

# The relationship between residual SYNTAX score and neutrophil/lymphocyte ratio in ST segment elevation myocardial infarction patients

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## Abstract

**Aim:** The objective of this study was to research the relation between residual SYNTAX score and neutrophil/lymphocyte ratio in patients with ST segment elevation myocardial infarction (STEMI).

**Material and Methods:** A total of 300 patients with STEMI were included from January 2015 to February 2020. Residual SYNTAX score (RSS) was calculated for each patient after primary percutaneous coronary intervention (PCI). RSS>8 was accepted as high RSS. Clinical and laboratory features of the patients including neutrophil/lymphocyte ratio were recorded.

**Results:** 109 (36.3%) of the patients had RSS over 8 and classified as high RSS. In the high residual SYNTAX group, while the neutrophil count was higher ( $p<0.001$ ), the lymphocyte count was lower ( $p<0.001$ ) and the N / L ratio was statistically higher ( $p<0.001$ ). In terms of multivariate analysis, glucose [( $p:0.023$ , OR: 1.005, 95% CI (1.001-1.009)], CRP [( $p: 0.033$ , OR: 1.018, 95% CI (1.001-1.035)], culprit vessel [( $p< 0.001$ , OR: 3.437, 95% CI (1.741-6.786)] and N/L ratio [( $p<0.001$ , OR: 1.559, 95% CI (1.364-1.780)] were independent predictors of high RSS. The threshold value of N/L ratio for RSS was calculated to be 4.50 [76.1 % sensitivity and 82.7 % specificity, AUC: 0.823,  $p<0.001$ , 95% CI: 0.771-0.876].

**Conclusion:** Neutrophil/ lymphocyte ratio is significantly associated with high residual SYNTAX score and also an independent predictor of coronary atherosclerotic burden after PCI.

**Keywords:** Neutrophil/lymphocyte ratio; residual SYNTAX score; ST segment elevation myocardial infarction

## INTRODUCTION

The recommended treatment at the appropriate time interval is primary percutaneous coronary intervention (PCI) in ST segment elevation myocardial infarction (STEMI) (1). Multi-vessel disease can be seen frequently in STEMI patients (2). It is associated with increased mortality (3). The Synergy between PCI with TAXUS (paclitaxel drug-eluting stent) and Cardiac Surgery (SYNTAX) score is an anatomically based angiographic scoring system, showing the extent and severity of coronary artery (4). The residual SYNTAX score (RSS) reveals the burden of coronary artery disease remaining after PCI. After PCI, RSS over 8 causes increased risk in death and composite end point of death, myocardial infarction and stroke in 5-year period (5). Similarly, RSS> 8 in moderate and high-risk acute coronary syndrome patients is associated with poor prognosis in a 1-year period (6). The role of inflammation in the pathogenesis of atherosclerosis is well-known. In studies on leukocytes, the ratio of neutrophil and lymphocyte counts (N/L) was

found to be associated with morbidity and mortality in acute myocardial infarction and stable coronary disease (7,8). N / L ratio was found to be related to the extent of atherosclerosis by calculating the SYNTAX score (9). In this study, it was aimed to investigate the relationship between N/L ratio and the extent of coronary artery disease remaining after PCI in STEMI patients.

## MATERIAL and METHODS

Three hundred patients who underwent primary PCI due to STEMI between January 2015 and February 2020 were retrospectively included in the study. The study was approved by institutional ethics committee. Informed consent was obtained from the patients and the study was carried out in compliance with the Helsinki Declaration Principles. Clinical, biochemical and echocardiographic data on patients were obtained by hospital database and file scanning. Patients with a history of previous coronary bypass, those with cardiogenic shock, end-stage renal failure and active infection or inflammatory disease were excluded from the study.

**Received:** 09.05.2020 **Accepted:** 21.08.2020 **Available online:** 22.09.2020

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Biochemical analyzes such as complete blood count, neutrophil and lymphocyte count, neutrophil / lymphocyte ratio, serum glucose, serum creatinine, cholesterol parameters were evaluated before the primary PCI procedure for STEMI.

The SYNTAX score was calculated according to coronary angiography for each patient using the SYNTAX score calculator Version 2.28 (available at <http://www.syntax-score.com>). Vessels with a diameter > 1.5 mm and lesions with 50% stenosis were included in the scoring. The parameters used to determine the SYNTAX score are: coronary domination; number of lesions; the number of segments per lesion; total occlusion, trifurcation, bifurcation, aorto-osteal stenosis, severe folded vessel, calcification, presence of thrombus, diffuse / small vessel disease and lesion length > 20 mm (10).

RSS was calculated after revascularization of the responsible lesion causing STEMI. RSS > 8 was defined as high RSS.

### Statistical analysis

Statistical evaluations in this study were made using the SPSS program (version 22.0; SPSS Inc., Chicago, IL, USA). Continuous variables are shown as mean  $\pm$  standard deviation (SD) or median (25% -75% percentile). Kolmogorov-Smirnov test was applied to investigate the distribution of variables. Independent t test or Mann-Whitney U test was conducted according to the distribution status to evaluate the continuous variables. Pearson's chi-square test was performed to compare categorical variables.

Variables found significant in univariate analysis were evaluated in multivariate analysis. The results were expressed as odds ratio (OR) using 95% confidence interval (GA) and p values.

ROC (Receiver Operating Characteristic) curve was created and threshold value, sensitivity, specificity, area under the curve (AUC) were determined for high residual SYNTAX value.

**Table 1. Comparison of clinical and laboratory features of patients with high and low residual SYNTAX scores**

	Low residual SYNTAX (n=191)	High residual SYNTAX (n=109)	p
Age	58.2 $\pm$ 11.1	62.6 $\pm$ 11.2	<b>0.001</b>
Gender (female), (n), %	43 (22.5)	22 (20.2)	0.745
Hypertension, (n), %	90 (47.1)	71(65.1)	<b>0.004</b>
Diabetes Mellitus,(n), %	71(37.4)	65(59.6)	<b>&lt;0.001</b>
Hyperlipidemia, (n), %	107 (56)	74(67.9)	0.058
Smoking, (n), %	55 (28.8)	42(38.5)	0.108
COPD, (n), %	11 (5.8)	18 (16.5)	<b>0.005</b>
PAD, (n), %	7(3.7)	13(11.9)	<b>0.012</b>
Culprit vessel, (n), % LAD	97 (50.8)	39 (35.8)	
Non-LAD arteries (CXA and RCA)	94 (49.2)	70(64.2)	<b>0.017</b>
Left ventricle EF, %	50 (45-55)	47 (40-55)	<b>0.028</b>
Creatinine, mg/dl	0.89 (0.78-1.06)	0.85(0.73-1.1)	0.710
Glucose, mg/dl	124(106-174)	176 (122-226)	<b>&lt;0.001</b>
Total cholesterol, mg/dl	192.6 $\pm$ 47.8	196 $\pm$ 42.2	0.541
LDL-Cholesterol, mg/dl	119 (96-145)	126(104-149.5)	0.114
HDL-Cholesterol, mg/dl	38 (32-45)	40 (34-46.5)	0.130
Triglycerides, mg/dl	141 (86-239)	136 (74-205)	0.172
CRP, mg/dl	3.7(1.7-9.6)	9.3 (2.25-17.5)	<b>0.001</b>
Hemoglobin, g/dl	14.4 (12.9-15.4)	13.8(12.3-15.0)	0.051
Leukocyte, $\mu$ l	11.2 (9.4-13.5)	12.7 (10.5-15.0)	<b>0.002</b>
Platelet, 103/ $\mu$ l	251 (220-300)	257 (219-298)	0.776
Neutrophils, $\mu$ l	6.77(5.28-9.37)	10.22(7.85-12.41)	<b>&lt;0.001</b>
Lymphocyte, $\mu$ l	3.0 (1.93-4.00)	1.60 (1.12-2.35)	<b>&lt;0.001</b>
N / L ratio	2.51 (1.5-3.88)	6.57(4.54-8.80)	<b>&lt;0.001</b>

## RESULTS

Three hundred STEMI patients undergoing primary PCI were included in the study. 109 (36.3%) of these patients were detected as RRS > 8 and defined as high residual SYNTAX group. In the high residual SYNTAX group, age ( $p < 0.001$ ), glucose ( $p < 0.001$ ), CRP ( $p < 0.001$ ) were higher. In high residual SYNTAX group, the neutrophil count was higher ( $p < 0.001$ ), the lymphocyte count was lower ( $p < 0.001$ ), and the N / L ratio was significantly higher ( $p < 0.001$ ). In addition, culprit vessel ( $p = 0.017$ ), hypertension ( $p = 0.004$ ), diabetes mellitus (DM) ( $p < 0.001$ ), peripheral artery disease (PAD) ( $p = 0.012$ ) and chronic obstructive pulmonary disease (COPD) ( $p = 0.005$ ) were found more in this group. Comparison of clinical, demographic and biochemical characteristics of patients in high and low residual SYNTAX groups can be seen in Table 1.

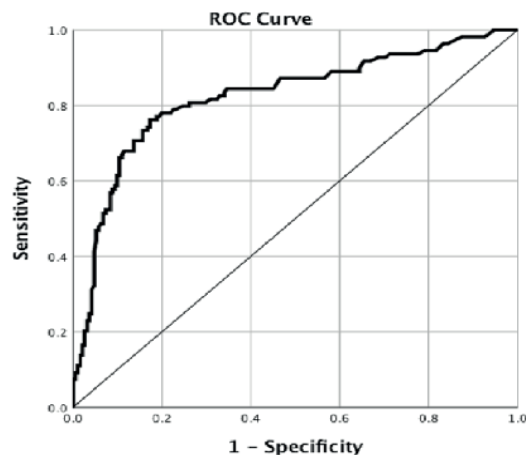


Figure 1. ROC analysis of high residual SYNTAX and N / L ratio

Table 2. Univariate and multivariate logistic regression analysis showing independent predictors for high residual SYNTAX score

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% confidence interval (Lower-upper)	p	Odds ratio	95% confidence interval (Lower-upper)	p
Age	1.036	1.014-1.059	0.001			
Hypertension	2.097	1.290-3.408	0.003			
Diabetes Mellitus	2.476	1.528-4.011	<0.001			
Hyperlipidemia	1.660	1.014-2.718	0.044			
COPD	3.237	1.467-7.141	0.004			
PAD	3.560	1.375-9.217	0.009			
Culprit vessel (Non-LAD arteries)	1.852	1.142-3.004	0.012	3.437	1.741-6.786	<0.001
Left ventricle EF	0.969	0.945-.995	0.020			
Glucose	1.005	1.002-1.008	0.001	1.005	1.001-1.009	0.023
CRP	1.026	1.010-1.041	0.001	1.018	1.001-1.035	0.033
Leukocyte	1.100	1.032-1.172	0.004			
N / L ratio	1.080	1.026-1.136	0.003	1.559	1.364-1.780	<0.001

In univariate analysis, age, hypertension, DM, hyperlipidemia, peripheral artery disease, chronic obstructive pulmonary disease, culprit vessel other than left anterior descending artery (LAD), left ventricle EF, glucose, CRP, leukocyte and N / L were related with high residual SYNTAX. When multivariate analysis was performed, glucose, CRP, culprit vessel and N / L ratio were determined as independent predictors. Glucose [(p: 0.023, OR: 1.005, 95% CI (1.001-1.009)], CRP [(p: 0.033, OR: 1.018, 95% CI (1.001-1.035)], culprit vessel [(p < 0.001, OR: 3.437, 95% CI (1.741-6.786)] and N / L ratio [(p < 0.001, OR: 1.559, 95% CI (1.364-1.780)] are independently associated with high residual SYNTAX. These results were depicted in Table 2.

In the ROC analysis, when the N / L ratio was taken as 4.50 threshold value, 76.1% sensitivity and 82.7% specificity were detected (AUC: 0.823,  $p < 0.001$ , 95% CI: 0.771-0.876). ROC curve was shown in Figure 1.

## DISCUSSION

This study shows that high residual SYNTAX score and N / L ratio are related in STEMI patients. The SYNTAX score was developed primarily for stable coronary artery disease. However, high SYNTAX score was found to be associated with mortality, stent thrombosis and adverse events in STEMI patients (11). RSS shows atherosclerotic burden after PCI and is an independent predictor for long-term clinical results (12). The role of inflammation

in the onset and progression of coronary atherosclerosis is well-documented (13). High levels of inflammatory markers have been found to be associated with prognosis after acute coronary syndrome and PCI (14). It has been demonstrated that N / L ratio, as an easily calculated marker of inflammation, shows the burden of coronary artery disease via the SYNTAX score for both stable coronary artery disease and acute coronary syndrome. Shen et al. investigated the relationship between N/L ratio and long-term mortality in STEMI patients, stated that the group with the highest N / L ratio had 4 times more deaths in the long term (15,16). However, the relationship between residual SYNTAX score and N / L was not previously investigated. With this study, the N / L ratio was also associated with the severity of coronary artery disease after PCI and was determined as an independent predictor. Knowing the N / L ratio in STEMI might be valuable in determining patients with high risk before the procedure. In addition, glucose, CRP and the culprit vessel being a non-LAD vessel were independent predictors of high RSS. It is proposed that culprit vessel other than LAD (CXA or RCA) increases the likelihood of residual coronary artery disease in LAD artery, thus rises SYNTAX score.

RSS is a parameter associated with long-term mortality and in-hospital mortality (17). The acute effect of high RSS on in-hospital mortality is explained by the disruption of myocardial perfusion and ischemia created by arteries other than the lesion responsible for MI. In the long term, this effect can be explained by the size of the affected myocardial tissue (2).

After revascularization of culprit vessel for STEMI with primary PCI, management of lesions in non-culprit vessels is a controversial issue. Recent randomized studies in this topic reveal that complete revascularization is more beneficial than revascularizing only the infarct-related artery (18-21). This shows the importance of residual atherosclerotic burden in the remaining vessels. However, it is uncertain whether complete revascularization will be in the same hospitalization or a separate hospitalization, as well as the next hospitalization time (1).

The relationship between atherosclerosis and increased N / L ratio can be explained by the effects of neutrophils and lymphocytes in this regard. Neutrophils secrete inflammatory markers and cause vascular degeneration, while lymphocytes exert anti-atherosclerotic effects. In inhibition of atherosclerosis, regulatory T cells are particularly effective (22). In addition, low lymphocyte count may be secondary to myocardial ischemia. In the current study, high residual SYNTAX was associated with increased neutrophil count and low lymphocyte count.

C-reactive protein (CRP) is another inflammatory marker that has been significantly associated with the risk of cardiovascular disease. CRP level is linked with neutrophil and N / L ratio (23,24).

The N / L ratio appears to be a potential marker of systemic inflammation in predicting CRP level. In this study, high residual SYNTAX was found to be related to CRP as well as N / L ratio. CRP was also an independent predictor for the high residual SYNTAX.

There are some limitations in the study. First of all, the study is single-centered, retrospectively designed, which tends to lead to possible bias. In the study, in-hospital and long-term mortality with N/L ratio were not investigated. In addition, although CRP was considered as an inflammatory marker other than N / L ratio in the study, the relationship between N / L ratio and CRP was not investigated separately.

## CONCLUSION

In STEMI patients, high residual SYNTAX score and N / L ratio are related. The N / L ratio is an independent predictor for the high residual SYNTAX score.

*Competing interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Ethical approval: Istanbul Yeni Yuzuil University Clinical Research Ethics Committee (13.02.2020/013).*

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