On-admission High Neutrophil to Lymphocyte Ratio as Predictor of In-hospital Adverse Cardiac Event in ST-elevation Myocardial Infarction

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ABSTRAK

Tujuan: *untuk meneliti peran rasio netrofil terhadap limfosit (rasio NL) dalam memprediksi terjadinya* adverse cardiac events *selama perawatan rumah sakit pada pasien infark miokard akut dengan elevasi segmen ST IMA-EST.* ***Metode:*** *penelitian kohort pada pasien IMA-EST dengan awitan ≤24 jam yang dirawat di ICCU. Rasio NL dihitung sebagai hitung netrofil absolut dibagi dengan hitung limfosit absolut yang diukur melalui penghitung sel darah otomatis saat masuk rumah sakit. Outcome yang dinilai adalah* adverse cardiac events *selama perawatan rumah sakit yang dinilai selama follow-up. Nilai cut-off rasio NL untuk memprediksi* outcome *ditentukan berdasarkan analisis kurva ROC. Analisis univariat dan multivariat dilakukan untuk menilai apakah rasio NL tinggi merupakan prediktor independen untuk terjadinya adverse cardiac events selama perawatan rumah sakit.* ***Hasil:*** *dari 165 subjek, adverse cardiac events selama perawatan rumah sakit terjadi pada 49 subjek (29%). Nilai cut-off rasio NL adalah 6,2. Analisis univariat menunjukkan bahwa rasio NL >6,2 mempunyai odd ratio 3,19 (95% CI 1,55-6,55, p=0,002) untuk mengalami adverse cardiac events selama perawatan rumah sakit. Analisis multivariabel menunjukkan bahwa rasio NL>6,2 merupakan prediktor independen terjadinya adverse cardiac events selama perawatan rumah sakit dengan odd ratio 4,10 (95% CI 1,59-10,54, p=0,003).* ***Kesimpulan:*** *rasio NL yang tinggi saat masuk rumah sakit merupakan prediktor independen terjadinya adverse cardiac events saat perawatan rumah sakit pada pasien yang dirawat dengan IMA-EST.*

Kata kunci: *rasio netrofil terhadap limfosit, adverse cardiac events, infark miokard akut dengan elevasi segmen ST IMA-EST.*

ABSTRACT

Aim: *to investigate the role of neutrophil-to-lymphocyte ratio (NLratio) in predicting in-hospital adverse cardiac events in patients with STEMI.* ***Methods:*** *this was a cohort study on patients with STEMI onset ≤24 hour hospitalised in ICCU. NLratio was calculated as absolute neutrophil count divided with lymphocyte count measured by automated blood cell counter on admission.The outcome was in-hospital adverse cardiac events, which were recorded during follow-up. The cut-off value of NLratio to predict outcome was determined by ROC curve analysis. Univariate and multivariable analysis to assess whether high NLratio was independent predictor for in-hospital adverse events were performed.* ***Results:*** *among165 subjects, in-hospital adverse*

cardiac events occurred in 49 subjects (29%). The cut-off value of NLratio was 6.2. The univariate analysis showed that NLratio >6.2 had an odd ratio of 3.19 (95% CI 1.55-6.55, p=0.002) to develop in-hospital adverse cardiac events. The multivariate analysis showed that NLratio was an independent predictor of in-hospital adverse cardiac events with an odd ratio of 4.10 (95% CI 1.59-10.54, p=0.003). ***Conclusion:*** *high on-admission NLratio is an independent predictor for in-hospital adverse cardiac events in patients hospitalised for STEMI.*

Key words: *neutrophil-to-lymphocyte ratio, adverse cardiac events, STEMI.*

INTRODUCTION

Acute myocardial infarction induces an exacerbation of acute inflammation and stress response, which are characterized by an exaggerated mobilisation of leucocytes in the necrotic area. Among leucocytes, neutrophils are mobilized the most during acute myocardial infarction. Elevated absolute neutrophil counts are associated with the development of heart failure and mortality in acute myocardial infarction.[1] On the other hand, lymphocyte count, another differentiated type of leucocytes, is depressed during acute stress condition due to the excess of stress hormones.[2] Low lymphocyte counts have been reported in acute myocardial infarction and associated with adverse clinical outcomes.[3,4]

The ratio of absolute neutrophil counts to lymphocyte counts (NLratio) indicates the equilibrium between neutrophils and lymphocytes in circulation.[5] It reflects the state of acute inflammation and ongoing stress response.[5] In acute myocardial infarction, the equilibrium might swing to the extreme edge such that NLratio increases due to excessive acute inflammation and stress response. Increased NLratio has been reported in acute myocardial infarction, both ST-elevation myocardial infarction (STEMI) and NSTEMI.[6,7] Most studies in patients with STEMI involved subjects undergoing primary PCI as the first treatment modality for STEMI in early hours.[8-10] However, in real world situation, several patients with STEMI can not reach PCI-capable hospital in the duration allowed for primary revascularisation, therefore other treatment modalities are given such as fibrinolysis and pharmaco-intensive treatments.

The study aims to investigate the role of NLratio as a predictor of in-hospital adverse cardiac events in patients with STEMI, either treated with primary revascularisation or not. This setting of the study is relevant in real world practices, since not all patients with STEMI can reach PCI-capable hospital to have primary PCI or be a candidate for fibrinolytic therapy.

METHODS

The design of the study was cohort study. The subjects were patients with STEMI admitted for intensive cardiac care hospitalisation in ICCU of Dr. Sardjito General Hospital, Yogyakarta, Indonesia. The subjects were recruited consecutively between August 2013 and September 2014. The inclusion criteria were (1) patients with STEMI based on anginal pain, ST-elevation criteria in electrocardiogram and elevated cardiac enzyme (troponin I and/or CK-MB), (2) patients with an onset of anginal pain $\leq$ 24 hours, (3) patients with age between 30 and 80 year old and (4) patients agreed by signing an informed consent. The exclusion criteria were (1) patients with known chronic heart failure, chronic kidney disease, hepatic cirrhosis, chronic inflammatory diseases and malignancy, (2) patients with concomitant acute infection and sepsis and (3) patients with concomitant acute stroke.

The diagnosis of STEMI was based on the criteria of ESC/ACCF/AHA/WHF.[11] The onset of anginal pain was determined by thorough anamnesis with the subjects or family witnessing the event. Demographic data, i.e age and gender, was collected and recorded. Cardiovascular risk factors were recorded. Diabetes mellitus was determined as subjects with previously known diabetic or those taking antidiabetic medication on admission. Hypertension was determined as subjects with previously known

hypertension, those taking antihypertensive medications or those with systolic blood pressure ≥150 and diastolic blood pressure ≥90 during hospitalization. Previous ischemic heart disease (IHD) was determined as subjects with known coronary artery disease, either stented or non stented, or previous hospitalisation of acute coronary syndrome or those taking antiischemic medication and antiplatelets. Chronic heart failure, chronic kidney disease, hepatic cirrhosis and malignancy were diagnosed by anamnesis of previous illnessess. Chronic inflammatory diseases was determined as rheumatoid arthritis, inflammatory bowel disease or psoriasis, which was known through anamnesis. Acute infection was determined as fever and known focal infection, whereas sepsis were determined based on standard criteria and confirmed by an internist in consultation. Acute stroke was determined as an infarct or hemorrhage stroke, confirmed by a neurologist in consultation.

Blood was collected from antecubital veins in supine position in each subject, centrifuged and inserted into an automated blood cell counter. Total leucocyte count and differential subtype counts, including absolute neutrophil and lymphocyte counts, were analyzed using an automated blood cell counter in hospital laboratory. The neutrophil to lymphocyte ratio (NLratio) was calculated as the absolute neutrophil count divided with lymphocyte count. Other routine laboratory examination was performed. Blood collection was done on admission before revascularisation and heparinisation therapy started.

The follow-up was conducted within hospitalisation timeframe. Adverse cardiac events were determined as in-hospital mortality, acute heart failure, cardiogenic shock, resuscitated cardiac arrest and reinfarction. In-hospital mortality was all cause of death during intensive hospitalization. Acute heart failure was the presence of symptom of breathlesness and fatique and signs of congestion with subsequent use of intravenous diuretics. Cardiogenic shock was low blood pressure (systolic blood pressure < 90 mmHg) and signs of low perfusion with subsequent use of vasopressor. Reinfarction was defined as recurrent chest pain, recurrent ST-segment elevation and a re-elevation of creatinekinase-MB. The adverse cardiac events were confirmed by attending cardiologists as well as the subsequent treatment of the events were in the discretion of attending cardiologist treating the patients.

Subjects were participated voluntarily and confirmed with an informed consent. The Medical and Health Research Ethics Committee Faculty of Medicine Universitas Gadjah Mada and Dr. Sardjito Hospital approved the study protocol and released the ethical clearance.

For statistics analysis, the SPSS 16.0 software was used. Continuous data was checked for normality distribution with Kolmogorov-Smirnov test. Comparison between normally distributed continuous data was performed with student's T-test, while Mann-Whitney test was used for not normally distributed continuous data after logarithmic transformation. Comparison between categorical data was performed with Chi-square test. Receiver-operating characteristics (ROC) curve analysis was performed to determine the cut-off value of NLratio in respect to in-hospital adverse cardiac events. Univariate and multivariable analysis were performed to variables which displayed statistics difference between groups with $p<0.200$. Logistic regression method was used as a multivariable analysis to determine the independent predictors among variables entered in the models. A scoring system was developed based on multivariate analysis. A value of $p<0.05$ was determined as statistical significancy.

RESULTS

A number of 165 subjects were recruited in this study, comprised of 131 male subjects (79%) with mean age of 58.1 years. Twenty-seven percent of subjects had diabetes mellitus, 69% had hypertension and 12% had previous ischemic heart disease. Fifty percent of subjects were smokers who still smoked actively when the infarct event occurred. The subjects characteristics were shown in **Table 1**.

Twenty-seven subjects (16 %) presented with Killip class II-IV on admission. Revascularisation procedure was accomplished in 118 subjects

(72%), consisted of 53 fibrinolysis (32%) and 61 primary PCIs (36%). Anticoagulant therapy during hospitalisation was administered in 153 subjects (93%), either with unfractionated heparin, low molecular weight heparin or fondaparinux. ACE inhibitor was given to 127 subjects (77%), whereas beta blocker was given to 87 subjetcs (53%).

Adverse cardiac events during hospitalisation occured in 49 subjects (29%). Compared with subjects without in-hospital adverse cardiac events, those with adverse cardiac events were more likely to be female (p=0.039 vs. male), have diabetes mellitus (p=0.031), be non smoker (p=0.012), have worse Killip class (p=0.001), have lower hemoglobin level (p=0.003), have higher absolute neutrophil count (p=0.007) and have higher blood creatinine and glucose levels (p=0.014 and p<0.001, respectively). The value of NLratio was significantly higher in subjects with in-hospital adverse cardiac events as compared to those without events (p<0.001). The parameters between two groups are shown in **Table 1**.

Receiver-operating characteristics curve (ROC) analysis showed that NLratio had an area under the curve (AUC) of 66% to predict the adverse cardiac events, as shown in **Figure 1**. Using this curve, the cut-off value of NLratio was set in the point of 6.2, which gave the sensitivity of 71% and specificity of 56%. Therefore, subjects with NLratio >6.2 was grouped and analysed with univariate and multivariable analysis.

Table 1. Baseline characteristic between subjects with and without in-hospital adverse cardiac events

Parameters	All subjects (n=165)	Adverse cardiac events (n=49)	No adverse cardiac events (n=116)	p value**
Age (year), mean±SD	58.1±9.1	58.9±8.8	57.7±9.2	0.446
Male gender, n (%)	131 (79)	34 (69)	97 (84)	0.039
Diabetes mellitus, n (%)	45 (27)	19 (39)	26 (22)	0.031
Hypertension, n (%)	107 (69)	33 (67)	74 (64)	0.662
Previous IHD, n (%)	19 (12)	6 (12)	13 (11)	0.849
Current smoker, n (%)	82 (50)	17 (35)	65 (56)	0.012
Body mass index*	23.4 (3.8)	23.4 (5.1)	23.4 (3.4)	0.763
Killip II-IV, n (%)	27 (16)	15 (31)	12 (10)	0.001
Hemoglobin (g/dL), mean±SD	13.7±1.9	13.0±2.0	13.9±1.7	0.003
Leucocyte ($x10^3/mm^3$), mean±SD	13.2±3.9	14.1±3.9	12.8±3.9	0.067
Neutrophil ($x10^3/mm^3$), mean±SD	10.3±3.9	11.5±3.6	9.7±3.9	0.007
Lymphocyte ($x10^3/mm^3$), mean±SD	1.8±0.9	1.7±1.0	1.9±0.8	0.201
NLratio*	6.6 (4.7)	7.9 (4.8)	5.7 (4.1)	0.001
Creatinine (mg/dL), mean±SD	1.1 (0.47)*	1.5±0.9	1.1±0.4	0.014
Glucose (mg/dL)*	184.3±96.7	202.0 (181.0)	137.0 (53.7)	<0.001
Fibrinolysis, n (%)	53 (32)	17 (35)	36 (31)	0.646
Primary PCI, n (%)	61 (36)	23 (47)	38 (33)	0.089
Heparin, n (%)				0.537
- Unfractionated	128 (77)	38 (78)	90 (77)	
- Low molecular weight	13 (8)	2 (4)	11 (10)	
- Fondaparinux	12 (7)	5 (10)	7 (6)	
ACE inhibitor, n (%)	127 (77)	35 (71)	92 (79)	0.272
Beta blocker, n (%)	87 (53)	22 (45)	65 (56)	0.317

* Data not normally distributed, value was depicted in median (interquartile range) and analysed with Mann-Whitney U test, ** A p value from analysis between subject with and without in-hospital adverse cardiac events

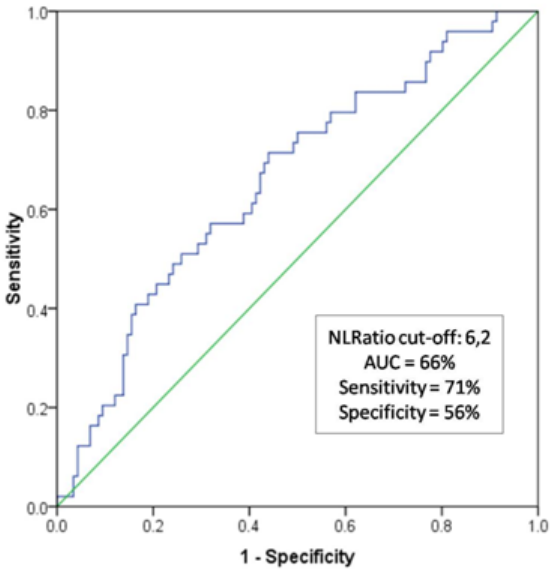

Figure 1. Receiver-operating characteristics curve (ROC) analysis gave NLratio cut-off value of 6.2 with sensitivity 71% and specificity 56% for in-hospital adverse cardiac events

The characteristics of subjects based on the value of NL ratio are shown in **Table 2**. The amount of subjects with NL ratio >6.2 was 86 subjects while the subjects with NL ratio ≤6.2 was 79 subjects.

The univariate analysis showed that NLratio >6.2 had an odd ratio of 3.19 (95% CI 1.55-6.55, p=0.002) to develop adverse cardiac events as compared NLratio <6.2. The multivariable analysis using logistic regression methods was performed with the adjustment of variables having p<0.200 in difference between groups (**Table 3**). The result of logistic regression analysis showed that NLratio was an independent predictor of in-hospital adverse cardiac events with an odd ratio of 4.10 (95% CI 1.59-10.54, p=0.003). Other independent predictors in this model were Killip class II-IV (odd ratio of 4.74 (95% CI 1.67-13.48, p=0.003) and creatinine >1.3 mg/dL (odd ratio of 4.53 (95% CI 1.83-11.17, p=0.001). The result of univariate and mutivariable analysis is shown in **Table 3**.

Based on multivariate analysis, the scoring system was developed incorporating variables with p value <0.05, i.e NL ratio >6.2, creatinine >1.3 and Killip class II-IV (**Table 3**). The total score was 9, out of three variables. We generated three risk category (low risk (score 0-2), medium risk (3-5) and high risk (6-9). (**Table 4**)

DISCUSSION

The result of this study shows that higher NLratio, with cut-off value 6.2, is an independent predictor of in-hospital adverse cardiac events in patients with STEMI. Patient with NLratio >6.2 had a four-time risk to develop in-hospital adverse cardiac events. Along with established predictors, i.e. Killip class and creatinine >1.3 mg/dl, on admission NL ratio >6.2 pose an increasing risk of hospital mortality and complication among patients admitted for STEMI, either primary revascularised or non-revascularised.

Other studies showed that high value of NLratio is associated with in-hospital major

Table 2. The characteristics of subjects according to the value of NL ratio

Parameters	NL ratio ≤6.2 (n=79)	NL ratio >6.2 (n=86)
Age (year), mean±SD	57.7±9.8	58.4±8.3
Male gender, n (%)	66 (84)	65 (76)
Diabetes mellitus, n (%)	23 (29)	22 (26)
Hypertension, n (%)	49 (62)	58 (67)
Previous IHD, n (%)	12 (15)	7 (8)
Current smoker, n (%)	38 (48)	44 (51)
Body mass index*	23.5 (3.4)	23.8 (3.4)
Killip II-IV, n (%)	13 (17)	14 (16)
Hemoglobin (g/dL), mean±SD	13.9±1.7	13.5±2.0
Leucocyte (x103/mm3), mean±SD	11.6±3.5	14.5±3.9
Neutrophil (x103/mm3), mean±SD	8.0±3.0	12.4±3.4
Lymphocyte (x103/mm3), mean±SD	2.4±1.1	1.3±0.4
NLratio*	4.2 (2.9)	8.8 (3.5)
Creatinine (mg/dL), mean±SD	1.4±2.0	1.2±0.4
Glucose (mg/dL)*	137.0 (83.0)	157.0 (120.7)
Fibrinolysis, n (%)	26 (33)	27 (31)
Primary PCI, n (%)	21 (27)	40 (46)
Heparin, n (%)		
- Unfractionated	62 (78)	66 (77)
- Low molecular weight	9 (11)	4 (5)
- Fondaparinux	5 (6)	7 (8)
ACE inhibitor, n (%)	60 (761)	67 (78)
Beta blocker, n (%)	46 (58)	41 (48)

* Data not normally distributed, value was depicted in median (interquartile range)

Table 3. Univariate and multivariable analysis among variables to predict in-hospital adverse cardiac events

Variables	Univariate		Multivariate	
	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Male gender	2.25 (1.03-4.92)	0.042	1.12 (0.35-3.59)	0.850
Diabetes mellitus	2.19 (1.07-4.51)	0.033	1.31 (0.51-3.34)	0.576
Current smoker	0.42 (0.21-0.83)	0.013	0.43 (0.16-1.17)	0.099
Killip II-IV	3.82 (1.63-8.97)	0.002	4.74 (1.67-13.48)	0.003
Hemoglobin	1.32(1.09-1.59)	0.005	0.86 (0.67-1.09)	0.218
Leucocyte	0.93(0.85-1.01)	0.070	1.05 (0.94-1.18)	0.380
NLratio>6.2	3.19(1.55-6.55)	0.002	4.10 (1.59-10.54)	0.003
Creatinine>1.3	3.68(1.80-7.55)	<0.001	4.53 (1.83-11.17)	0.001
Reactive hyperglycemia	3.07(1.48-6.38)	0.003	1.62 (0.67-3.94)	0.283
Primary PCI	1.76(0.89-3.47)	0.103	1.00 (0.44-2.27)	0.994

Table 4. Scoring system based on multivariate analysis

Variables	Score
Killip II-IV	3
Creatinine >1.3	3
NLratio >6.2	3
Total score	9

adverse cardiac events in STEMI patients regardless primary revascularisation therapy, i.e. primary PCI or fibrinolysis.[6] Nunez et al. (2008) revealed that the high quintile value of NLratio were associated with in-hospital mortality and a worse clinical picture during hospitalisation such as worse Killip class, left ventricular dysfunction, higher arrhytmia, maximum troponin I level and the need for rescue PCI in patients with STEMI.[6] This study showed that increased NLratio occurred from hospital admission and reached its peak level in 12-14 hour after admission.

Most studies on the role of NLratio in STEMI patients involving those whom treated with primary PCI as a the first principal treatment strategy. Arbel et al.[8] (2014) showed that high NLratio was independently associated with lower ejection fraction, cardiogenic shock and acute kidney failure in STEMI patients referred for primary PCI. However, acute heart failure did not associated with high NLratio according to the study.[8] Among STEMI patients with primary PCI, high NLratio associated with no re-flow following PCI and subsequent in-stent thrombosis, in-hospital mortality and major adverse cardiac events.[12-14] In our study, primary revascularisation procedure was accomplished in 114 subjects (71%), i.e. primary PCI in 61 subjects (36%) and fibrinolysis in 53 subjects (32%). Combined with subjects without undergoing primary revascularisation, high NLratio increases the risk for in-hospital adverse outcome.

Similar to our study, Ghaffari et al.[15] (2014) enrolled about 400 patients with STEMI regardless of primary revascularisation and reported the increasing incidence of left ventricular pump failure and major tachyarrhytmias. The study reported the incidence of in hospital cardiac events occurred in the first day of hospitalisation, which implicated the direct impact of NL ratio which was measured on admission. In our study, the adverse cardiac events were also observed from early hospitalisation. Furthermore, our study showed NL ratio predicted adverse cardiac events independently to Killip class which was determined on admission.

In STEMI patients, a higher NL ratio is associated with the severity of coronary artery disease and predicted higher Syntax score on coronary angiography analysis. This relationship is independent with other predictors such as diabetes mellitus, age and ejection fraction.[16] This may implicate the role of NL ratio as one of the supporting factor in coronary atherosclerosis development. Not only in acute phase of coronary artery disease, higher NL ratio also implicates

on the presence and severity of coronary artery disease in stable coronary artery disease.[17] The severity of coronary artery disease, in addition to culprit vessel, affects the outcome of STEMI both in hospital or long term prognosis.

NLratio is combined value of neutrophil count as an inflammatory marker and lymphocyte count as a stress response marker. The neutrophils release inflammatory mediators and orchestrate tissue inflammation. Increased neutrophil count is associated with the acute inflammatory response due to tissue injury or infarction. During myocardial infarction, neutrophil mobilisation aims as a repair process of an infarcted myocardia, however several maladaptive processes occur and contribute a worse clinical outcome.[6] Maladaptive impacts of neutrophil mobilisation for instances intravascular plugging, extensive myocardial necrosis, reperfusion injury, oxidative stress, plaque infiltration and disruption and neutrophil-platelet interaction.[6] In contrast, low lymphocyte count in myocardial infarction contribute to increased circulating apoptotic lymphocytes that induce secretion of inflammatory cytokines.[13] Taken together, higher NLratio reflects the increasing acute inflammation and ongoing stress that cause maladaptive responses during acute phase of infarct myocardial.

Our study clearly showed that high NLratio is associated with a 4-fold increased risk to develop in-hospital adverse events in patients with STEMI. The risk encompassess both primary revascularised and non-revascularised patients. The result of our study conveys additional evidence that NLratio measurement on admission in STEMI is necessary to predict subsequent worsened event. Measurement of NLratio is routinely done in the first blood withdrawal for routine laboratory examination, therefore no additional cost or effort is needed. This simple and practical examination is available in all hospital treating patients with STEMI.

CONCLUSION

A high NLratio on-admission is an independent predictor for in-hospital adverse cardiac events in patients hospitalised for STEMI.

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REFERENCES

1. Arruda-Olson AM, Reeder GS, Bell MR, Weston SA, Roger VL. Neutrophilia predicts death and heart failure after myocardial infarction: a community-based study. Circ Cardiovasc Qual Outcomes. 2009;2:656-62.
2. Onsrud M, Thorsby E. Influence of in vivo hydrocortisone on some human blood lymphocyte subpopulations. I. Effect on natural killer cell activity. Scand J Immunol. 1981;13:573–9.
3. Blum A, Sclarovsky S, Rehavia E, Shohat B. Levels of T-lymphocyte subpopulations, interleukin-1 beta, and soluble interleukin-2 receptor in acute myocardial infarction. Am Heart J. 1994;127:1226-30.
4. Horne BD, Anderson JL, John JM, et al. Which white blood cell sub-types predict increased cardiovascular risk? J Am Coll Cardiol. 2005;45:1638-43.
5. Kalay N, Dogdu O, Koc F, et al. Hematologic parameters and angiographicprogression of coronary atherosclerosis. Angiol. 2012;63:213–7.
6. Nunez J, Nunez E, Bodi V, et al. Usefulness of the neutrophil to lymphocyte ratio in predicting long-term mortality in ST segment elevation myocardial infarction. Am J Cardiol. 2008;101:747-52.
7. Azab B, Zaher M, Weiserbs KF, et al. Usefulness of neutrophil to lymphocyte ratio in predicting short- and long-term mortality after non–ST-elevation myocardial infarction. Am J Cardiol. 2010;106:470-6.
8. Arbel Y, Shacham Y, Ziv-Baran T, et al. Higher neutrophil/lymphocyte ratio is related to lower ejection fraction and higher long-term all-cause mortality in ST-elevation myocardial infarction patients. Can J Cardiol. 2014;30:1177-82.
9. Kaya MG, Akpek M, Lam YY, et al. Prognostic value of neutrophil/lymphocyte ratio in patients with ST-elevated myocardial infarction undergoing primary coronary intervention: a prospective, multicenter study. Int J Cardiol. 2013;168:1154-9.
10. Chia S, Nagurney JT, Brown DF, et al. Association of leukocyte andneutrophil counts with infarct size, left ventricular function and out-comes after percutaneous coronary intervention for ST-elevation myocardial infarction. Am J Cardiol. 2009;103:333-7.
11. Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. J Am Coll Cardiol. 2007;22:2173-95.
12. Akpek M, Kaya MG, Lam YY, et al. Relation of neutrophil/lymphocyte ratio to coronary flow to in-hospital major adverse cardiac events in patients with ST-elevated myocardial infarction undergoing primary coronary intervention. Am J Cardiol. 2012;110:621-7.

13. Sen N, Afsar B, Ozcan F, et al. The neutrophil to lymphocyte ratio was associated with impaired myocardial perfusion and long term adverse outcom e in patients with ST-elevated myocardial infarction undergoing prim ary coronary intervention. Atherosclerosis. 2013;228:203-10.
14. Ayca B, Akın F, Celik O, et al. Neutrophil to lymphocyte ratio is related to stent thrombosis and high mortality in patients with acute myocardial infarction. Angiol. 2014; DOI 0003319714542997, first published online.
15. Ghaffari S, Nadiri M, Pourafkari L, et al. The predictive value of total neutrophil count and neutrophil/ lymphocyte ratio in predicting in-hospital mortality and complications after STEMI. J Cardiovasc Thorac Res. 2014;6:35-41.
16. Sahin DY, Elbasan Z, Gur M, et al. Neutrophil to lymphocyte ratio is associated with the severity of coronary artery disease in patients with st-segment elevation myocardial infarction. Angiol. 2012;64:423-9.
17. Papa A, Emdin M, Passino C, et al. Predictive value of elevated neutrophil-lymphocyte ratio on cardiac mortality in patients with stable coronary artery disease. Clin Chim Acta. 2008;395:27-31.