NEUTROPHIL TO LYMPHOCYTE RATIO CORRELATE WITH SYNTAX SCORE IN PATIENTS WITH NON ST ELEVATION ACUTE CORONARY SYNDROME

Sh. M. Abyaneh¹, M. Jalalyazdi*,²

¹Resident of Cardiology, school of Medicine, Mashhad University of Medical Sciences
²MD Cardiologist, assistant professor, school of Medicine, Mashhad University of Medical Sciences

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ABSTRACT

Introduction : In this study we aimed to investigate the correlation between the neutrophil to lymphocyte ratio (NLR) and severity of coronary artery disease (CAD) in patients with Non ST elevation acute Coronary Syndrome (NSTE-ACS) using the SYNTAX score (SXscore).

Method: A total of 150 patients with NSTE-ACS who underwent coronary angiography were enrolled in the study. NLR was measured for all patients at presentation. The study population was then divided into 3 tertiles based on the SYNTAX trial results (1). The low syntax group (n = 25) was defined as those with an SXscore ≤ 22, the intermediate syntax group (n = 78) was defined as an SXscore ≥ 23 and < 33, and the high syntax group (n = 47) as those with an SXscore ≥33.

Result: NLR was significantly lower in patients with a low SXscore compared to patients with an intermediate SXscore or high SXscore (2.4 ± 2 to 4.8 ± 2 and 6.9 ± 3, P < 0.001). Linear regression analysis revealed that NLR (coefficient β = 0.470, 95%CI: 1.273-1.935, P < 0.001) was significantly associated with the SXscore in patients with NSTE-ACS.

Author Correspondence, e-mail: author@gmail.com
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Conclusion: Our results indicate that NLR is independently associated with the severity of CAD in patients with NSTE-ACS.

1. INTRODUCTION
Non ST elevation acute coronary syndrome (NSTE-ACS) is one of the leading causes of death in patients with coronary artery disease (CAD) (2,3). Patients with NSTE-ACS include patients with non ST elevation elevation myocardial infarction and patient with unstable angina. Several treatment strategies including intensive medical treatment and invasive procedures have been successful in decreasing the morbidity and mortality of NSTE-ACS (4). However, the severity of CAD in coronary angiography is the leading factor in determining the most useful treatment strategy. The SYNTAX score (SXscore) is an anatomic scoring system which quantifies the properties of a lesion including complexity, morphology, and location in the coronary vasculature (5). It has been shown that the SXscore may predict short and long-term mortality in patients with CAD intervention (6).

The role of inflammation in the initiation and progression of coronary atherosclerosis is well described (7-10). Increased levels of inflammatory markers have been found in association with the severity of coronary atherosclerosis and prognosis in acute coronary syndromes (11,12). The neutrophil to lymphocyte ratio (NLR) is an indicator of baseline inflammatory response. Although the predictive value of NLR on the severity of CAD in patients with STEMI and stable CAD is well known, its role in NSTE-ACS is less clear. Therefore, the aim of the present study was to investigate whether there is an association between NLR and severity of CAD in patients with NSTE-ACS using the SXscore.

2. METHODS
Patient selection: A total of 150 patients (100 males, mean age, 61 ± 8 years) were consecutively selected from among patients with NSTE-ACS who underwent coronary angiography in the catheterization laboratory of the Emam Reza Education and Research Hospital between June 2014 and July 2015. NSTE-ACS defined as any group of clinical symptoms compatible with acute myocardial ischemia and included unstable angina (UA), non—ST-segment elevation myocardial infarction (NSTEMI).To diminish any confounder that might influence NLR, patients with a history of congestive heart failure, previous percutaneous coronary
intervention, coronary artery bypass grafting surgery history, active infectious disease, inflammatory or immunologic disease, cirrhosis, peripheral arterial disease, chronic obstructive pulmonary disease, chronic kidney disease, malignancy, or cardiogenic shock on admission were excluded.

Blood samples were collected at the admission to the emergency department and after fasting 12-hour next day. All measurements were performed within 30 minutes after blood collection. Complete blood count, fasting blood glucose, creatinine levels, lipid profile and were analyzed for all patients.

Quantitative coronary angiography was performed using the Judkins technique by 2 experienced interventional cardiologists unaware of the clinic and laboratory results of the patients. Significant CAD was defined as > 50% stenosis in at least 1 coronary artery. Each coronary lesion producing a ≥ 50% luminal obstruction in vessels ≥ 1.5 mm was separately scored and added to provide the vessel SXscore. The SXscore was calculated using dedicated software that integrates the number of lesions with their specific weighting factors based on the amount of myocardium distal to the lesion according to the score of Leaman et al and the morphologic features of each single lesion, as previously reported (13,14). The study population was then divided into 3 tertiles based on the SYNTAX trial results (1). The low syntax group (n = 25) was defined as those with a SXscore ≤ 22, the intermediate syntax group (n = 78) as a SXscore ≥ 23 and < 33, and the high syntax group (n = 47) as those with an SXscore ≥ 33.

Statistical analysis was performed using the SPSS software version 15. Continuous variables are presented as the mean ± standard deviation and categorical variables as a percentage. Linear regression analysis was performed to identify the significance of the relation between the SXscore and several variables.

3. RESULTS

The clinical characteristics and laboratory parameters of the patients with NSTE-ACS are listed in Table 1. NLR was significantly lower in patients with a low SXscore compared to patients with an intermediate or high SXscore (2.4 ± 2 to 4.8 ± 2 and 6.9 ± 3, P < 0.001). Linear regression analysis revealed that NLR (coefficient β = 0.470, 95% CI: 1.273-1.935, P < 0.001), age (coefficient β = 0.211, 95% CI: 0.110-0.235, P < 0.001) and LDL cholesterol level
(coefficient $\beta = 0.104$, $95\%$CI: 0.004-0.052, $P = 0.024$, Table I) were significantly associated with SXscore in patients with NSTE-ACS (Table 1).

### Table 1. Clinical and laboratory parameters of the patients

|                        | Mean ± SD / percentage | Coefficients $\beta$ | 95% CI       | $P$    |
|------------------------|------------------------|----------------------|--------------|--------|
| Age                    | 61±8 years             | 0.211                | 0.110-0.235  | < 0.001|
| Diabetes               | 52 (35%)               | 0.036                | -0.680-2.868 | 0.423  |
| Hypertension           | 58 (39%)               | -0.058               | -2.955-0.675 | 0.324  |
| Smoking                | 25 (17%)               | 0.074                | -0.310-3.664 | 0.094  |
| NLR                    | 5.3 ± 4.7              | 0.470                | 1.273-1.935  | < 0.001|
| LDL                    | 135±25                 | 0.104                | 0.004-0.052  | 0.024  |
| Type of NSTE-ACS       |                        |                      |              |        |
| unstable angina        | 23 (16%)               | 0.047                | -0.570-3.244 | 0.344  |
| NSTEMI                 | 127 (84%)              |                      |              |        |

### 4. DISCUSSION

Our results clearly demonstrate that patients with NSTE-ACS had high NLR. Our results also show that there is a significant association between NLR and severity of CAD in patients with NSTE-ACS. In this study we showed that patients with a high SXscore had higher NLR compared to those with a low or intermediate SXscore in NSTE-ACS.

Non-ST segment elevation ACS is one of the most frequent presentations of patients with CAD. Although in-hospital mortality in patients with NSTE-ACS is lower than those with ST segment elevation, 6-month mortality is similar. Moreover, 4-year mortality in patients with NSTE-ACS is two-fold higher than patients with ST segment myocardial infarction (3,4,15). Therefore, risk stratification, management of patients with NSTE-ACS in the acute phase, and long-term follow-up are crucial to prevent increased mortality and morbidity in these patients.

The SXscore, a lesion-based angiographic scoring system, has been introduced to grade the complexity of coronary artery disease. Since the initial trial, several trials have demonstrated that the SXscore can be used to risk-stratify patients with complex coronary disease. These studies have shown that patients with a relatively high SXscore have worse cardiovascular outcomes, and
that the score is an independent predictor of MACE for percutaneous coronary intervention (PCI) (16-18). Therefore, SXscore can be used in the selection of optimal treatment by identifying those patients at highest risk of adverse events following PCI.

NLR has been proposed as a prognostic marker and shown to be related with a pro-inflammatory state and resultant worse clinical outcomes in cardiovascular disease. NLR has been evaluated as a prognostic marker for several cardiovascular diseases including coronary artery ectasia, stable CAD, NSTEMI, and STEMI (7,19-21). NLR has also been shown in association with complexity of CAD in patients with stable CAD and acute coronary syndromes. In a recent study, Sahin, et al showed that NLR was significantly associated with severity of CAD in patients with STEMI. They also showed that NLR was an independent predictor for SXscore in patients with STEMI (16). Another study conducted by Kaya, et al showed that NLR was significantly associated with both the presence and severity of CAD in patients with stable CAD (17). In a more recent study, Altun, et al. showed that in patients with acute coronary syndrome, high sensitive troponin T and NLR were significantly correlated with the severity of CAD.

Similar to previous investigations, our study demonstrates that NLR, an indicator of systemic inflammatory response, is significantly associated with severity of CAD and may predict the SXscore in patients with NSTEMI-ACS. The role of inflammation in the initiation and progression of atherosclerosis is well established. During the early stages of atherosclerotic plaque development, inflammatory monocytes are provoked to move into the vascular wall by several adhesion and chemoattractant molecules released from endothelial cells (18). These monocytes differentiate to macrophages to contribute to the formation of the lipid core in advanced stages of atherosclerotic plaque development. In mature atherosclerotic plaque, various inflammatory mediators play a role in the expression of proteolytic enzymes which may weaken the fibrous cap and result in plaque rupture (19,20). With this background in mind, we suggest that the inflammatory state, represented by NLR, contributes to the formation of coronary atherosclerosis in patients with NSTE-ACS.

Our study has several limitations. First, this is an observational, single-institution, cross-sectional study. Second additional markers of inflammation were not assessed in our study. Also, the lack of longitudinal data regarding the association of NLR and prognosis of NSTE-ACS is another limitation of the study.
In conclusion, NLR is a widely available parameter around the world. In patients with NSTE-ACS, NLR was higher in the high-SXscore group than in the low-SXscore group and was independently associated with SXscore. Also, there was a significant correlation between the SXscore and NLR ratio. Thus, we suggest that patients with NSTE-ACS who have more atherosclerotic involvement also have a higher NLR and we also suggest that a preprocedural NLR, which is an inexpensive and universally available marker, can be used for the risk stratification of patients with NSTE-ACS. Additionally, these results might play an important role in better understanding the role of inflammation in the pathogenesis of atherosclerosis and may lead to improved treatment strategies in patients with NSTE-ACS.

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