1.2±4.3	4.7±12.2	P<0.001
Cholesterol, mg/dL		165.6±42.2	170.6±51.6	P=0.571
Triglyceride, mg/dL		124.6±64.6	125.6±69.5	P=0.739
High-density lipoprotein (HDL), mg/dL		106.3±47.3	103.0±40.0	P=0.531
Low-density lipoprotein (HDL), mg/dL		39.7±15.1	40.6±9.5	P=0.916
Platelet to lymphocyte ratio		110.7±99.1	151.2±48.5	P<0.001
Neutrophil to lymphocyte ratio		2.7±4.6	4.4±1.9	P<0.001
Type of acute coronary syndrome	UA	72 (53.7)	52 (23.0)	P<0.001
	STEMI	35 (26.1)	120 (53.1)	
	NSTEMI	27 (20.1)	54 (23.9)	
number of involved arteries	1	46 (50.0)	55 (25.7)	P<0.001
	>1	46 (50.0)	159 (74.3)	

Table 3 Possible predictors of significant coronary artery stenosis based on regression analysis

Variables	Univariate			Multivariate		
	Wald	OR (95% CI of OR)	P-value	Wald	Adjusted OR (95% CI of OR)	P-value
Male sex	3.53	0.657 (0.424-1.02)	0.06	3.567	2.081 (0.973-4.45)	0.059
Age	2.63	1.015 (0.997-1.032)	0.104	1.436	0.982 (0.955-1.01)	0.231
Coronary artery bypass surgery	8.42	8.62 (2.01-36.94)	0.004	9.66	13.02 (2.58-65.74)	0.002
ACS(STIMI)	34.64	4.74 (2.87-7.97)	<0.001	6.95	3.63 (1.39-9.48)	0.008
ACS(NSTIMI)	11.70	2.76 (1.54-4.96)	0.001	0.006	1.037 (0.407-2.643)	0.940
Left ventricle ejection fraction	4.57	1.74 (1.05-2.89)	0.032	1.016	0.653 (0.302-1.415)	0.280
Troponin I	10.57	1.10 (1.04-1.17)	0.001	1.88	1.047 (0.981-1.117)	0.170
Platelet to lymphocyte ratio	18.37	1.01 (1.00-1.015)	<0.001	24.93	1.028 (1.017-1.039)	<0.001
Neutrophil to lymphocyte ratio	18.27	1.29 (1.15-1.46)	<0.001	11.11	1.27 (1.10-1.46)	0.001

* ACS: Acute coronary syndrome

patients to the non-SRG group. The study consisted of 360 patients (224 males and 136 females) with a mean age of 60.7 ± 12.3 years. According to the angiography, 134 (37.2%) patients were assigned to the SRG group and 226 (62.8%) patients to the non-SRG group.

Angiographic and laboratory data

STIMI syndrome was more common in the non-SRG group than in the SRG group, while the UA was higher in the SRG group (P <0.001). According to the number of involved arteries, 159 patients in the non-SRG group (74.3%) had more than one arterial involvement. There was a significant association between the number of involved arteries and grouping SRG and non-SRG (P <0.001) (Table 1). Comparison of laboratory findings in the two groups of SRG and non-SRG showed that non-fasting blood sugar levels, white blood cell count, platelet count, neutrophil count, and troponin I, NLR and PLR were significantly higher in the abnormal group (Table 2).

Diagnostic value of PLR and NLR

The best cut-off point of PLR and NLR in the non-SRG prediction was 103 and 3.3 in the ACS patients, respectively. The area under the ROC curve, sensitivity and specificity of obtained cut-off points were determined to be 66.6, 73.1%, and 54.5% for the PLR (95% CI=61.5-71.4), and 68.3, 46.9%, and 82.0% for NLR (95% CI=63.2-73.1), respectively. In addition, logistic regression analysis showed that considering the probable markers related to spontaneous reperfusion, only PLR and NLR indices, history of cardiac surgery and STEMI diagnosis had significant association (Table 3).

DISCUSSION

The aim of this study was to investigate the association of PLR and NLR with angiographic findings in ACS patients. The findings of this study showed that both of these parameters were significantly associated with the severity of impaired coronary circulation. The aim of this study was to investigate the association of PLR and NLR with angiographic findings in ACS patients. The findings of this study showed that both of these parameters were significantly associated with the severity of impaired coronary circulation. In addition, our study showed that these two criteria could be helpful in predicting more severe coronary circulatory problems because they remain as factors associated with impaired coronary circulation in the regression model, in addition to having suitable diagnostic features. This was the first study in the Iranian race, whose findings could help to complete the puzzle of "Association of Platelet and Leukocyte Indexes with the Severity of

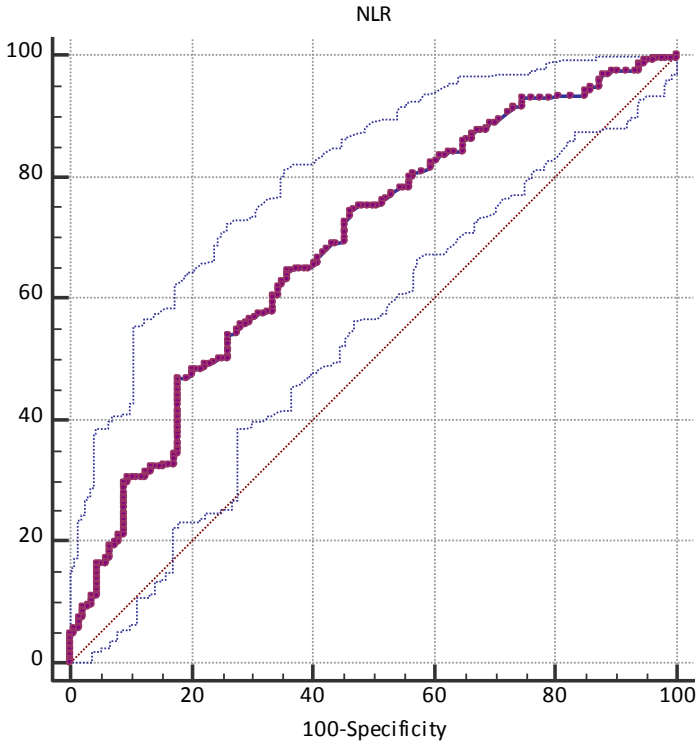

Figure 1 Receiver operating characteristic (ROC) curve of Neutrophil-to-lymphocyte ratio (NLR) level in the prediction of non-spontaneous reperfusion in patients with acute coronary syndrome

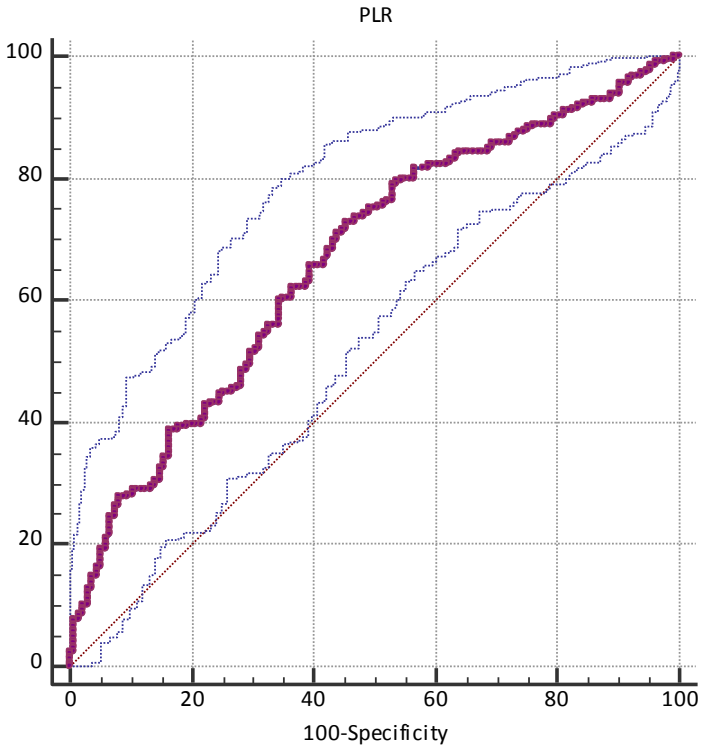

Figure 2 Receiver operating characteristic (ROC) curve of platelet-to-lymphocyte ratio (PLR) level in the prediction of non-spontaneous reperfusion in patients with acute coronary syndrome

CAD." More than dozens of studies have so far examined the association of leukocyte and platelet indexes with the CAD severity in other races, mainly in the USA, Western Europe and East Asia, whose overall findings were consistent with our results (6-8, 15).

The measurement of troponin is still considered as one of the most selective markers in detecting myocardial damages. The long-term elevation in serum levels and the need for examination in successive sequences caused ambiguity in the use of troponin in the rapid triage of ACS patients (16, 17). Therefore, efforts are continuing to find markers

capable of accelerating diagnostic and decision-making processes for ACS patients (18, 19). The important point about PLR and NLR is the high speed of examinations and very low cost, which help not only save a lot of time in the decision process, but also reduce the cost of treatment and prevent further diagnostic measures on admission at the emergency department. In our study, it was shown that the sensitivity of PLR and the specificity of NLR in predicting severe impaired coronary circulation in the ACS patients were 73.1% and 82.0% respectively, while the specificity of PLR and the sensitivity of NLR were about 50%. Although the findings for NLR are still insufficient in the studies, another study found that the sensitivity of PRL was about 56% and the specificity of PRL was about 52%, with specificity values similar to our study (5). In a study by Lee et al., the sensitivity and specificity of PLR values were estimated to be about 60% (6). In our study, the cut-off points for PLR and NLR were 103 and 3.3, which are roughly in line with the values found in other studies. In the study of Lee et al., the cut-off point was 137 for PLR. In the study of Kurtul et al., the cut-off point for PLR was 116 with the sensitivity and the specificity of 71% and 66%, respectively, which were close to the cut-off point determined in our study (6, 11). Therefore, according to reports on the diagnostic value of PRL and NLR in predicting more severe impaired coronary circulation and poorer prognosis of patients, our findings, along with other studies, show that these two factors alone cannot be used to make decisions. In fact, the simultaneous increase of PLR and NLR can be helpful as a tool for decision-making with physicians; for example, at a time when primary troponin level, despite clinical evidence and electrocardiographic findings, is still not in the diagnostic value for MI.

Regardless of the discussion on the diagnostic value of PLR and NLR, we measured the association between the severity of impaired coronary circulation measured by TIMI and other markers. Interestingly, a significant association was found between impaired coronary circulation with higher troponin levels, white blood cell count, platelet count, neutrophil count, PLR and NLR. Other studies also looked at this in a variety of ways other than the TIMI criterion in angiography and reported findings consistent with our results. Kurtul et al. showed that the subjects with PLR≥116 had higher TPI, lower hemoglobin, lower LVEF, further involvement of multiple arteries and higher mortality (11). However, no significant association was found between PLR and the number of involved arteries in our study. Perhaps the reason for this is the difference in the evaluated samples, that we studied patients with unstable angina while Kurtul et al. examined merely MI patients. Other studies also showed that higher levels of PLR are associated with a poorer heart condition, such as higher prevalence of peripheral arterial occlusion and reduced collateral circulation (20, 21).

Further studies have documented that higher levels of PLR have also been associated with a greater variety and severity of coronary artery involvement and increased mortality (11, 20). These findings, similar to our study, suggest the high value of PLR and NLR in relation to poorer prognosis and worse coronary artery disease in patients. In the study of Acet et al., infarct-related artery patency in STEMI patients was associated with lower LVEF and a higher level of PLR and NLR, and in line with our study, PLR and NLR were introduced as variables with the ability to predict patency rate of coronary arteries (20). In a study in Turkey on in-hospital mortality patients with ACS, the results revealed that PLR was associated with in-hospital mortality in these patients and suggested that it could be used as a measure for risk stratification (12). An interesting point in our study was that after the regression analysis and the placement of probable factors in relation to impaired coronary circulation, it was found that both the PLR and NLR indices remained as relevant factors, highlighting the value of these two indicators in the initial decision-making process.

The reason for association between increased levels of PLR and NLR can be attributed to the interaction of platelets and leukocytes, which leads to vascular endothelial dysfunction. Relative thrombocytosis and platelet activation and accumulation predispose platelet-rich thrombosis. In fact, platelets and coagulation cascades play a key role in the development of ACS (15, 21). In response to physiological stress during myocardial infarction or ischemia, the secretion of cortisol and catecholamines increases and leads to redistribution of lymphocytes in lymphatic organs and their apoptosis and ultimately lymphopenia (9, 20). However, very rapid changes in the size and function of the blood cells under different clinical conditions may be one of the biggest constraints in using PLR and NLR for the ACS patients. On the other hand, limited studies measured the sampling time of patients relative to the time of the onset of symptoms, and its effect has not yet been measured in changing the diagnostic value of PLR and NLR (7); this can be an idea for future research.

Perhaps the most important application of the findings of this study can be summarized in the statement that the increased PLR and NLR appear to be presented as markers with potential for risk assessment and decision making to nominate patients for angiography, although further studies are still needed for a definitive conclusion. Particularly, the angiography is an invasive diagnostic action and has many local and systemic side effects. As a result, the use of these markers in the CBC, which are simple, inexpensive and available, can lead to a significant reduction in unnecessary angiography. Our study also had some limitations. One of the limitations of our study is the measurement and evaluation of PLR and NLR from one CBC, so that different results may be obtained in multiple measurements and different days. The second limitation is the small sample size, the study limitation to a hospital, and the low mortality rates, which are not statistically reliable. A greater percentage of patients were male, and this might have an impact on the outcome. In addition, many latent inflammatory diseases and infections could affect PLR, which could not be excluded in the study.

CONCLUSION

Based on the findings of this study, it seems that PLR and NLR could be used to assess the severity of involvement and impaired coronary circulation in the ACS patients. Although using both of PLR and NLR as diagnostic tests could be helpful but NLR could be more useful. However, there are several other factors involved in increasing the risk in these patients, including age, LVEF, underlying disease, especially history of cardiovascular disease and increased TPI, which provide the feasibility of using PLR and NLR for risk stratification of these patients. Other uncertainties, such as the frequency of measurement, the time of measurement, and the final cut-off point associated with the application of PLR and NLR in the risk stratification of ACS patients, remain unanswered, which require further studies in various clinical settings.

REFERENCES

1. Ansari MA, Mohebati M, Poursadegh F, Foroughian M, Shamloo AS. Is echocardiographic epicardial fat thickness increased in patients with coronary artery disease? A systematic review and meta-analysis. Electronic physician. 2018;10(9):7249-58.
2. Zhou D,Wang G, Fan Y, Wan Z, Liu X. Platelet to lymphocyte ratio is associated with the severity of coronary artery disease and clinical outcomes of percutaneous coronary intervention in the Chinese Han population. Experimental and therapeutic medicine. 2017;13(2):731-8.

3. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acutemyocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European heart journal. 2018;39(2):119-77.
4. Sharma KH, Shah KH, Patel I, Patel AK, Chaudhari S. Do circulating blood cell types correlate with modifiable risk factors and outcomes in patients with acute coronary syndrome (ACS)?. Indian heart journal. 2015;67(5):444-51.
5. Karakurt A, Yildiz C. Predictive values of inflammatory cell ratios for complexity of coronary artery disease in patients with acute coronary syndrome. International Journal of the Cardiovascular Academy. 2018;4(4):70.
6. Lee YSG, Baradi A, Peverelle M, Sultani R, Adams H, Garlick J, et al. Usefulness of Platelet-to-Lymphocyte Ratio to Predict Long-Term All-Cause Mortality in Patients at High Risk of Coronary Artery Disease Who Underwent Coronary Angiography. The American journal of cardiology. 2018;121(9):1021-6.
7. Besli F, Ilter A, Gungoren F. The Link Between Mean Platelet Volume to Lymphocyte Ratio and Complexity of Coronary Artery Disease. Angiology. 2018;69(4):358-9.
8. Bressi E, Mangiacapra F, Ricottini E, Cavallari I, Colaiori I, Di Gioia G, et al. Impact of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio on 5-Year Clinical Outcomes of Patients with Stable Coronary Artery Disease Undergoing Elective Percutaneous Coronary Intervention. Journal of cardiovascular translational research. 2018;11(6):517-23.
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 medicine. 2015;5(2):96-104.
10. Bekler A, Gazi E, Yilmaz M, Temiz A, Altun B, Barutcu A, et al. Could elevated platelet-lymphocyte ratio predict left ventricular systolic dysfunction in patients with non-ST elevated acute coronary syndrome? Anatolian journal of cardiology. 2015;15(5):385-90.
11. Kurtul A, Murat SN, Yarlioglues M, Duran M, Ergun G, Acikgoz SK, et al. Association of platelet-to-lymphocyte ratio with severity and complexity of coronary artery disease in patients with acute coronary syndromes. The American journal of cardiology. 2014;114(7):972-8.
12. Oylumlu M, Yildiz A, Oylumlu M, Yuksel M, Polat N, Bilik MZ, et al. Platelet-to-lymphocyte ratio is a predictor of in-hospital mortality patients with acute coronary syndrome. Anatolian journal of cardiology. 2015;15(4):277-83.
13. Cong YL, Jin DM, Wang HL, Okada T, Peng ZH. [Establishing the reference range of venous blood measured by automated haematology analyzer in Chinese adults]. Zhonghua yi xue za zhi. 2003;83(14):1201-5.
14. 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). European heart journal. 2016;37(3):267-315.
15. Acar G, Kalkan ME, Avci A, Alizade E, Tabakci MM, Toprak C, et al. The relation of platelet-lymphocyte ratio and coronary collateral circulation in patients with stable angina pectoris and chronic total occlusion. Clinical and applied thrombosis/hemostasis : official journal of the International Academy of Clinical and Applied Thrombosis/Hemostasis. 2015;21(5):462-8.
16. Wu AH, Christenson RH. Analytical and assay issues for use of cardiac troponin testing for risk stratification in primary care. Clinical biochemistry. 2013;46(12):969-78.
17. Reihani H, Sepehri Shamloo A, Keshmiri A. Diagnostic Value of D-Dimer in Acute Myocardial Infarction Among Patients With Suspected Acute Coronary Syndrome. Cardiology research. 2018;9(1):17-21.
18. Wu AH, Smith A, Christenson RH, Murakami MM, Apple FS. Evaluation of a point-of-care assay for cardiac markers for patients suspected of acute myocardial infarction. Clinica chimica acta; international journal of clinicalchemistry. 2004;346(2):211-9.
19. Ghaderi F, Eshraghi A, Shamloo AS, Mousavi S. Assosiation of Epicardial and Pericardial Fat Thickness with Coronary Artery Disease. Electronic physician. 2016;8(9):2982-9.
20. Acet H, Ertas F, Akil MA, Ozyurtlu F, YildizA, Polat N, et al. Novel predictors of infarct-related artery patency for ST-segment elevation myocardial infarction: Platelet-to-lymphocyte ratio, uric acid, and neutrophil-to-lymphocyte ratio. Anatolian journal of cardiology. 2015;15(8):648-56.
21. Sunbul M, Gerin F, Durmus E, Kivrak T, Sari I, Tigen K, et al. Neutrophil to lymphocyte and platelet to lymphocyte ratio in patients with dipper versus non-dipper hypertension. Clinical and experimental hypertension (New York, NY : 1993). 2014;36(4):217-21.
22. Maher MA, Gutbi SS. Assessment of dietary pattern among coronary heart disease outpatients attended El-Shaap teaching hospital, Khartoum state. Medical Science, 2017, 21(86), 160-172

Article Keywords
Acute coronary syndrome, inflammatory marker, platelet-to-lymphocyte ratio, platelet, neutrophil-to-lymphocyte ratio

Acknowledgments
The current study has been adapted from the findings of a specialty thesis written by Dr. Hamidreza Bagherian in Emergency Medicine at Mashhad University of Medical Sciences. This study was conducted with the financial and spiritual support of the Deputy of Research of Mashhad University of medical sciences as a proposal approved by code of 950087.

Conflict of interest
The authors declare any conflicts of interest regarding the publication of this manuscript.

Article History
Received: 17 December 2018
Accepted: 8 February 2019
Published: March-April 2019

Citation
Javad Ramezani, Hamidreza Bagherian Kalat, Amir Masoud Hashemian, Neema John Mehramiz, Mahdi Foroughian. Association of neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios with coronary artery disease severity. *Medical Science*, 2019, 23(96), 211-216