ROLE OF NEUTROPHIL TO LYMPHOCYTE RATIO AS A PREDICTOR IN RISK STRATIFYING PATIENTS WITH NSTE-ACS

Sameh Mosaad Abdul-Wahab[1], Ali Ahmed El Abd[2], Abeir Ramadan El Hinnawy[3] and Ehab Mohamed El Fekky[2]

[1]Cardiovascular Medicine Department, Faculty of Medicine, Modern Technology & Information (M.T.I.) University, Cairo, Egypt
[2]Cardiovascular Medicine Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt.
[3]Cardiovascular Medicine Department, Faculty of Medicine, October 6 University, Giza, Egypt
Corresponding author:
Sameh Mosaad Abdul-Wahab
Mobile: +2 01005022068
E-mail:
samehcardio75@gmail.com
Received: 31/7/2023
Accepted: 19/8/2023

Online ISSN: 2735-3540

ABSTRACT:

Background: *Acute myocardial infarction is known to be accompanied by elevated leukocyte count. The differentiation of leukocyte types gives an added benefit of judging the severity of A.C.S. & predicting its clinical outcomes. Collecting peripheral blood samples is an easy & inexpensive test.*

Aim: *To test the significance of Neutrophil to Lymphocyte ratio in risk stratifying patients with acute coronary syndromes and its early outcomes.*

Methods: *One hundred patients with UA and NSTEMI were prospectively evaluated at Ain Shams University Hospital (63% UA and 37% NSTEMI). The patients were followed-up for clinical outcomes for 48 hours in-hospital & for one month after discharge.*

Results: *The median (IQR) NLR was 8.4 (5.3 to 9.7) in NSTEMI group versus 1.8 (1.2 to 2.8) in unstable angina group, NLR > 3.9 had a sensitivity of 100%, & specificity of 92% as a diagnostic value. The patients were categorized into three groups: low risk, intermediate risk, & high risk, according to TIMI score. In unstable angina patients, the quartiles of NLR in "low risk", "intermediate risk" and "high risk" groups were 3 (2.0, 4.3), 3.4 (2.4, 5.1) and 5.5 (3.4, 9.65). In NSTEMI patients, the quartiles of NLR in "low risk", "intermediate risk", and "high risk" groups were 5.1 (3.1, 8.1), 5.2 (3.0, 9.0) and 6.5 (3.9, 11.7). Meaning that there is positive correlation, as NLR values were found to be significantly elevated in high-risk groups.*

Conclusion: *NLR on presentation, is a powerful & independent predictor of cardiovascular outcomes in patients with NSTE-ACS. It represents a good marker for stratifying patients with NSTE-ACS. It appears to have the chance of revitalization as a practical biomarker with high clinical predictability and prognostication. The easiness and swiftness of doing this test make it simple, cheap, and flawless early predictor for risk stratification in patients with NSTE-ACS.*

Keywords: *NLR, NSTE-ACS, Cardiovascular outcomes.*

INTRODUCTION:

Acute coronary syndrome (A.C.S.) refers to patients who are suspected or proved to have unstable angina or infarction. Acute coronary syndrome comprises NSTEMI, STEMI, and U.A. It is noteworthy that the expanded use of the high-sensitivity troponin test, has rehashed most of patients previously diagnosed with UA into non-STEMI patients. This has happened as those patients previously diagnosed with UA have abnormally raised high-sensitivity troponin values. Classically, unstable angina is defined as clinical and/or electrocardiographic changes with normal biomarker level**(1)**.

Inflammation has a pivotal role in the development of atherosclerotic lesions in coronary arteries[2]**.** During the process of atherosclerosis development & progression, a huge number of inflammatory mediators are secreted. This can be considered as a maker for the monstrosity of atherosclerosis[3&4]**.**

Neutrophils are marker of inflammation, while lymphocytes are marker of its regulation, both are seen in the affected areas. Both stimulate major cell types involved in the inflammatory process. The Neutrophil-to-Lymphocyte ratio (The absolute count of neutrophils divided by the absolute count of lymphocytes), is used to assess the prognosis of an inflammatory process. It is a part of routine blood count assay done in the emergency room. The utilization of NLR as marker for inflammation has been previously stated[5&6]**.**

Normal NLR values in a healthy, adult, population are between 0.78 and 3.53[7]**.**

AIM OF THE WORK:

To test the significance of neutrophil to lymphocyte ratio in risk stratifying patients with NSTE-ACS, and its early outcomes.

PATIENTS AND METHODS:

Type of study:

A prospective, observational study.

Study setting:

It was performed in Ain shams University Hospital.

Study period:

From 20/5/2021 until 20/11/2021.

Inclusion criteria:

Patients with NSTEMI and unstable angina.

Exclusion criteria:

Patients with bacterial sepsis, infectious or inflammatory diseases such as cholecystitis, nephritis, upper &/or lower respiratory tract infections, urinary tract infections, …etc, patients with renal impairment and STEMI patients.

Sampling method:

Probability stratified random sampling.

Sampling size:

One hundred patients**.**

Ethical consideration:

Informed consent was taken from every participant after explanation to him the aim of work. The agreement of Ain Shams university ethical committee was acquired in accordance with the ethical guidelines of the declaration of Helsinki (revised in 2008).

Study tools:

All the following was applied to the study patients:

Collecting full history data:

Concentrating on the risk factors for atherosclerosis, as: Age, gender, smoking, hypertension, diabetes mellitus, dyslipidemia & family history of IHD.

Full clinical examination:

General examination:

Especially measuring blood pressure and pulse & auscultation of lung bases.

Local examination of the heart:

Concentrating on auscultation of heart sounds, additional sounds & murmurs (for possible mechanical complications of myocardial infarction)**.**

Laboratory investigations, including:

Differential C.B.C.:

To get the total leukocyte count (T.L.C.) and calculate neutrophils to lymphocyte ratio (NLR). On admission the whole blood sample was withdrawn under aseptic conditions, from peripheral vein, un-centrifuged and anticoagulated using ethylene-diamine-tetra-acetic acid (EDTA). Normal values of white blood cells count 4,000 to 11,000/cmm. NLR was obtained by

dividing absolute number of neutrophils by the absolute number of lymphocytes. The normal values of NLR in a healthy, adult personnel are between 0.78 and 3.53.[8]

Serial Creatine kinase MB (ck-MB):

On admission & every 8 hours for 24 hours. numeric measurement by getting the serum specimen anticoagulated with E.D.T.A. and centrifuged, using automated analyzer Bechman coulter. Normal reference value of ck-MB (5-25) IU /L.[9]

Cardiac troponin (TnT):

Numeric measurement by collecting the serum specimen on admission and being anticoagulated with E.D.T.A. and centrifuged using automated analyzer Bechman coulter. Reference value: hs-TnT >30 ng/L → probable Myocardial infarction. [10]

Echocardiography:

Transthoracic echocardiography was performed to assess systolic and diastolic functions, RWMA and mechanical complications of MI in-hospital, before discharge and one month follow up after discharge.

The test was done with the patients lying down in left lateral decubitus position. The ejection fraction of the left ventricle (LVEF) was measured in accordance with the recommendations of American Society of Echocardiography by using modified Simpson's.

Normal reference value for mean LVEF is (62 ± 5 %). [11]

Follow-up:

Forty-eight hours in hospital monitoring of:

Reinfarction**,** anginal pains. mortality of cardiac causes.

One month follow up of:

Ischemic symptoms, reinfarction, arrhythmias, heart failure symptoms and mortality of cardiac cause.

Statistical Methods:

Statistical analysis of the data collected was done using IBM© SPSS© Statistics version 26 (IBM© Corp., Armonk, NY) and Med-Calc® Statistical Software version 20 (Med-Calc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021).

Categorical variables are expressed as counts and percentages and the intergroup differences are compared using the Pearson chi-squared test or Fisher's exact test. Ordinal data are collated using the chi-squared test for trend.

Non-normally distributed continuous variables are expressed as median and interquartile range. The differences are compared with the Mann-Whitney test (for two-group comparison) or the Jonckheere-Terpestra trend test (to assess the significance of trend in multiple-group comparison). The Conover test is used for post hoc pairwise comparison.

Correlations between numerical variables are tested using the Spearman rank correlation or Pearson correlation. The correlation coefficients (Spearman rho or Pearson r) are interpreted as follows: <0.2 = very weak, 0.2 to 0.39 = weak, 0.4 to 0.59 = moderate, 0.6 to 0.79 = strong, ≥ 0.8 = very strong

Repeated-measures analysis of variance (ANOVA) with logarithmic transformation is used to analyze within-subjects and between-subjects effects on the change in CK-MB. Serial measurements analysis of log-transformed data is used to calculate the area under the time-CK-MB curve (AUC). The unpaired t-test is used to compare different AUCs.

Multivariable binary logistic regression analysis is used to examine the relation between NLR and NSTEMI as adjusted for the effect of possible confounding factors.

P-values <0.05 are considered statistically significant.

Case examples:

65 years old male patient. Known to be diabetic, hypertensive, dyslipidemic and smoker, came to the emergency room complaining of recurrent typical chest pain of two days duration. On examination the patient had a blood pressure of 155/110, pulse of 93 beat per minute and the rest of examination was irrelevant. ECG showed ST segment depression in the precordial leads. His laboratory test results revealed NLR:14.2, Troponin T :223, CK-MB: 81. The patient had a high risk TIMI score.

Another case, 72 years old female patient. Known to be dyslipidemic with no other history of medical importance, came to the emergency room complaining of typical chest pain. Her examination was irrelevant. With no specific changes on ECG. Her laboratory results showed NLR: 1.5, Troponin T :7.5, CK-MB:25. The patient had a low risk TIMI score.

RESULTS:

Table 1. Demographic characteristics

Variable	All population (N=100)	UA (N=63)	NSTEMI (N=37)	P-value†
Age (yr), median (IQR)	63.0 (57.0 to 68.5)	61 (56.3 to 66.0)	65 (60.0 to 72.3)	**0.011†**
Male sex, n (%)	77 (77.0%)	51 (81.0%)	26 (70.3%)	0.220‡
DM, n (%)	57 (57.0%)	32 (50.8%)	25 (67.6%)	0.102‡
Hypertension, n (%)	45 (45.0%)	24 (38.1%)	21 (56.8%)	0.070‡
Smoking, n (%)	39 (39.0%)	18 (28.6%)	21 (56.8%)	**0.005‡**
Dyslipidemia, n (%)	46 (46.0%)	24 (38.1%)	22 (59.5%)	**0.038‡**
Risk stratification, n (%)				**<0.001§**
Low	52 (52.0%)	48 (76.2%)	4 (10.8%)	
Intermediate	30 (30.0%)	13 (20.6%)	17 (45.9%)	
High	18 (18.0%)	2 (3.2%)	16 (43.2%)	

†. Mann-Whitney test ‡. Pearson chi-squared test §. Chi-squared test for trend IQR = interquartile range

Table (1) shows that patients in the NSTEMI group were significantly older than those in the unstable angina group (P = 0.011). The percentage of patients with history of smoking and dyslipidemia was significantly higher in the NSTEMI group (P = 0.005 and 0.038, respectively). The patients were categorized into three groups: low risk, intermediate risk, & high risk, according to TIMI score. The percentage of patients classified as at low, intermediate, and high risk was 10.8%, 45.9% and 43.2% in the NSTEMI group compared with 76.2%, 20.6% and 3.2% in the unstable angina group, respectively. These differences were statistically significant (P < 0.001). Both groups were comparable as regards the male/female ratio (P = 0.220) and prevalence of DM (P = 0.102) or hypertension (P = 0.070).

Table 2. Neutrophil, lymphocyte and NLR

Variable	Total population (N=100)	Unstable angina (N=63)	NSTEMI (N=37)	P-value
Neutrophils (x1,000/µl, median (IQR)	6.4 (4.2 to 8.4)	4.9 (3.8 to 6.8)	9.6 (7.4 to 12.7)	<0.0001†
Lymphocytes (x1,000/µl), median (IQR)	1.9 (1.2 to 3.5)	2.9 (1.8 to 4.0)	1.1 (0.9 to 1.5)	<0.0001†
NLR, median (IQR)	2.9 (1.6 to 5.9)	1.8 (1.2 to 2.8)	8.4 (5.3 to 9.7)	<0.0001†

†. Mann-Whitney test IQR = interquartile range

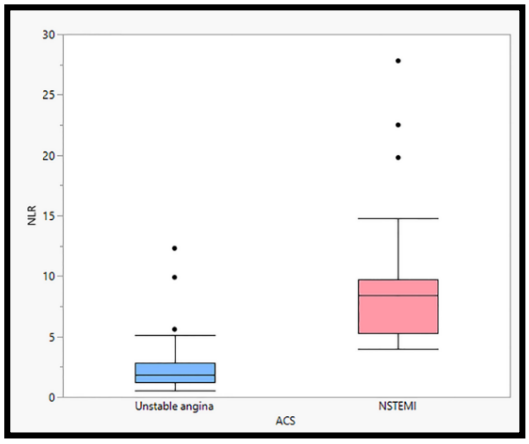

Figure (1): Box plot illustrating NLR in patients suffering NSTEMI or unstable angina. Box represents the interquartile range (25th to 75th percentile). The line inside the box represents the median (50th percentile). Whiskers constitute the minimum and maximum values excluding outliers and extreme values (rounded markers)

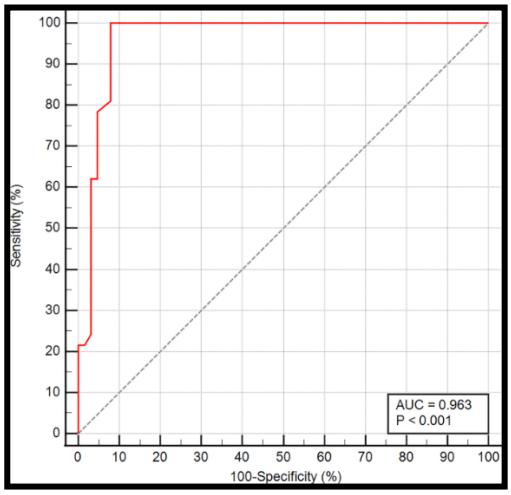

Figure (2): Receiver-operating characteristic (ROC) curve for discrimination between patients with NSTEMI or unstable angina using NLR. NLR has excellent diagnostic value with an area under the ROC curve (AUC) of 0.963 (95% CI = 0.905 to 0.990, P <0.0001). An NLR > 3.9 has a sensitivity of 100%, specificity of 92%, positive predictive value (PPV) of 88% and a negative predictive value (NPV) of 100%, likelihood ratio positive (LR+) of 12.6, likelihood ratio negative (LR-) of 0.0, J index of 0.92 and an overall accuracy of 92%

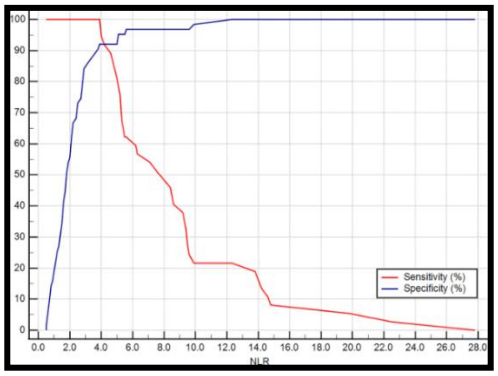

Figure (3): Plots of Sensitivity and Specificity versus NLR Criterion. Best cut-off criterion is an NLR > 3.9 which has a sensitivity of 100%, specificity of 92%, positive predictive value (PPV) of 88% and a negative predictive value (NPV) of 100%, likelihood ratio positive (LR+) of 12.6, likelihood ratio negative (LR-) of 0.0, J index of 0.92 and an overall accuracy of 92%

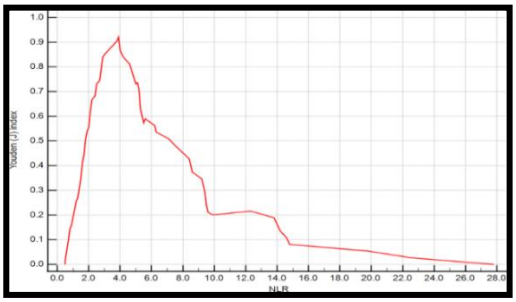

Figure (4): Plot of Youden index versus NLR Criterion. Best cut-off criterion is an NLR > 3.9 which has a sensitivity of 100%, specificity of 92%, positive predictive value (PPV) of 88% and a negative predictive value (NPV) of 100%, likelihood ratio positive (LR+) of 12.6, likelihood ratio negative (LR-) of 0.0, J index of 0.92 and an overall accuracy of 92%.

Table 3. Multivariable binary logistic regression analysis for the relation between NLR and NSTEMI as adjusted for effect of possible confounding factors.

Variable	Coefficient	SE	Wald	P value	Odds ratio	95% CI
NLR	1.327	0.347	14.621	<0.001	3.769	1.909 to 7.441
Age (years)	-0.033	0.059	0.313	0.576	0.968	0.862 to 1.086
Male sex†	-0.069	0.895	0.006	0.938	0.933	0.161 to 5.393
Moderate risk‡	0.810	1.189	0.464	0.496	2.248	0.218 to 23.124
High risk‡	-4.444	2.365	3.532	0.060	0.012	0.0001 to 1.210
Constant	-4.211	3.413	1.523	0.217		

†. Reference category is female sex ‡. Reference category is low risk

Table 4. Correlation between NLR and cardiac enzymes and EF

	NLR		
Variable	Count	Spearman's rho	P-value
Troponin	100	0.872	<0.001
CK-MB at admission	100	0.752	<0.001
CK-MB at 8 h	98	0.778	<0.001
CK-MB at 16	98	0.720	<0.001
CK-MB at 24 h	98	0.716	<0.001
EF at admission	100	-0.670	<0.001
EF at 1 month	100	-0.632	<0.001

Table 4 shows the correlation between NLR and cardiac enzymes or EF. There is a very strong positive correlation between NLR and troponin and CK-MB. On the other hand, there was moderate negative correlation between NLR and EF.

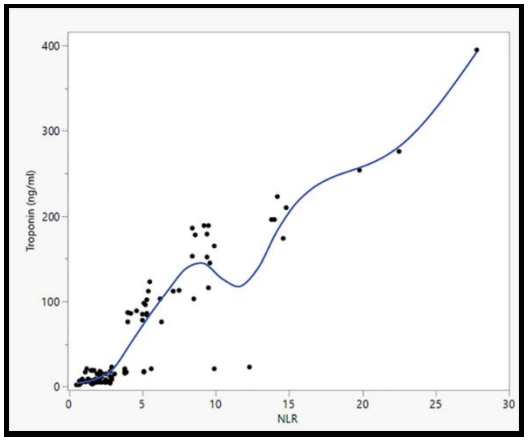

Figure (5): Scatter plot illustrating the correlation between NLR and troponin. Scatters represent individual observations. Fitted line represents local regression smoothing trend line. There is very strong positive correlation between both variables (Spearman's rho = 0.872, P-value <0.001).

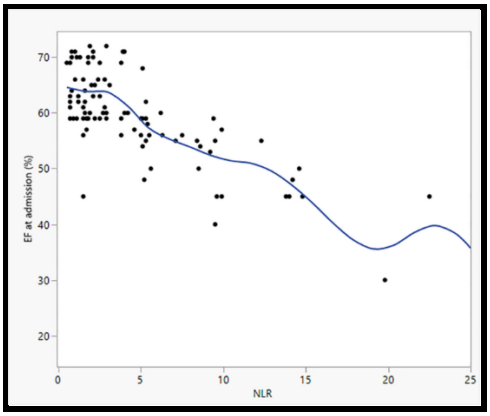

Figure (6): Scatter plot illustrating the correlation between NLR and EF at admission (%). Scatters represent individual observations. Fitted line represents local regression smoothing trend line. There is moderate negative correlation between both variables (Spearman's rho = -0.670, P-value <0.001).

Table 5. Relation between NLR and ST segment depression or cardiac risk.

Variable		Count	NLR, median (IQR)	P-value
ST segment	Normal	35	1.6 (1.0 to 2.1)	<0.001†
	Depressed	65	5.1 (2.7 to 9.2)	
Risk stratification	Low	52	1.8 (1.2 to 2.5)	<0.001‡
	Intermediate	30	5.1 (2.9 to 5.5) a	
	High	18	11.1 (9.4 to 14.6) b	

†. Mann-Whitney test ‡. Jonckheere-Terpstra trend test a. P-value <0.01 versus Low-Risk Group (Conover post-hoc test) b. P-value <0.01 versus Intermediate-Risk Group (Conover post-hoc test)
IQR = interquartile range

Table 5 shows comparison of NLR in patients with depressed or normal ST segment. The median (IQR) NLR was 5.1 (2.7 to 9.2) versus 1.6 (1.0 to 2.1) in either group, respectively. The difference is statistically significant (P < 0.001). The NLR was significantly higher in patient at high cardiac risk (median = 11.1, IQR = 9.4 to 14.6) compared with those at low risk (median = 1.8, IQR = 1.2 to 2.5, P < 0.01) or at intermediate risk (median = 5.1, IQR = 2.9 to 5.5, P < 0.01).

DISCUSSION:

The expression of acute coronary syndrome (ACS) is expressed for patients with either query or confirmed acute myocardial ischemia or infarction. STEMI, NSTEMI, and UA are the three forms of acute ischemic events. The three entities can be distinguished by performing an ECG and measuring cardiac biomarkers specifically troponins. STEMI is diagnosed with the appearance of an elevated ST segment and high cardiac troponins, whereas NSTEMI and unstable angina can have ECG abnormalities in the form of depressed ST segment and/or inverted T wave. The differentiating character between Non-STEMI and UA is the occurrence of the rise of cardiac troponins. **(12)**

The expansive utilization of the high sensitivity cardiac troponin has switched the diagnosis of UA to NSTEMI in majority of patients previously diagnosed to have unstable angina. This has happened as those patients previously diagnosed with unstable angina, in-fact, have raised high-sensitivity cardiac troponin levels. **(13)**

Neutrophils and lymphocytes comprise the front line of protection inside the human being to face the different invading agents. Neutrophils and lymphocytes are in the foreground inflammatory and regulatory agents, respectively, seen in the affected areas. They stir the major cell types concerned with acute and chronic inflammatory reactions. The Neutrophil-Lymphocyte ratio (NLR) -obtained by dividing the absolute count neutrophils count by the absolute count of lymphocytes- is used to assess the prognostication of the inflammation.**(14)**

The utilization of NLR as a marker of inflammation has been prescribed before. Additionally, NLR has also been correlated with unpleasant outcomes in different states, including atherosclerosis, myocardial infarction, coronary artery disease, and chronic obstructive air-way diseases. **(15)**

In our study, we found that the neutrophil and lymphocyte counts were significantly correlated with ACS subtypes, patients with NSTEMI had significantly higher neutrophils and lower lymphocytes than patients with unstable angina having lower neutrophils and higher lymphocytes. Thus, the Neutrophil to Lymphocyte ratio shows statistically significant difference between both NSTEMI and unstable angina groups with the median NLR was 8.4 (5.3 to 9.7) versus 1.8 (1.2 to 2.8) in either group, respectively. Moreover, significantly higher levels of cardiac troponin and peak CK-MB were seen in those with higher NLR.

In agreement with our study, ***Mansiroglu et al.*** **(16)** conducted a single-centered study of 426 patients who were admitted to Bolu Abant Izzet university hospital, to assess the relation between NLR and ACS. They realized that neutrophil and NLR were higher in NSTEMI patients that in unstable angina patients, also ***El Shafey et al.*** **(17)** concord with our study that higher NLR counts for NSTEMI patients unlike lower NLR for unstable angina.

Furthermore, ***Tahto et al.***[18] who conducted a cross-sectional study, on one hundred patients with ACS, agreed with our study stating that TLC count, neutrophils, and monocytes were significantly elevated in acute myocardial infarction group than in unstable angina group. NLR was also found to be significantly more elevated in myocardial infarction group compared to those with unstable angina. Significantly more elevated levels of hsTnI and CK-MB were found in patients with myocardial infarction. NLR had significantly positive correlation with the readings of hsTnI, CK-MB, CRP & TLC.

In our study -after adjustment for the effect of age, sex, and risk score- NLR was an independent predictor for NSTEMI. Additionally, NLR is correlated with the monstrosity of acute coronary syndromes according to TIMI Score.

The patients were assorted into three groups: “low risk”, “intermediate risk”, & “high risk”, according to TIMI score. In unstable angina patients, the quartiles of NLR in “low risk”, “intermediate risk” and “high risk” groups were 3 (2.0, 4.3), 3.4 (2.4, 5.1) and 5.5 (3.4, 9.65). In NSTEMI patients, the quartiles of NLR in “low risk”, “intermediate risk”, and “high risk” groups were 5.1 (3.1, 8.1), 5.2 (3.0, 9.0) and 6.5 (3.9, 11.7). Meaning that there is positive correlation, as NLR values were significantly elevated in high-risk groups.

In the present study, patients with NSTEMI had significantly higher Troponin and CK-MB at admission. CK-MB at 8 hours, 16 hours and 24 hours were also significantly more elevated in patients with NSTEMI & showed positive correlation with the NLR.

In agreement to our study, ***Seaoud et al.*** [19] showed that the NLR and WBC count, were markedly elevated in the high-risk group, while the mean lymphocyte count was highest in the low-risk group., ***El Shafey et al.*** [17] found that there were statistically significant differences between the three studied groups regarding neutrophil count, lymphocyte count and TLC.

Moreover, in concordance with our study ***Soylu et al.*** [20] who raised a study of 300 patients admitted to cardiology clinic at Ondokuz Mayis University with NSTE-ACS, agreed with our study in reporting that the mean NLR was highest in the high-risk groups with significant difference.

In consensus with our study, ***Gul et al.*** [21] -who conducted a prospective study included 308 patients, who were admitted to the emergency room with NSTEMI and UA- reported that there were significantly higher levels of peak CK-MB, NLR and WBC count in the higher-risk group.

On the other hand, the capacity of NLR in prognostication of in-hospital and one month follow up complications in both groups (NSTEMI and UA), showed that NLR has an excellent predictive value. As in our study showed that complications occurred more for those with high NLR.

In accordance with our study, ***Gul et al.*** [21] reported that the adverse outcomes at 30 days, hospitalization for heart failure, reinfarction and cardiovascular mortality were higher in high-NLR group.

Neutrophil-to-Lymphocyte ratio is a novel addendum to the long list of biomarkers, which is cheap, easy to get, & universally available marker of inflammation, which can help in the risk stratification of patients with different cardiovascular diseases along with the other traditionally used markers. Studies have been carried-out to suggest an acceptable cut-off value of it, with fruitful clinical use in different patient groups. [19]

Shumilah et al. [22]**,** stated in their study, that was conducted on one hundred patients who were admitted to the E.R. and were proved to have ACS, that the acceptable cut-off value of NLR for the diagnosis of ACS was found to be 2.95 with 90% sensitivity, 88% specificity, 89.7% negative predictive value (NPV), and 88.2% positive predictive value (PPV).

In our present study, NLR had excellent diagnostic value in differentiation between UA patients & those with NSTEMI. Using the receiver-operating characteristic (ROC) curve, the analysis showed that NLR > 3.9 had a sensitivity of 100%, specificity of 92%, positive predictive value (PPV) of 88%, negative predictive value (NPV) of 100% and an overall accuracy of 92% in differentiating patients with UA from those with NSTEMI.

Conclusion:

Admission NLR is a powerful and independent prognostication marker of cardiovascular outcomes in patients with NSTE-ACS. Therefore, with the other privileges of NLR, it represents a good marker for risk stratifying patients with NSTE-ACS. The feasibility and swiftness in doing these tests make them an independent,

simple, cheap, and accurate early markers of high-risk patients with ACS.

Recommendations:

Using NLR in patients with suspected A.C.S. on presentation to E.R. for early, feasible & cheap accurate marker -along with other markers- is recommended for early risk stratification & differentiating patients with UA from those with NSTEMI.

Limitations:

The sample size of the included patients in our study was relatively small and from a single center. Another limitation is that we could not compare NLR with other inflammatory markers, such as C-reactive protein, fibrinogen, myeloperoxidase, TNF-α or IL-6, because they were not routinely obtained in our study population. Lastly a longer-term (more than one month) of follow-up may be needed for a more comprehensive assessment of the relationship between NLR and long-term outcomes.

Conflict of interest:

There is no conflict of interest.

List of abbreviations:

ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
CAD	Coronary artery disease
CK	Creatine kinase
cTnI	Cardiac troponin I
cTnT	Cardiac troponin T
EDTA	Ethylene-diamine-tetra-acetic acid
MI	Myocardial infarction
NLR	Neutrophil-to-lymphocyte ratio
NSTEMI	Non-ST-elevation myocardial infarction
NSTE-ACS	Non-ST-elevation Acute coronary syndrome
RWMA	Regional wall motion abnormality
STEMI	ST-elevation myocardial infarction
TLC	*Total leucocyte count*
UA	*Unstable angina*
WBC	*White blood cell count*

REFERENCES:

1. **Braunwald, E., & Morrow, D. A. (2013).** Unstable angina: is it time for a requiem?. Circulation, 127(24), 2452-2457.
2. **Christodoulidis, G., Vittorio, T. J., Fudim, M., Lerakis, S., & Kosmas, C. E. (2014).** Inflammation in coronary artery disease. Cardiology in review, 22(6), 279-288.
3. **Ungan, I., Caglar, F. N. T., Biyik, İ., Ciftci, S., Sahin, A., & Akturk, I. F. (2016).** The correlation between plasma human neutrophil peptide 1-3 levels and severity of coronary artery disease. Archives of medical sciences. Atherosclerotic diseases, 1(1), e133.
4. **Lyu, Y., Jiang, X., & Dai, W. (2015).** The roles of a novel inflammatory neopterin in subjects with coronary atherosclerotic heart disease. International immunopharmacology, 24(2), 169-172.
5. **Kolaczkowska, E., & Kubes, P. (2013).** Neutrophil recruitment and function in health and inflammation. Nature reviews immunology, 13(3), 159-175.
6. **Oncel, R. C., Ucar, M., Karakas, M. S., Akdemir, B., Yanikoglu, A., Gulcan, A. R., ... & Demir, I. (2015).** Relation of neutrophil-to-lymphocyte ratio with GRACE risk score to in-hospital cardiac events in patients with ST-segment elevated myocardial infarction. Clinical and applied thrombosis/hemostasis, 21(4), 383-388.
7. **Katayev, A., Balciza, C., & Seccombe, D. W. (2010).** Establishing reference intervals for clinical laboratory test results: is there a better way?. American journal of clinical pathology, 133(2), 180-186.
8. **Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M (2017):** What is the normal value of the neutrophil-to-lymphocyte ratio?. BMC research notes. Dec;10(1):12.
9. **Walker HK, Hall WD, Hurst JW (1990):** Boston: Butterworths.
10. **Leistner D, Klotsche J, Pieper L et al.** Circulating Troponin As Measured by a Sensitive Assay for Cardiovascular Risk Assessment in Primary Prevention. Clinical Chemistry. 2012. 58:1 200–208 (2012).
11. **Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P (2015):** Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography

and the European Association of Cardiovascular Imaging. European Heart Journal-Cardiovascular Imaging. 16(3):233-71.

12. Thygesen, K., Alpert, J. S., Jaffe, A. S., Simoons, M. L., Chaitman, B. R., & Vasileva, E. Y. (2012). Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction. Nature Reviews Cardiology, 9(11), 620-633.

13. **Bergmann, I., Büttner, B., Teut, E., Jacobshagen, C., Hinz, J., Quintel, M.,... & Roessler, M. (2018).** Pre-hospital transthoracic echocardiography for early identification of non-ST-elevation myocardial infarction in patients with acute coronary syndrome. Critical Care, 22(1), 1-6.

14. **Liu, C. C., Ko, H. J., Liu, W. S., Hung, C. L., Hu, K. C., Yu, L. Y., & Shih, S. C. (2019).** Neutrophil-to-lymphocyte ratio as a predictive marker of metabolic syndrome. Medicine, 98(43).

15. **King, A. H., Schmaier, A. H., Harth, K. C., Kumins, N. H., Wong, V. L., Zidar, D. A.,... & Cho, J. S. (2020).** Elevated neutrophil-lymphocyte ratio predicts mortality following elective endovascular aneurysm repair. Journal of vascular surgery, 72(1), 129-137.

16. Mansiroglu, A. K., Sincer, I., & Gunes, Y. (2020). Assessment of neutrophil and neutrophil/lymphocyte ratio in coronary collateral developed patients with acute coronary syndrome. Revista da Associação Médica Brasileira, 66, 954-959.

17. **El Shafey, W. E. H., Emara, A. M., Mosa, W. F., & El-Sharnouby, K. H. (2018).** Predictive Value of Neutrophil-to-Lymphocyte Ratio in Outcomes of Patients with Acute Coronary Syndrome. World Journal of Cardiovascular Diseases, 8(5), 265-275.

18. **Tahto, E., Jadric, R., Pojskic, L., & Kicic, E. (2017).** Neutrophil-to-lymphocyte ratio and its relation with markers of inflammation and myocardial necrosis in patients with acute coronary syndrome. Medical Archives, 71(5), 312.

19. **Seaoud, E., Mohamed, A. A. H. A., & Elkot, M. A. (2020).** The Role of the Platelet/Lymphocyte Ratio and Neutrophil/Lymphocyte Ratio in Predicting High-Risk Heart Score in Patients Admitted with Non-ST Elevation Acute Coronary Syndrome. Pulse, 8(1-2), 66-74.

20. **Soylu, K., Gedikli, Ö., Dagasan, G., Aydin, E., Aksan, G., Nar, G.,... & Yilmaz, Ö. (2015).** Neutrophil-to-lymphocyte ratio predicts coronary artery lesion complexity and mortality after non-ST-segment elevation acute coronary syndrome. Revista Portuguesa de Cardiologia, 34(7-8), 465-471.

21. **Gul, M., Uyarel, H., Ergelen, M., Ugur, M., Isık, T., Ayhan, E.,... & Uslu, N. (2014).** Predictive value of neutrophil to lymphocyte ratio in clinical outcomes of non-ST elevation myocardial infarction and unstable angina pectoris: a 3-year follow-up. Clinical and Applied Thrombosis/ Hemostasis, 20(4), 378-384.

22. Papa, A., Emdin, M., Passino, C., Michelassi, C., Battaglia, D., & Cocci, F. (2008). Predictive value of elevated neutrophil–lymphocyte ratio on cardiac mortality in patients with stable coronary artery disease. Clinica chimica acta, 395(1-2), 27-31.

23. **Shumilah, A. M., Othman, A. M., & Al-Madhagi, A. K. (2021).** Accuracy of neutrophil to lymphocyte and monocyte to lymphocyte ratios as new inflammatory markers in acute coronary syndrome. *BMC Cardiovasc Disord* **21,** 422.

دور نسبة خلايا الدم البيضاء العدلة إلى خلايا الدم البيضاء الليمفاوية في تحديد درجة الخطورة في المرضى اللذين يعانون من الذبحة الصدرية الغير مستقرة و الجلطة الغير مكتملة بالشرايين التاجية

سامح مسعد عبدالوهاب [١] ، علي أحمد العبد [٢] عبير رمضان الحناوي[٣]

، إيهاب محمد الفقي [٢]،

قسم القلب و الأوعية الدموية ، كلية الطب ، الجامعة الحديثة للتكنولوجيا و المعلومات[١]
قسم القلب و الأوعية الدموية ، كلية الطب ، جامعة عين شمس[٢]
قسم القلب و الأوعية الدموية ، كلية الطب ، جامعة ٦ أكتوبر[٣]

الخلفية: من المعروف أن احتشاء عضلة القلب الحاد يكون مصحوبًا بارتفاع عدد كرات الدم البيضاء. يعطي التمايز بين أنواع الكريات البيضاء فائدة إضافية للحكم على شدة متلازمة القصور الحاد في الشرايين التاجية والتنبؤ بنتائجها السريرية. يعد جمع عينات الدم من الأوردة الطرفية اختبارًا سهلاً وغير مكلف.

الهدف من الدراسة: اختبار أهمية نسبة العدلات إلى الخلايا الليمفاوية في تصنيف درجات الخطورة للمرضى الذين يعانون من متلازمات الشريان التاجي الحادة (الذبحة الصدرية الغير مستقرة و الاحتشاء القلبي غير مرتفع القطعة ST ونتائجها المبكرة.

طريقة إجراء الدراسة: هذه الدراسة هي دراسة رصدية مستقبلية ، تم من خلالها تقييم مائة مريض يعانون من نوبات ذبحة صدرية غير مستقرة وآخرون يعانون من احتشاء قلبي حاد غير مرتفع القطعة ST ، في مستشفى جامعة عين شمس (٦٣٪ ذبحة صدرية غير مستقرة و ٣٧٪ احتشاء قلبي حاد غير مرتفع القطعة ST). تمت متابعة النتائج السريرية للمرضى لمدة ٤٨ ساعة في المستشفى ولمدة شهر بعد الخروج.

النتائج: كان متوسط النسبة بين العدلات الى الخلايا الليمفاوية ٨,٤ (٥,٣ إلى ٩,٧) في مجموعة المرضى اللذين يعانون من احتشاء قلبي حاد غير مرتفع القطعة ST ، مقابل ١,٨ (١,٢ إلى ٢,٨) في مجموعة الذبحة الصدرية غير المستقرة ، وكانت نسبة العدلات إلى الخلايا الليمفاوية الأعلى من ٣,٩ لديها حساسية بنسبة ١٠٠٪ ، ونوعية ٩٢٪ كقيمة تشخيصية لتمييز المرضى اللذين يعانون من احتشاء قلبي حاد غير مرتفع القطعة ST من اللذين يعانون من ذبحة صدرية غير مستقرة. كما تم تصنيف المرضى إلى ثلاث مجموعات: منخفضة المخاطر ، ومتوسطة المخاطر ، ومخاطر عالية ، وفقًا لدرجة TIMI. في مرضى الذبحة الصدرية غير المستقرة ، كانت الشرائح الربعية لنسبة العدلات إلى الخلايا الليمفاوية في المجموعات "منخفضة المخاطر" و "المخاطر المتوسطة" و "عالية المخاطر" ٣ (٢,٠ ، ٤,٣) ، ٣,٤ (٢,٤ ، ٥,١) و ٥,٥ (٣,٤ ، ٩,٦٥). و في مجموعة الاحتشاء القلبي الحاد غير مرتفع القطعة ST ، كانت الشرائح الربعية لنسبة العدلات إلى الخلايا الليمفاوية في المجموعات "منخفضة المخاطر" و "المخاطر المتوسطة" و "عالية المخاطر" ٥,١ (٣,١ ، ٨,١) ، ٥,٢ (٣,٠ ، ٩,٠) و ٦,٥ (٣,٩ ، ١١,٧). بمعنى أن هناك ارتباطًا إيجابيًا ، حيث تم العثور على قيم مرتفعة لنسبة العدلات إلى الخلايا الليمفاوية بشكل ملحوظ في المجموعات المعرضة للخطر.

الخلاصة: تعد نسبة العدلات إلى الخلايا الليمفاوية عند حضور المريض لقسم الطوارئ بالمستشفى ، مؤشر قوي ومستقل للتنبؤ بمدى خطورة الحالة و كذلك خطورة حدوث مضاعفات مستقبلية على مستوى القلب والأوعية الدموية في المرضى الذين يعانون من نوبات قصور حاد بالشرايين التاجية غير مرتفع القطعة ST. كما أنه يمثل وسيلة جيدة لتقسيم المرضى إلى درجات خطورة مختلفة. إن سهولة وسرعة إجراء هذا الاختبار تجعله مؤشرًا مبكرًا بسيطًا ورخيصًا يمكن الاعتماد عليه لتقييم درجات الخطورة في مرضى الذبحة الصدرية الغير مستقرة و مرضى الاحتشاء القلبي الحاد غير مرتفع القطعة ST.