

# Neutrophil/Lymphocyte Ratio and Echocardiographic Parameters in Suspected Acute Coronary Syndrome

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## BACKGROUND/AIMS

The aim of this study is to evaluate the relationship between the neutrophil-lymphocyte ratio and echocardiographic parameters and the role of these in predicting critical coronary stenosis requiring urgent intervention in patients with suspected acute coronary syndrome.

## MATERIAL AND METHODS

This is a prospective, observational, analytical clinical study. A total of 88 patients who were hospitalized in the cardiology department with the suspicion of acute coronary syndrome were included in the study. All the patients underwent echocardiography and angiography. Of those, 24 patients had no critical stenosis requiring coronary intervention, and they were assigned to the control group.

## RESULTS

The ratio of patients with critical coronary stenosis on angiography was 72.7% (n=64). The median neutrophil/lymphocyte ratio value was 2.78 in the patient group and 2.42 in the control group; the difference was not statistically significant (P=0.38). There were no significant differences between the systolic/diastolic septum and posterior wall thicknesses of the patients depending on whether critical stenosis.

## CONCLUSION

We did not find any statistically significant relation between neutrophil/lymphocyte ratio and echocardiographic parameters and critical stenosis. Although no critical stenosis that required intervention was identified in these patients, coronary stenosis and plaque in varying degrees were observed.

**Keywords:** Acute coronary syndrome, neutrophil/lymphocyte ratio, echocardiography

## INTRODUCTION

In the USA, approximately 7 million patients are admitted to emergency departments (EDs) with chest pain annually and 15–25% of these patients are diagnosed with acute coronary syndrome (ACS) (1). In Turkey, approximately 420,000 coronary events occur yearly (2).

Due to the time required for the changes to occur in cardiac biomarkers, patients usually spend 8–12 h in the emergency department in order to be diagnosed with ACS. This duration leads to overloading and extra costs in the emergency departments (3, 4). In addition, in the ED, early identification of the patients requiring percutaneous coronary intervention will facilitate early transfer of these patients to the appropriate centers.

Neutrophil/lymphocyte ratio (NLR) has been shown to be useful in predicting sixth-month mortality and is considered to be an independent risk factor in patients with ACS (5). NLR is associated with the number of thrombosed coronaries

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and has been shown to be an independent risk factor of the severity of coronary artery disease, impairment of myocardial perfusion and prognosis of revascularization surgery (6, 7). It is also correlated with other risk factors and clinical classifications and is easily accessible, simple, fast, inexpensive, and reproducible (8, 9).

Echocardiography has been used in the differential diagnosis of chest pain in the ED, and to evaluate the complications of ACS. It is portable, inexpensive, and reproducible (10, 11). Wall thickening occurs and the distance between endocardium and epicardium increases by at least 20% during systole. In case of myocardial ischemia, ventricular contraction does not occur. Shortly after the onset of symptoms, both systolic and diastolic functions deteriorated. After coronary circulation stops, myocardium loses its function and regional impairments of wall movements occur in a very short period of time (5–15 min.). These findings can persist for up to 48 h, even after adequate blood flow is provided.

Using wall thickness for the diagnosis of suspected ACS is a class I recommendation, when electrocardiogram findings are not diagnostic and cardiac markers do not help (12). First dys-synchrony, (difference of time with the adjacent segments), then, hypokinesia (decrease in the amount of contraction), then akinesia (completely dysfunctional segments) and finally paradoxical movement dyskinesia develop in the ischemic area of the heart. Hyperkinesia develops as a result of increased sympathomimetic activity and acute compensatory mechanisms in the normal areas of the heart other than the infarction area (13).

The primary aim of this study is to evaluate the relationship between the neutrophil-lymphocyte ratio and echocardiographic parameters in patients admitted to the emergency department with chest pain who are investigated for ACS. The secondary aim is to study the role of these parameters in predicting critical coronary stenosis requiring urgent intervention.

## MATERIAL and METHODS

This is a prospective, observational, analytical clinical study. Ethics committee approval was received for this study from the ethics committee of Ankara Atatürk Training and Research Hospital (2014/191). It was conducted in the emergency department of a training and research hospital between July 2014 and November 2014. The annual number of patient admissions in our institution is about 140,000. The local ethics committee approved the study protocol. The patients who were admitted to the emergency department between these dates and hospitalized in the cardiology department with a preliminary diagnosis of ACS and underwent angiography were included in the study. The patients with oncological, hematological, and autoimmune diseases, clinical signs or symptoms of infection, patients who developed cardiac arrest before percutaneous coronary intervention, who were on steroids or chemotherapy, who underwent surgical procedures or had trauma within the last 30 days, and patients who did not undergo percutaneous coronary intervention or did not agree to participate in the study were excluded from the study. All patients were informed about the study and informed consents were obtained.

A total of 88 patients who were hospitalized in the cardiology department with suspicion of ACS were included in the study.

All the 88 patients included in the study underwent angiography. In 24 of the 88 patients, no critical stenosis requiring coronary intervention was detected. These 24 patients were assigned to the control group.

The patients' sex, age, family history, history of coronary artery disease, dyslipidemia, chronic renal failure, hypertension, and diabetes mellitus, and the duration between onset of the symptoms and time of admission were recorded in the study forms.

All patients' electrocardiograms were taken on admission and venous blood samples were collected for complete blood count, biochemistry tests (glucose, urea, creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), sodium, potassium), and cardiac markers (highly sensitive troponin T and creatine kinase MB, CK-MB). Troponin T and CK-MB levels were measured and recorded at 4h intervals until the patients were admitted to the cardiology department.

In the emergency department, an experienced cardiologist performed echocardiography for all patients. End-diastolic and end-systolic diameters and systolic and diastolic septum and the posterior wall thickness of the left ventricle were measured using echocardiography in M-mode through the parasternal short-axis view. In addition, the anteroposterior diameter of the left atrium (LA) was measured by two-dimensional imaging. Left ventricular ejection fraction was calculated by using the modified Simpson's method of the apical 4-chamber view. Presence of segmental wall motion abnormalities in apical four-chamber and parasternal long axis views was recorded.

Coronary angiographies were performed for all patients by experienced cardiologists, within 48 h. The patients diagnosed with ST-elevation myocardial infarction on admission were immediately transferred to the catheterization laboratory and coronary angiography was performed.

The cut-off point for critical coronary stenosis requiring intervention was accepted to be 70%. Because coronary interventions for only study purposes in patients admitted to the emergency department with chest pain but who were not suspected to have ACS is not appropriate, the patients who underwent angiography with initial diagnosis of ACS, but have no critical coronary stenosis were assigned to the control group. According to the results of angiography, patients without critical coronary stenosis, patients in whom re-flow was provided by percutaneous coronary intervention, patients who need only medical treatment and patients who required emergency surgery were recorded.

Measurements were recorded using study forms. The appropriateness of the data to normal distribution was evaluated. A *t*-test was used in the comparison of parametric data between the groups and Mann-Whitney U test and Kruskal-Wallis test were used in the comparisons of non-parametric data. Correlation analysis was used to define the relationships between two variables. Chi-square test was used in the analysis of the relationship between the numerical data. The Statistical Package for the Social Sciences (SPSS) ver. 18 (IBM, SPSS Corp.; Armonk, NY, USA) software was used in the analysis of the data.

## RESULTS

The study included 88 patients; 63.6% (n=56) of them were male. The mean age was 58.3±12.3. Regarding risk factors of coronary artery disease, hypertension was present in 55.7% (n=49), diabetes in 29.5% (n=26), smoking in 48.9% (n=43), family history in 39.8% (n=35), history of coronary artery disease in 35.2% (n=31), and dyslipidemia in 2.3% (n=2) of the patients.

The mortality rate was 4.5% (n=4), the ratio of those who received only medical treatment according to the results of angiography was 39.8% (n=35), the ratio of those who received interventional treatment was 56.8% (n=50), and the ratio of those who underwent surgery was 4.5% (n=4). The mean of NLO in patients who died was 5.74±3.17; in patients who lived was 3.65±3.34. Although the average of NLO was found to be higher in dead patients, the difference was not statistically significant. (p=0.22)

The ratio of patients with critical coronary stenosis on angiography was 72.7% (n=64), and the ratio of those without a critical stenosis was 27.3% (n=24). During coronary angiography, right coronary artery (RCA) occlusion was seen in 38.6% (n=34) of the patients, left main coronary artery (LMCA) occlusion in 3.4% (n=3), left anterior descending artery occlusion (LAD) in 51.1% (n=45), and circumflex artery (x) occlusion in 36.4% (n=32) of the patients.

The participants with critical stenosis were assigned to the patient group, and those without critical stenosis were assigned to the control group. The mean duration between the onset of the symptoms and coming to the ED were 4 h in patient group and 9 h in the control group. The duration between the onset of symptoms and coming to the ED was significantly shorter for the patient group (p<0.01). The median values of troponin and CK-MB on admission were significantly higher in the patient group than those in the control group (p<0.01, p=0.02). The median NLR value was found to be 2.78 in the patient group and 2.42 in the control group; the difference was not statistically significant (p=0.38).

When the groups were compared according to echocardiographic parameters, the average of the Ejection fraction (EF) was found to be 44%±12 in the patient group and 58±9% in the control group. Mean EF value of the patient group was lower than that of the control group and the difference was statistically significant (p<0.01).

When the patients were compared according to NLR values, the mean of the EF was found to be 52%±12 in patients with lower NLR values and 44±14% in patients with higher NLR; the difference was statistically significant (p<0.01). There was no statistical relationship between NLR and left ventricle end systolic diameter (LVESD) and left ventricle end diastolic diameter (LVEDD).

Wall motion abnormalities were observed in 83.1% of the patient group, whereas this ratio was 16.9% in the control group; the difference was statistically significant (p<0.01). There were no significant differences between the groups in terms of LA diameter. There were no significant differences between the septum's systolic/diastolic septum thicknesses, posterior wall

systolic/diastolic thicknesses, systolic septum/posterior wall thicknesses, diastolic septum/posterior wall thicknesses of the patients, depending on whether critical stenosis was present or not in LAD, Cx, RCA, and LMCA.

## DISCUSSION

The overall mean age in our study was younger than in the literature, whereas the ratios of the sexes were similar (14, 15). Hypertension, diabetes, and smoking rates were similar to those reported in the literature (16). In our study, dyslipidemia rate was lower as compared to that reported in the literature; it may be because our patients have not been diagnosed yet.

Neutrophil/lymphocyte ratio, which was similar to that reported in the literature, was higher in patients who died in hospital, but there were no statistically significant differences between the mortality group and lived patients group (5, 17). This may be due to low number in-hospital mortality in our study.

In the literature, NLR was also significantly higher in patients with higher troponin levels (8, 16). In our study, myocardial necrosis markers were significantly higher in the patient group. However, although NLR was also higher in the patient group, there were no statistically significant differences between patient and control groups. This may be because, in our study, rather than people with completely normal coronaries, the control group comprised the patients who underwent angiography due to suspected ACS and no critical stenosis was identified. Although no critical stenosis that required intervention was identified in these patients, coronary stenosis and plaque in varying degrees were present.

Consistent with the literature, the mean EF of the patients whose NLR's were increased were significantly lower (18). A higher neutrophil-lymphocyte ratio and a lower EF can be helpful in detecting ACS in the emergency department.

Anteroposterior diameter of the left atrium has not been useful for the diagnosis of ACS in the emergency department. The average of the left ventricular end-systolic and end-diastolic diameters in our study is consistent with those reported in the literature (19). Neutrophil-lymphocyte ratio and left ventricular end-systolic and end-diastolic diameters were not useful in predicting the presence of critical stenosis.

Wall segment changes that occur in the infarcted and normal regions following the first moments of coronary occlusion in ACS have been examined in several studies (20-22). In our study, we could not find any correlation between the systolic and diastolic wall thicknesses of the posterior wall and the septum and the neutrophil-lymphocyte ratio. The relationship between the neutrophil-lymphocyte ratio and systolic and diastolic wall thicknesses of the septum and posterior wall are not guiding in predicting critical stenosis.

Our findings may be due to the presence of non-critical coronary stenosis in the control group, measurement location to be affected by the stunned and hibernating areas of myocardium, the lack of significant changes in the acute phase that can guide diagnosis, and the measurements being done only on two walls, for providing practicality in the emergency department.

The patients who underwent angiography with an initial diagnosis of ACS, but no critical coronary stenosis was detected were assigned to the control group rather than people with completely normal coronaries. Although no critical stenosis that required intervention was identified in these patients, coronary stenosis and plaque in varying degrees were present. This may be the reason expected differences between the groups were not observed.

In conclusion, in our study, we aimed to detect critical coronary stenosis, which requires intervention by echocardiography to be performed quickly on two locations in the early phase and NLR in the emergency department. However, we could not find any parameter indicating a significant relation between the echocardiography findings and a critical coronary artery disease. Further studies are needed to evaluate the role of echocardiography in this area. In addition, we also compared NLR with other echocardiographic findings, but could not find any significant relationship.

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**Informed Consent:** Verbal informed consent was obtained from patients who participated in this study.

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