# NEUTROPHIL TO LYMPHOCYTE RATIO AS MORTALITY PREDICTOR IN ACUTE CORONARY SYNDROME PATIENTS

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## Abstract

**Introduction:** Inflammation plays important role in atherosclerosis which is the primary mechanism in acute coronary syndrome (ACS). Neutrophil to lymphocyte ratio (NLR) as an indication of systemic inflammation has been researched to be associated with morbidity and mortality in ACS. There are little data available about the association between NLR, levels with GRACE and TIMI risk score. Purpose of this study was to determine the association of NLR with GRACE and TIMI score in ACS patients. Methodology. A total of 1000 ACS patients were recruited into this study retrospectively from patients that admitted to Cardiology Department at Dustira Army Hospital. Patient assessment and medical record review were performed from January 2019 to January 2020. Results. The GRACE risk score was significantly higher in the group with high NLR value compared to those with moderate and low NLR value respectively 155 (132,2-178), 134 (115-156), 125 (107,5-144,25), p<0.001). Similarly, TIMI score for UAP, NSTEMI and STEMI significantly higher in the group with high NLR value compared to those with moderate and low NLR value respectively (3 (3-4), 3 (3-4), 3 (3-3), p<0.001), (5 (4-5), 4 (4-5), 4.5 (4-6 5), p<0.001) and (6 (5-7), 6 (5-6), 6 (5.5-6), p<0.001). Moreover, both GRACE (r=0,402, p<0.000) and TIMI (r=0.221, r=0.234, r=0.295, in UAP, NSTEMI, and STEMI respectively, p<0.000) score showed a significant positive correlation with NLR respectively. Conclusions. NLR is convenient, inexpensive and reproducible biomarker for ACS prognosis.

Keyword: Neutrophil, Lymphocyte, Acute coronary syndrome, GRACE score, TIMI score

## INTRODUCTION

Cardiovascular diseases are the number one cause of morbidity and mortality globally [1]. Acute coronary syndrome (ACS) is one of the prevalent that are responsible for fatal heart attack and heart failure [2]. Acute coronary syndrome impairs vascular perfusion and reperfusion, cause the damage to myocardium, depending on the duration of ischemia, severity and metabolic demand of tissue [3]. As a consequence, local and systemic inflammation process can be triggered for remodeling and scar formation of myocardium [4]. There are two main phases of inflammation in acute coronary syndrome, inflammatory phase and proliferative phase. In the first phase, the first leukocytes can be found in the damaged areas are neutrophils [1,4]. Lymphocytes play vital roles in the second phase for remodeling the myocardium [5]. Therefore, neutrophils are seen as a marker of ongoing inflammation and lymphocytes as a marker of remodeling phase [6].

Neutrophil to lymphocyte ratio (NLR) as an indication of systemic inflammation has been researched to be associated with poor clinical outcome in various cardiovascular diseases, including acute coronary syndrome [7–9]. Adverse clinical outcome in ACS patient can be measured by scoring system, GRACE (Global Registry of Acute Coronary Events) score and TIMI (Thrombolysis in Myocardial Infarction) score, that have a high diagnostic performance for adverse outcome in ACS [2]. In countries with a lack of resources, these relatively inexpensive and very available parameter can be importance for diagnosis, risk stratification and predict mortality in patients with ACS [1].

Recent multicenter study found that NLR level significantly higher in ACS patients [10]. The previous studies have shown that NLR is associated with morbidity and mortality in ACS patient [5,10]. The relationship between NLR and ACS has been demonstrated in several studies, but there are little data available about the association between NLR levels with GRACE and TIMI risk score [11]. The purpose of

this study was to determine the association of concomitant hematological indices such as NLR with GRACE and TIMI score in ACS patients.

## METHODOLOGY Study Population

The sample of this study was obtained retrospectively from patients that admitted to Cardiology Department at Dustira Army Hospital. Patient assessment and medical record review were performed in ACS patients in Dustira Army Hospital from January 2019 to June 2020. 1000 patients were recruited into this study. The inclusion criteria of this study were the following: (a) Adult (age > 18 years old); (b) ACS patient (STEMI and non-ST-segment elevation acute coronary syndrome (NSTE-ACS)) that diagnosed according to the criteria recommended by 2020 ESC guidelines [12]. Meanwhile, the exclusion criteria of this study were: (a) Patients who had inflammatory diseases such as gastritis, chronic cholecystitis, nephritis, rhinitis, pharyngitis, bronchitis, myocarditis, rheumatoid arthritis, gout, immune disorder, ongoing infection and cancer; (b) significant valvular heart disease; (c) significant congestive heart failure; (d) sever renal or liver disease, and (e) the history of trauma or surgery within 30 days.

## **Clinical Assessment**

All ACS patients that fulfilled inclusion and exclusion criteria were recruited into this study. Information on demographic (age, gender and BMI) and clinical characteristic (hypertension, diabetes mellitus, systolic blood pressure, diastolic blood pressure, heart rate, serum glucose, total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), complete blood count (CBC) such as hemoglobin (Hb); white blood count (WBC); hematocrit; platelet count (PC), MCV,MCH, MCHC, RDW, natrium, potassium, uric acid, creatinine, blood urea nitrogen (BUN), cardiac marker, SGOT, SGPT, Killip class, GRACE risk score and TIMI risk score) were collected.

#### Definition of acute coronary syndrome

Patients with chest pain that persisted for at least 20 min, ST segment elevation > 1 mm in at least 2 contiguous leads or new onset complete left bundle branch block or new onset complete right bundle branch block on 12-lead electrocardiogram and elevated cardiac markers such as troponin T/I or creatine kinase myocardial band were diagnosed with ST-segment elevated myocardial infarction (STEMI). The definition of NSTEACS included unstable angina pectoris (UAP) and non-ST segment elevated myocardial infarction on electrocardiogram and/or positive cardiac enzyme in patients with angina or equivalent. UAP was defined as the presence ST-segment depression on electrocardiogram and/or negative cardiac enzyme in patients with angina or equivalent.

#### Laboratory parameters

Venous blood samples were obtained from the patients within an hour of admission to the emergency room. The NLR and PLR were calculated by dividing the absolute neutrophil count (NC) to the absolute lymphocyte count (LC) and the absolute plate PC to the absolute LC respectively. Fasting biochemical parameters such as TC, HDL, LDL, TG, glucose level and uric acid were tested 1 day after hospital admission. In this present study, we use single measurement for cardiac marker, troponin I, considering, 0.02 ng/ml to be an elevated cardiac marker.

#### **Risk Scoring**

In this study, we used GRACE risk score and TIMI risk score to stratify patients who diagnosed ACS to estimate their in-hospital, 6 months to 3 years mortality and risk for having or dying from a heart related event in the next 14 days respectively. The variables used in the calculation of the GRACE score include age, systolic blood pressure, heart rate, baseline creatinine level, Killip level of congestive heart failure, history of cardiac arrest at admission, elevation cardiac marker and ST segment deviation. The variables used in the calculation of the TIMI risk score for STEMI patients include age, history of diabetes, hypertension or angina, systolic blood pressure, heart rate, Killip class of congestive heart failure, weight, anterior ST elevation or LBBB and history of time to treatment > 4 hours. The variables used in the

calculation of TIMI risk score for NSTEAC patients include age, history of coronary artery disease (CAD) such as hypertension, diabetes, family history of CAD, and current smoker, recent CAD (stenosis  $\geq$  50%), ASA use in past 7 days, severe angina ( $\geq$ 2 episodes in 24 hours), ECG ST changes  $\geq$ 0.5 mm and positive cardiac masker. NLR classified into 3 groups, low NLR (<2.6), medium NLR (2.6-4.5) and high NLR (>4.5).

#### Statistical analysis

GRACE risk score and TIMI risk score were independent variables. Dependent variable in this study was NLR. Data were analysed with SPSS 22.0 statistical software. Descriptive analyses included mean ± SD/ median (Q1-Q3) for continuous numerical outcomes and percentage frequency distribution for categorical data. Correlation between data was tested with Pearson's correlation analysis. Receiving operating characteristic curve analysis was used for NLR. Chi-square, Fisher's exact, independent t-test, Mann–WhitneyU-tests, ANNOVA and Kruskal Wallis tests were used to compare occurrence of categorical factors and numerical data, respectively, between the two groups.

#### RESULTS

In this study, records were analyzed of 1000 patients whom were admitted with diagnosis of Acute Coronary Syndrome (STEMI and non-ST-segment elevation acute coronary syndrome (NSTE-ACS)). The demographic, clinical, and laboratory characteristics of the patients are presented in Table 1. The patients in the group with high NLR were older and had higher serum glucose levels, higher LDL cholesterol levels, lower hemoglobin, higher heart rate, higher Killip class, more ST-segment changes, and higher troponin and creatinine levels. GRACE risk score was significantly higher in the high NLR group than in those with moderate or low NLR (159 (143-180), 134 (116.75-153) and 123 (104-146), respectively, p<0.000). Whereas, TIMI risk score in UAP was slightly higher in the group with high NLR value compared to those with moderate and low NLR value (4 (3-4), 3 (3-4), and 3(3-4), respectively, p<0.000). In NSTEMI, the TIMI risk score was also slightly higher in the group with high NLR value compared to those with moderate and low NLR value (4 (4-5), 4 (4-5), and 4 (4-4.75), respectively, p<0.000). Similarly, TIMI risk score in STEMI was slightly higher in the group with high NLR value compared to those with moderate and low NLR value (4 (5-7), 6 (5-6), and 5.5 (4.75-6), respectively, p<0.000).

Low NLR (<2.6),	Medium NLR	High NLR	P value	
n=291	(2.6-4.5), n=462	(>4.5), n=247		
54(48-61)	55(49-63)	64(55-70)	<0.000	
147(50.5%)	259(56.1%)	156(63.2%)	0.013	
144(49.5%)	203(43.9%)	91(36.8%)	0.013	
	24.44(21.94-	24.65(22.31-		
24.7(22.19-27.24)	26.89)	26.84)	0.481	
104(35.7%)	144(31.2%)	76(30.8%)	0.35	
14(4.8%)	21(4.5%)	9(3.6%)	0.788	
30(10.3%)	35(7.6%)	14(5.7%)	0.13	
2(0.7%)	2(0.4%)	3(1.2%)	0.493	
(%) 15(5.2%) 16(3.5%)		15(6.1%)	0.248	
78(26.8%)	119(25.8%)	31(12.6%)	<0.000	
18(6.2)	27(5.8%)	27(10.9%)	0.032	
115(39.5%)	155(33.5%)	83(33.6%)	0.202	
114(39.2%)	174(37.7%)	108(43.7%)	0.286	
	n=291 54(48-61) 147(50.5%) 144(49.5%) 24.7(22.19-27.24) 104(35.7%) 14(4.8%) 30(10.3%) 2(0.7%) 15(5.2%) 78(26.8%) 18(6.2) 115(39.5%)	n=291 $(2.6-4.5), n=462$ $54(48-61)$ $55(49-63)$ $147(50.5%)$ $259(56.1%)$ $144(49.5%)$ $203(43.9%)$ $24.44(21.94 24.7(22.19-27.24)$ $26.89)$ $104(35.7%)$ $144(31.2%)$ $14(4.8%)$ $21(4.5%)$ $30(10.3%)$ $35(7.6%)$ $2(0.7%)$ $2(0.4%)$ $15(5.2%)$ $16(3.5%)$ $78(26.8%)$ $119(25.8%)$ $18(6.2)$ $27(5.8%)$ $115(39.5%)$ $155(33.5%)$	n=291 $(2.6-4.5), n=462$ $(>4.5), n=247$ $54(48-61)$ $55(49-63)$ $64(55-70)$ $147(50.5%)$ $259(56.1%)$ $156(63.2%)$ $144(49.5%)$ $203(43.9%)$ $91(36.8%)$ $24.44(21.94 24.65(22.31 24.7(22.19-27.24)$ $26.89$ $26.84$ $104(35.7%)$ $144(31.2%)$ $76(30.8%)$ $14(4.8%)$ $21(4.5%)$ $9(3.6%)$ $30(10.3%)$ $35(7.6%)$ $14(5.7%)$ $2(0.7%)$ $2(0.4%)$ $3(1.2%)$ $15(5.2%)$ $16(3.5%)$ $15(6.1%)$ $78(26.8%)$ $119(25.8%)$ $27(10.9%)$ $115(39.5%)$ $155(33.5%)$ $83(33.6%)$	

#### Table 1. Demographic characteristics of patient with Acute Coronary Syndrome

Physical examination					
Heart Rate Systolic Blood Pressure	95(79-105)	102(90-109)	109(98-120)	<0.000	
(mmHg) Diastolic Blood Pressure	120(110-140)	120(110-140)	110(110-120)	<0.000	
(mmHg)	80(80-90)	80(80-90)	80(80-90)	0.154	
<b>Biochemical Parameters</b>					
Serum glucose (mg/dl)	115(97-135)	124(99-150)	124(100-164)	<0.000	
Total cholesterol (mg/dl)	165(134-185)	165(134-198.75)	165(135-205)	0.113	
LDL cholesterol (mg/dl)	106(86-139)	108(91-135)	123(97-151)	<0.000	
HDL cholesterol (mg/dl)	32(28-38)	32(28-38)	32(28-38)	0.869	
Triglycerides (mg/dl)	121(89-172)	128(98-165)	123(91-170)	0.235	
Creatinin (mg/dl)	0.7(0.5-1)	0.8(0.6-1)	1(0.7-1.2)	<0.000	
Ureum (mg/dl)	27(21-33)	27(23-33)	29(23-37)	0.006	
Troponin I (ng/ml)	0.01(0.01-0.13)	0.04(0.01-0.7)	0.4(0.01-3.04)	<0.000	
Natrium (mmol/l)	138(137-141)	138(137-140)	139(137-141)	0.108	
Kalium (mmol/l)	3.9(3.7-4.1)	3.9(3.7-4)	3.8(3.6-4)	0.414	
Hemogram parameters					
Hemoglobin (g/l)	13.3(12.3-14.3)	13.2(11.9-14.2)	13.1(12.1-14.3)	0.279	
RBC	4.6(4.3-5.2)	4.7(4.3-5.3)	4.8(4.3-5.3)	0.211	
Hematocrit, %	37.5(34.8-41.3)	36.9(33.2-41.1)	37.2(34.5-42.2)	0.083	
Leukosit	7.3(6.3-8.7)	8.6(7.4-9.5)	9.5(8.1-11.8)	<0.000	
	2275.2(1934.4-	1792.1(1494.52-	1219.4(924-		
Limfosit Count	2692.8)	2070.6)	1466.1)	< 0.000	
		548.1(393.6-	667(507.6-		
Monosit Count	472.5(333.7-663.3)	712.3)	952.2)	< 0.000	
Basofil Count	40.8(20.8-58.1)	49.2(19.1-77.7) 88.7(52.15-	42(21.9-66.4)	0.001	
Eosinofil Count	183.6(85.8-320.4)	169.27)	94.5(51.1-153)	<0.000	
Losmoni Count	4135.6(3329.4-	6149.9(5341.25-	7464.6(6240-	<b>NO.000</b>	
Netrofil Count	5030.4)	6976.67)	9231.3)	<0.000	
Netronii Count	253000(187000-	225000(172000-	242000(185000-	<b>NO.000</b>	
Platelet	299000)	295500 (172000-	320000)	0.003	
MCV (fL)	81.7(75-85)	81.1(72.3-84.6)	81.8(73.2-85)	0.003	
MCV (IL) MCH (fL)	28(26.3-30)	27.8(23.4-30.1)	27.8(23.7-30)	0.323	
	34.1(32.6-35.2)			0.238	
MCHC (fL)		33.7(31.8-35)	33.7(31.9-34.9)	0.075	
ם זם	103.62(83.7-	130.39(103.12-	199.21(155.18-	<0.000	
PLR	133.96)	162.06)	272.51)	<0.000	
RDW	12.8(11.6-14)	12.7(8.2-13.9)	15(12.7-18.4)	<0.000	
ST-Segment deviation, n	222/76 682	20((92.57))	010/06 091	0.000	
(%) V:11: 1	223(76.6%)	386(83.5%)	213(86.2%)	0.009	
Killip class		252/00 523	100/00 57	0.0-1	
I	239(82.1%)	373(80.7%)	199(80.6%)	0.871	
II	30(10.3%)	43(9.3%)	26(10.5%)	0.871	
III	14(4.8%)	28(6.1%)	11(4.5%)	0.871	
IV IV	8(2.7%)	18(3.9%)	11(4.5%)	0.871	
GRACE risk score TIMI	123(104-146)	134(116.75-153)	159(143-180)	<0.000	
UAP	3(3-4)	3(3-4)	4(3-4)	<0.000	
NSTEMI	4(4-4.75)	4(4-5)	4(4-5)	<0.000	
STEMI	4(4-4.75) 5.5(4.75-6)	4(4-3) 6(5-6)	4(4-3) 6(5-7)	<0.000	
SIEMI	J.J(+.75-0)	0(0-0)	0(3-7)	NU.UUU	

Data are presented as median (interuartile range) or n (%).

CAD: Coronary Artery Disease; PCI: Percutaneous Coronaru Intervention; CABG: Coronary Artery Bypass Graft; AMI: Acute Myocardial Infarction; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; RBC:Red Blood Cells; WBC: White Blood Cell; MCV: Mean Cell Volume; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin; Content attraction p<0.000) and TIMI (r=0.221, r=0.234, r=0.295, in UAP, NSTEMI, and STEMI respectively, p<0.000) score showed a significant positive correlation with NLR.

Table 2. Correlation analysis for patient with acute coronary syndrome					
	NLR				

	r	р			
GRACE score	0.402	<0.000			
TIMI score					
UAP	0.221	<0.000			
NSTEMI	0.234	<0.000			
STEMI	0.295	<0.000			

Receiving operating characteristic (ROC) analysis showed that the best cutoff value of the NLR was 4.51. The ROC analysis revealed that the area under the ROC (AUROC) for the GRACE score in predicting mortality was 0.756 and the best cutoff value of the GRACE score for predicting mortality was 146.5 (sensitivity: 71.2%, specificity: 70.78%), with a positive predictive value of 44.44% and a negative predictive value of 88.2% (figure 1). The ROC analysis revealed that the area under the ROC (AUROC) for the TIMI score in predicting mortality in STEMI patient was 0.677 and the best cutoff value of the TIMI score for predicting mortality in STEMI patient was 5 (sensitivity: 98.9%, specificity: 18.42%), with a positive predictive value of 49.18% and a negative predictive value of 95.45% (figure 2). The ROC analysis revealed that the area under the ROC (AUROC) for the TIMI score in predicting mortality in STEMI patient was 5 (sensitivity: 98.9%, specificity in NSTEMI patient was 0.606 and the best cutoff value of the TIMI score in predicting mortality in NSTEMI patient was 4 (sensitivity: 97.8%, specificity: 7.75%), with a positive predictive value of 27.21% and a negative predictive value of 90.9% (figure 3). The ROC analysis revealed that the area under the ROC (AUROC) for the TIMI score in predicting mortality in UAP patient was 3 (sensitivity: 96.92%, specificity: 3.14%), with a positive predictive value of 14.58% and a negative predictive value of 85.71% (figure 4).

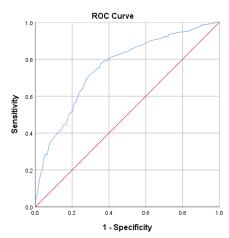


Figure 1. Receiver operating characteristic curve analysis of GRACE risk score (area under the curve=0.756) for inhospital mortality

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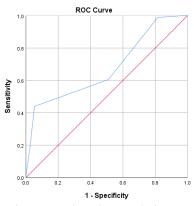


Figure 2. Receiver operating characteristic curve analysis of TIMI risk score (area under the curve=0.677) in STEMI patient for mortality

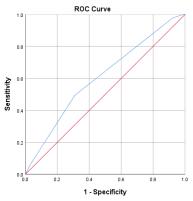


Figure 3. Receiver operating characteristic curve analysis of TIMI risk score (area under the curve=0.606) in NSTEMI patient for mortality

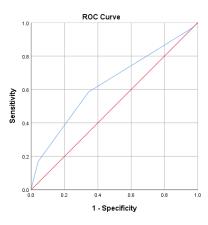


Figure 4. Receiver operating characteristic curve analysis of TIMI risk score (area under the curve=0.634) in UAP patient for mortality

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	AUC	SE	P-value	CI%95		Specifi	Sensiti	NPV	PPV	Cut off
				Lower limit	Upper limit	city	vity			value
GRACE	0.759	0.018	0.000	0.721	0.791	70.78	71.2	88.2	44.44	146.5
TIMI UAP	0.634	0.040	0.001	0.556	0.712	3.14	96.92	85.71	14.58	3
TIMI	0.606	0.034	0.003	0.539	0.673	7.75	97.80	90.9	27.21	4
NSTEMI TIMI	0.667	0.038	0.000	0.602	0.752	18.42	98.9	95.45	49.18	5
STEMI	0.007	0.038	0.000	0.002	0.752	10.42	90.9	95.45	49.10	5
OTENII										

Table 3. Receiver operating characteristic (ROC) analyzes of GRACE risk score, TIMI risk score for UAP. TIMI risk score for NSTEMI, and TIMI risk score for STEMI

## DISCUSSION

In this study, subject's age characteristic was similar with several studies in China and Turkey. [3] [5] The subject's BMI in this study was also similar with the study in China. Most subjects in other several studies have similar risk factors with subject in this study, which includes hypertension, diabetes, dyslipidemia, and smoking. Hypertension number significantly fewer in this study compared with the study conducted by Soylu et al. (2015) in Turkey (26.8% vs 42.9% in low NLR group, 25.8% vs 36.8% in medium NLR group, 12.6% vs 49.1% in high NLR group) [3]. Similarly, diabetes number is also significantly fewer in this study compared with the study conducted in Turkey (6.2% vs 22.9% in low NLR group, 5.8% vs 19.8% in medium NLR group, 10.9% vs 35.8% in high NLR group) [3]. This difference might carry different prognostic outcome. In this study, subject's hemoglobin level was similar with study in Turkey (p<0.001) and China (p=0.169) [3,5]. A study suggest that anemia was associated with increased comorbidities and higher-risk features on presentation [13]. In this study, subject's heart rate is higher than the previous study conducted in Turkey, but have lower systolic blood pressure (HR: 95 vs 74.9 in low NLR group, 102 vs 79.2 in medium NLR group, 109 vs 86.6 in high NLR group, p<0.001) (SBP: 120 vs 152.3 in low NLR group, 120 vs 147.5 in medium NLR group, 110 vs 141 in high NLR group, p=0.059) [3]. The subject's serum glucose was lower than the study conducted by Soylu et al. (2015) in Turkey (115) vs 157.1 in low NLR group, 124 vs 143.5 in medium NLR group, 124 vs 171 in high NLR group, p=0.017) [3]. The study suggests that the difference might be related to different food variants among various countries [14]. Compared with the study conducted by Chen et al. (2018) in China, subject's WBC and its differential count is quite similar in this study (WBC: 7.3 vs 6.9 in low NLR group, 9.5 vs 9.6 in high NLR (DC(LYM/MON/BAS/EOS/NEU): 2275.2/472.5/40.8/183.6/4135.6 group. p=0.000)vs 2363.9/538.3/23.1/167.6/3825.3 group, 1219.4/667/42/94.5/7464.6 in low NLR vs 1503.6/676.4/24.5/90.2/7385.1 in high NLR group, p=0.000, p=0.000, p=0.764, p=0.000, p=0.000, respectively) [5]. In this study, subject's LDL cholesterol level and creatinine level was similar with other several studies in China and Turkey [3,5]. The subject's troponin I level was significantly lower than the study conducted by Soyu et al. [3] in Turkey (0.01 vs 10.1 in low NLR group, 0.04 vs 19.7 in medium NLR group, 0.4 vs 29.2 in high NLR group, p < 0.001). The study suggest the difference might be health care conditions [15].

## Neutrophil to Lymphocyte Ratio

In this study, we found higher GRACE and TIMI risk scores in patients with high NLR values. We also found that NLR correlated with GRACE and TIMI scores. This study demonstrates an association between NLR and mortality in patients with ACS. Neutrophil to lymphocyte ratio has emerged as a useful and easy-to-assess prognostic tool and biomarker of cardiovascular risk [16,17]. Moreover, the NLR has been shown to predict cardiac arrhythmias, risk of recurrent major ischemic events, as well as short- and long-term mortality in patients with acute coronary syndromes (ACS) [4,6,18,19]. There are various possible mechanisms that can explain the relationship between elevated NLR and risk of cardiovascular events. Systemic factors like inflammation, endothelial dysfunction, and oxidative stress may play a role [20–22]. Neutrophils secrete inflammatory mediators that can lead to vascular wall degeneration [23,24]. Neutrophils may also make plaques more vulnerable through the release of proteolysis enzymes, arachidonic acid derivatives, and superoxide radicals [20]. Conversely, lymphocytes regulate the

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inflammatory response and have an anti-atherosclerotic role in which regulatory T-cell, a subclass of lymphocyte, may have an inhibitory effect on atherosclerosis [23,25]. B1a cells are the primary producers of natural IgM antibodies. IgM antibodies are believed to protect against atherosclerosis [26]. Previous studies also showed that a low lymphocyte count served as an early marker of physiologic stress and systemic collapse secondary to myocardial ischemia mediated by cortisol release. Increased cortisol levels result in a reduction in the relative level of lymphocytes [23].

## **GRACE Risk Score**

The Global Registry of Acute Coronary Events (GRACE) risk scores have a high diagnostic performance for adverse outcomes in ACS and are the preferred scoring system that current European Acute Coronary Syndrome guidelines recommend to apply on admission and at discharge in daily clinical practice [2]. The present study shows that the GRACE risks score significantly correlateswith NLR. This result is also shown in a study conducted by Soylu et al. (2015) and Acet et al. (2016) in which the GRACE risk score also significantly correlates with NLR (p<0.001, p<0.001 and p<0.001 respectively) [2,3]. A study conducted at BRSU Tabanan on March 2018also demonstrated a significant correlation between NLR and GRACE risk score in ACS patients [27]. On ROC analysis, GRACE risk score with a threshold of 146.5 has a higher negative predictive value than positive predictive value. Low GRACE risk score may be interpreted as a good predictor of good prognosis and survival, which may be more useful than the positive role of increased GRACE risk score. In this study, the cutoff value of the GRACE score was similar with score in Turkey (146.5 vs >140).

## **TIMI Risk Score**

TIMI risk score for STEMI presented good discriminatory power as a predictor of in-hospital mortality [11]. The TIMI risk score therefore should be used in conjunction with clinical judgment for ED chest pain patient risk stratification [28,29]. Correia et al. (2014) have recently evaluated the discriminatory power of the TIMI risk score in comparison to the GRACE risk score in 152 STEACS patients, showing a similarity between the scores, but better calibration for the TIMI risk score [30]. On ROC analysis, TIMI risk score with a threshold of 5, 4, 3 (for STEMI, NSTEMI, and UAP respectively) has a higher negative predictive value than positive predictive value. Low TIMI risk score may be interpreted as a good predictor of good prognosis and survival, which may be more useful than the positive role of increased TIMI risk score either in STEMI patient, NSTEMI patient, or UAP patient.

## CONCLUSION

In the present study, a strong correlation between NLR with GRACE and TIMI scores has been demonstrated, particularly in the high NLR group. Therefore, in addition to the relation of low and moderate NLR values with low morbidity, it may be assumed that a high NLR would be associated with increased morbidity and mortality.

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