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RESEARCH

NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A PREDICTOR OF SEVERE CORONARY ARTERY DISEASE AND LEFT VENTRICULAR SYSTOLIC DYSFUNCTION OF ANY DEGREE IN GERIATRIC PATIENTS PRESENTING TO EMERGENCY DEPARTMENT WITH ACUTE CORONARY SYNDROME

Abstract

Introduction: We examined the role of the neutrophil-to-lymphocyte ratio (NLR) for predicting severe coronary artery disease and left ventricular systolic dysfunction of any degree in geriatric patients presenting to emergency department with non-ST-elevation acute coronary syndrome.

Materials and Method: We retrospectively reviewed data for patients aged ≥65 years with non-ST-elevation acute coronary syndrome who underwent coronary angiography between April 2011 and January 2016. Patients were divided into Group 1 (101 patients; severe [>50%] lesions in one or more epicardial artery or branch) and Group 2 (65 patients; no severe lesions). The key clinical parameters, including NLR were compared among the groups and the power of NLR as a predictor of severe coronary artery disease and left ventricular systolic dysfunction of any degree was determined.

Results: Group 1 included more patients who were male, older, or smoked; these had higher troponin I, mass CK-MB, NLR, but a lower left-ventricular ejection fraction. NLR was an independent predictor of severe coronary disease and left ventricular systolic dysfunction of any degree with good sensitivity and moderate specificity.

Conclusion: Neutrophil-to-lymphocyte ratio is a simple, rapid, and cheap parameter that can predict severe coronary artery disease and left ventricular systolic dysfunction of any degree in geriatric patients with non-ST-elevation acute coronary syndrome.

Anahtar Sözcükler: Akut koroner sendrom; Yaşlı; Nötrofil; lenfosit

ARAŞTIRMA

AKUT KORONER SENDROMLA ACİL SERVİSE BAŞVURAN GERİATRİK HASTALARDA CİDDİ KORONER ARTER HASTALIĞININ VE HERHANGİ BİR DERECEDE SOL VENTRİKÜL SİSTOLİK DİSFONKSİYONUNUN ÖNGÖRDÜRÜCÜSÜ OLARAK NÖTROFİL LENFOSİT ORANI

Öz

Giriş: Bu çalışmada, akut koroner sendrom ile acil servise başvuran geriatrik hastalarda nötrofil/lenfosit oranının (NLR) ciddi koroner arter hastalığını ve herhangi bir derecede sol ventrikül sistolik disfonksiyonunu göstermedeki rolü araştırılmıştır.

Gereç ve Yöntem: Nisan 2011 ile Ocak 2016 tarihleri arasında ST elevasyonsuz akut koroner sendrom ile acil servise başvuran ve koroner anjiyografi uygulanan 65 yaş ve üzeri hastaların verileri retrospektif olarak incelendi. Hastalar Grup 1 (bir ya da daha fazla epikardiyal koroner arter ya da dalında ciddi [≥50%] lezyonları olan 101 hasta) ve Grup 2 (ciddi lezyonları olmayan 65 hasta) olarak ikiye ayrıldı. NLR dahil anahtar klinik parametreler gruplar arasında karşılaştırıldı ve NLR'nin ciddi koroner arter hastalığı ve herhangi bir derecede sol ventrikül sistolik disfonksiyonunu öngördürücü gücü hesaplandı.

Bulgular: Grup 1'de daha fazla erkek, daha yaşlı hasta, daha yüksek sigara içme sıklığı, daha yüksek troponin I, kütle CK-MB ve NLR düzeyleri ve daha düşük sol ventrikül ejeksiyon fraksiyonu saptandı. NLR hem ciddi koroner arter hastalığını hem de herhangi bir derecede sol ventrikül sistolik disfonksiyonunu iyi bir duyarlılık ve ortalama özgüllükle öngörebiliyordu.

Sonuç: Basit, hızlı ve ucuz bir parametre olan NLR, ST elevasyonsuz akut koroner sendromla acil servise başvuran geriatrik hastalarda ciddi koroner arter hastalığını ve herhangi bir derecede sol ventrikül sistolik disfonksiyonunu öngörebilir.

Key Words: Key Words: Acute coronary syndrome; Aged; Neutrophils; lymphocytes

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INTRODUCTION

Acute coronary syndromes (ACS) in geriatric patients are a common emergency department presentation (1). Geriatric patients with ACS may present with atypical symptoms, non-specific electrocardiographic changes (ECG) and non-cardiac troponin elevations (1-3). They are also more sensitive to the side effects of interventional procedures, particularly stroke and bleeding (1). Therefore, it is vital in this population to correctly predict coronary artery disease severity and myocardial dysfunction to eliminate diagnostic uncertainty, avoid unnecessary procedures, and prevent inappropriate discharges from the emergency department.

It is known that inflammatory mechanisms occur in ACSs, so various studies have been conducted to determine the role of inflammatory markers in coronary artery thrombosis, both as a diagnostic and prognostic tool (4,5). Neutrophil-to-lymphocyte ratio (NLR), an inflammatory parameter calculated from routinely studied complete blood counts, has been reported to reflect the severity of obstructive coronary artery lesions (6,7) as well as left ventricular dysfunction (8,9) or prognosis in ACSs (10,11). However, there is little information about its role in predicting CAD severity and left ventricular dysfunction in geriatric patients with ACS. Therefore, we explored the predictive role of NLR for angiographical single- or multi-vessel severe coronary artery disease (CAD) and echocardiographic left ventricular systolic dysfunction of any degree in geriatric patients free of a history of CAD presenting to an emergency department with ACS.

MATERIALS AND METHOD

This study was approved by Baskent University Institutional Review Board (Project No: KA16/177; Date: 05.05.2016) and supported by Baskent University Research Fund. This was a retrospective review of the medical records of geriatric patients who presented with ACS to the Emergency Department of Başkent University Ankara Hospital and underwent invasive coronary angiography between April 2011 and January 2016. The medical records of our patients were accessed via the hospital's data automation system.

The study population consisted of geriatric patients (>65 years old) without known CAD presenting to our emergency department with chest pain or angina equivalents (dyspnea, sweating, altered consciousness, syncope, embolic events, acute heart failure, or hypotension) within 3 hours of symptom onset. All patients underwent ECG testing, biochemistry and blood count analysis, plain chest X-ray, and standard transthoracic echocardiography (performed by experienced senior residents or expert cardiologists). The troponin I levels were measured at the emergency department admission and 3-6 hours later, depending on the assay used (i.e regular vs high-sensitive troponin I assays). Echocardiographic data including the left-ventricular ejection fraction (LVEF), any segmental wall motion abnormalities, and left ventricular systolic dysfunction of any degree (LVEF<52% for men and 54% for women) were recorded. All patients were hospitalized by the cardiology department and examined with invasive coronary angiography on the basis of clinical presentation, ischemic ECG findings, or elevated troponin I measurements, alone or in combination. Therefore, patients both with unstable angina pectoris (resting chest pain without troponin I elevation) and non-ST elevation myocardial infarction (NSTEMI) (resting chest pain with troponin I elevation) who underwent coronary angiography were included in the study. NSTEMI was diagnosed on the basis of a rise and/or fall in the troponin I levels in an appropriate clinical setting with or without typical ECG findings.

Patients with severe coronary artery stenoses (>50%) in one or more major epicardial coronary artery or branch, necessitating intervention, were assigned to Group 1. Those patients with non-significant lesions (normal coronary arteries, minimal plaque burden or coronary arterial irregularities, stenoses<50%, with no thrombus burden in single or multiple coronary arteries) were assigned to Group 2. We excluded the following patients from the study: those with known significant CAD and prior revascularization; those with ST elevation >20 minutes in two consecutive ECG leads or persistent

left bundle branch block; those with atrial fibrillation or supraventricular tachyarrhythmias with rapid ventricular response or ventricular tachycardia, idioventricular rhythm, advanced (second or third degree) atrioventricular block, asystole, profound bradycardia (<40 beats per minute), or respiratory or circulatory arrest; sepsis or septic shock; those using non-steroidal antiinflammatory drugs, immunomodulators, immunosuppressants, or steroids; those with connective tissue disorders, inflammatory or rheumatological disorders, active cancer, or hematological malignancies, particularly lymphoproliferative disorders or a recent history of chemotherapy or radiotherapy; and those with known lymphopenia, lymphocytosis, neutropenia, neutrophilia, or leukocytosis.

We studied and compared the following parameters between the groups: demographic properties; ischemic changes on admission ECG (segmentary wall motion abnormalities, numerical value of LVEF, and the presence of left ventricular systolic dysfunction of any degree (LVEF<52% for men and 54% for women) on echocardiography performed at the emergency department or coronary care unit, biochemical and complete blood count parameters, cardiac biomarkers, and NLR. The following were considered to indicate ischemic changes on ECG: ST depression (especially horizontal or downsloping in character); transient (defined as<20 minutes) ST elevation; T-wave inversion or flattening presumed to be new; pseudonormalization of T waves; QT prolongation presumed to be secondary to ischemia; new onset pathological Q waves or U waves; and new onset poor anterior precordial R wave progression.

Statistical analysis

The normality of continuous variables was tested with the Kolmogorov–Smirnov test, and all normally and non-normally distributed variables were then expressed as mean±standard deviation or as median (range), respectively. When the variables were normally distributed, they were compared between the groups using the Student's *t* test; when not, they were compared using the Mann–Whitney *U* test. Categorical variables were compared using the chi-squared test.

Variables that were significantly correlated with severe CAD and left ventricular systolic dysfunction of any degree were determined using univariate analysis, which was followed by a logistic regression analysis to identify the independent significant predictors of both parameters. Receiver operating characteristic (ROC) curves were then drawn to examine the power of NLR to predict severe CAD and left ventricular systolic dysfunction of any degree. The significance level was set to $p<0.05$ for all statistical analyses.

RESULTS

The study population comprised 166 patients aged 73.7±6.6 years, of whom 97 (58.4%) were men and 69 (41.6%) were women. Groups 1 and 2 included 101 and 65 patients, respectively. The overall in-hospital mortality rate was 3.01% (n=5), with all deaths occurring in Group 1.

By coronary angiography, severe single- and multi-vessel CAD was identified in 30 (29.7%) and 71 patients (70.3%), respectively, in Group 1. Of those with severe multi-vessel CAD, 34 (47.9%) underwent coronary artery bypass graft surgery; percutaneous coronary intervention was performed to the circumflex artery in 17 (23.9%), to the left anterior descending artery in three (4.2%), and to the right coronary artery in seven (9.9%) (or their major branches in each case), or to two separate major epicardial vessels in two cases. Eight (11.3%) patients with multi-vessel disease had unfavorable lesional/clinical/myocardial characteristics and did not undergo any percutaneous or surgical intervention. Among those with significant single-vessel disease, percutaneous intervention was to the left anterior descending artery in 11 (36.7%), to the circumflex artery in three (10%), and to the right coronary artery in 10 (33.3%) (Or their major branches in each case). Six (20%) patients with significant single-vessel disease were unsuitable for percutaneous or surgical intervention because of unfavorable characteristics.

Group 1 included significantly older patients, more men, and more current or past smokers. Other demographic and clinical variables were similar between the groups (Table 1). Although there were

similar rates of ischemic changes on admission ECG in both groups, Group 1 had a significantly higher rate of segmental wall motion abnormalities, significantly reduced LVEF on echocardiography; however, the rate of left-ventricular hypertrophy was also similar (Table 2).

Table 1. Comparison of characteristics by severity of CAD

Characteristics	Group 1 (n, %)	Group 2 (n, %)	P
Age (years)	74 (65–91)	71 (65–87)	<0.05*
Sex (male)	51 (50.5%)	19 (28.2%)	<0.05**
Typical angina pectoris on admission	89 (88.1%)	51 (78.5%)	0.12
Diabetes mellitus	35 (34.6%)	18 (27.7%)	0.39
Hypertension	81 (80.1%)	54 (83.1%)	0.68
Hyperlipidemia	50 (49.5%)	34 (52.3%)	0.75
Family history for CAD	29 (28.7%)	16 (24.6%)	0.59
Chronic renal disease	18 (17.8%)	5 (7.7%)	0.16
Current or past smoking history	51 (50.5%)	20 (30.3%)	<0.05**
Current smoking history	22 (21.8%)	8 (12.3%)	0.15

*Student's t test, ** Chi-squared test. Group 1=severe; Group 2=non-severe. CAD: coronary artery disease.

Table 2. Comparison of electrocardiographic, echocardiographic, and laboratory findings by severity of CAD

Parameter	Group 1 n (%) or n (range)	Group 2 n (%) or n (range)	P
Signs of acute ischemia on ECG	57 (56.4%)	24 (36.9%)	0.16
LVEF (%)	46 (23–63)	58 (34–63)	<0.001*
s	55 (54.5%)	14 (%21.5)	<0.001**
Echocardiographic segmentary wall motion abnormalities	69 (68.3%)	10 (15.4%)	<0.001**
Echocardiographic left-ventricular hypertrophy	63 (62.4%)	31 (47.7%)	0.13
Mass CK-MB	1.53 (0–181.31)	0.95 (0–17.92)	<0.05*
Troponin I	0.16 (0–67.8)	0.006 (0–2.38)	<0.001*
Neutrophil	3.03 (0.90–24.59)	2.31(0.52–17.56)	<0.05*
Lymphocyte	2.00 (0.62–5.21)	2.33 (0.67–5.59)	<0.05*
NLR	3.03 (0.90–24.59)	2.32 (0.53–17.57)	<0.01*

*Mann–Whitney *U* test, **Chi-squared test. Group 1=severe; Group 2=non-severe. CAD: coronary artery disease. ECG: Electrocardiography, LVEF: left-ventricular ejection fraction.

Comparison of the biochemical and hematological parameters indicated that Group 1 had a significantly higher median blood urea nitrogen, creatinine, mass CK-MB, troponin I, neutrophil count, lymphocyte count, and NLR levels (Table 2). However, levels of other parameters were similar to those in Group

2. Univariate analysis then revealed that NLR was significantly correlated to severe CAD and the presence of left ventricular systolic dysfunction of any degree, and a multivariate logistic regression analysis confirmed that NLR was a significant independent predictor of both parameters (Table 3). A low in-hospital mortality rate prevented any statistical analysis of the relationship between NLR and mortality.

Table 3. Multivariate logistic regression analyses showing the significant independent predictors of severe single- or multi-vessel CAD and left ventricular systolic dysfunction of any degree

	Predicted parameter	
Predictor parameter HR (95% CI)	**Severe CAD**	**Left ventricular systolic dysfunction of any degree**
NLR	1.25 (1.05–1.48)*	1.22 (1.06–1.40)*
Male sex	2.40 (1.09–5.27)*	2.27 (1.11–4.59)*
Typical angina pectoris on admission	3.59 (1.33–9.70)*	–
Age	–	1.08 (1.03–1.14)*

*p<0.05. NLR: neutrophil-to-lymphocyte count, CAD: coronary artery disease, HR: hazard ratio, CI: confidence interval

The ROC curve drawn to determine the power of NLR to predict severe CAD showed an area under the curve of 0.638 (95% confidence interval 0.55–0.72). At a cut-off level of 1.815, it could predict severe CAD with a sensitivity of 80.2%, specificity of 40%, positive predictive value of 67.5%, and negative predictive value of 56.5% (Figure 1). As for the ROC curve drawn to determine the power of NLR to predict left ventricular systolic dysfunction of any degree, the area under the curve was 0.696 (confidence interval 0.61–0.78). At a cut-off level of 2.419, this could predict left ventricular systolic dysfunction of any degree with a sensitivity of 76.9%, specificity of 57.1%, positive predictive value of 69.5%, and negative predictive value of 50.7% (Figure 2).

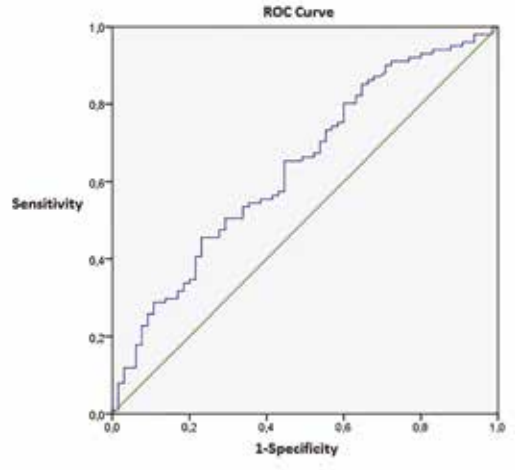

Figure 1. Receiver Operating Characteristic Curve for Neutrophil-to-Lymphocyte Ratio to Predict Severe Single- or Multi-Vessel Coronary Artery Disease

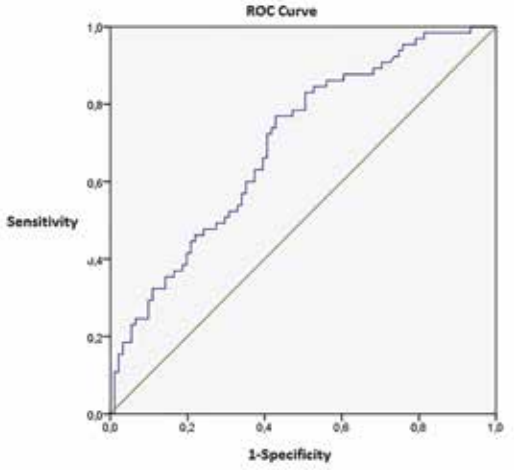

Figure 2. Receiver Operating Characteristic Curve for Neutrophil-to-Lymphocyte Ratio to Predict Left Ventricular Systolic Dysfunction of any Degree

DISCUSSION

In the geriatric population, ACSs are characterized by atypical presentations and non-specific or unreliable ECG and cardiac biomarker findings (1,2). These factors may collectively cause excess hospitalizations and coronary angiography procedures, and when coupled by a high comorbidity burden and increased fragility of this population, they increase the risk of hemorrhage, contrast nephropathy, allergic reactions, infections, and mortality. The alternative is also possible, with the high rate of non-specific signs, symptoms, ECG changes, and troponin I elevations potentially reducing the perceived reliability of these parameters among clinicians, leading to premature or inappropriate discharge from the emergency department without admission or intervention. Therefore, sensitive, specific, and cheap markers are still needed that can be used to predict severe CAD or myocardial injury requiring intervention.

ACSs are characterized by an increased leukocyte count in the early phase (12). ACSs, particularly when myocardial injury occurs, cause neutrophilia in the peripheral blood, and by means of substances released by activated neutrophils, lead to atherosclerotic plaque rupture and further myocardial injury (13-15). In addition, highly inflammatory conditions like ACSs may give rise to relative lymphopenia that is driven by lymphocyte apoptosis and that eventually leads to proinflammatory cytokine release, which further exacerbates the inflammation and myocyte damage (16). It is also known that inflammation is closely related to severity of stable and unstable CAD (17,18). Therefore, leukocytosis, neutrophilia, relative lymphopenia, and increased NLR may be useful for guiding clinicians in the assessment of inflammatory burden, and thus CAD severity and myocardial injury in the ACS setting. Supporting this idea, NLR was found by previous studies to be linked to CAD severity in myocardial infarction (6,7). It was also reported to be an independent predictor of left-ventricular dysfunction (8) and all-cause mortality in ACSs (10,11). In this study, we showed that NLR level was significantly higher in geriatric patients with severe CAD on invasive coronary angiography compared with those without such lesions. We also revealed that NLR could independently predict severe single- or multi-vessel CAD requiring intervention, and could also predict left ventricular systolic dysfunction of any degree. An elevated NLR level in ACS could either be an indicator of the inflammatory milieu causing plaque rupture (i.e., *the cause*) or be a reflection of inflammatory events activated in response to plaque rupture, intravascular thrombosis, or myocardial injury (i.e., *the effect*), or both. A higher NLR in this setting likely indicates a higher grade of inflammation, which underlies a more severe CAD and a higher rate of myocardial dysfunction (19,20). Although both type I (primary plaque rupture or erosion) and type II (myocardial oxygen supply–demand mismatch) myocardial injury may occur in ACS, the higher NLR in those with severe CAD suggests a greater plaque burden and that type I MI is more plausible in our patient population. Nevertheless, in at least some patients, increased NLR levels may have developed also from myocardial injury due to type I or Type II MIs with accompanying inflammatory response with neutrophilia and relative lymphopenia. This is the first study to examine the role of NLR for determining CAD severity in the geriatric ACS setting. Although a similar ACS study also showed that NLR was independently correlated to the SYNTAX score, a surrogate marker of CAD severity and extent, the mean age of the study participants was 62.0±12.7 years, which was younger than in our study (mean age 73.7±6.6 years) (21). Similarly, in a study in non-ST elevation myocardial infarction that correlated SYNTAX score for CAD extent to NLR, the mean age of the study population was 63.8±12 years, which was considerably lower than that in our population (22).

Inflamamatory markers such as NLR may perform better than troponins for predicting both CAD burden and myocardial dysfunction as a result of an intense inflammatory state in these conditions (19,20). In support of this hypothesis, our study revealed that troponin I, unlike NLR, was not an independent predictor of neither severe CAD nor myocardial dysfunction. This may have stemmed from the fact that not all severe coronary lesions on

coronary angiography are unstable, but rather they are incidentally detected and thus may not cause troponin elevation, limiting the association between troponin I level and severe CAD. Although the group with severe CAD had a significantly greater troponin I level, this difference may not necessarily indicate widespread CAD since a partial or complete obstruction of a relatively small coronary artery and, sometimes, the injury of a relatively small myocardial territory may produce substantial troponin I release. There was also no significant difference between the two groups with regard to the rate of ischemic changes on ECG despite the difference in CAD burden, possibly because of a greater prevalence of secondary ST-T changes due to non-coronary causes (eg. left ventricular hypertrophy) in this age group, obscuring any significant difference in ischemic ECG changes between the study groups, non-coronary ischemia producing ischemic ST-T changes despite normal or only minimally diseased coronary arteries, and normal or minimally abnormal ECG in some patients with acute coronary syndrome, irrespective of having severe CAD, which was reported to occur in upto 6% of cases (23). Hence, as a result of the inherent limitations of the clinical presentation, ECG findings, and troponin I levels, NLR offers a promise to predict severe CAD and left ventricular dysfunction that necessitate intervention, both saving available resources and avoding unnecessary complications in geriatric populations.

NLR may increase in some inflammatory conditions and risk factors, such as smoking (24). This may also be considered to have occurred to some degree in our study; however, as stated in the methods section, we excluded major inflammatory conditions such as connective tissue disorders and rheumatologic disorders, conditions characterized by neutrophilia, steroid use, active infection or cancer, sepsis, and septic shock. Although cigarette smoking may induce inflammation and increase NLR, the ratio of current smoking was similar in both groups. Therefore, it is unlikely that elevated NLR levels resulted from neither active smoking nor other inflammatory conditions, and they likely reflected severe CAD and myocardial injury.

Our results do not imply that a low NLR level can be used to determine geriatric patients without significant coronary lesions or LV dysfunction in whom ACS treatment can be deferred. ACS is a clinical diagnosis where neither biomarkers nor angiography and echocardiography can be used alone to make treatment decisions. Therefore, neither NLR nor any other biomarker alone should guide clinicians for the treatment of ACS. Rather, as stated above, NLR can be used to pick up patients with a more severe CAD or LV dysfunction that justify coronary intervention.

Study limitations

Our study has some limitations. First, it was a retrospective study with the limitations inherent to this design. Second, the results of both regular troponin I and high-sensitive troponin I assays were used. Third, coronary artery lesions<50% were considered insignificant, even though it is already known that some ACSs originate from such lesions. However, because our aim was to identify those lesions necessitating coronary intervention, not those patients in need of ACS treatment, we consider it appropriate that such lesions were considered insignificant. Fourth, this study did not provide any information as to which conditions may have caused secondary ACS/MI in patients without severe CAD; but, it should be noted that this was beyond the scope of this research. Fifth, we could not provide any meaningful comparison for in-hospital mortality because of the low mortality rate.

In conclusion, we showed that NLR, a test that can be performed rapidly and without added cost in all emergency departments, could predict severe angiographic CAD and left ventricular systolic dysfunction of any degree in geriatric patients with ACS in this study. Therefore, NLR shows promise for identifying geriatric patients likely to have a more extensive disease and require intervention. Further studies are needed to confirm our findings, particularly in terms of addressing the limitations.

Conflict of Interest

The authors declare no conflict of interest.

REFERENCES

1. Dai X, Busby-Whitehead J, Alexander KP. Acute coronary syndrome in the older adults. J Geriatr Cardiol 2016;13(2):101–8. (PMID:27168733).
2. Tanindi A, Cemri M. Troponin elevation in conditions other than acute coronary syndromes. Vasc Health Risk Manag. 2011;7:597-603. (PMID:22102783).
3. Carro A, Kaski JC. Myocardial infarction in the elderly. Aging Dis. 2011;2(2):116-37. (PMID:22396870).
4. Tasin V, Kuvandik G, Karakus A, et al. Role of inflammatory mediators in the prediction angiographic thrombus in patients with acute coronary syndrome. J Clin Anal Med 2015;6:9-12.
5. Wagdy S, Sobhy M, Loutfi M. Neutrophil/Lymphocyte ratio as a predictor of in-hospital major adverse cardiac events, new-onset atrial fibrillation, and no-reflow phenomenon in patients with st elevation myocardial infarction. Clin Med Insights Cardiol 2016;10(10): 19-22. (PMID:26884687).
6. Akin F, Köse N, Ayca B, et al. Relation between red cell distribution width and severity of coronary artery disease in patients with acute myocardial ınfarction. Angiology 2013;64(8):621-5. (PMID:23070683).
7. Sahin DY, Elbasan Z, Gür M, et al. Neutrophil to lymphocyte ratio is associated with the severity of coronary artery disease in patients with ST-segment elevation myocardial infarction. Angiology 2013;64(6):423-9. (PMID:22802534).
8. Bekler A, Erbag G, Sen H, Gazi E, Ozcan S. Pak Predictive value of elevated neutrophil-lymphocyte ratio for left ventricular systolic dysfunction in patients with non ST-elevated acute coronary syndrome. J Med Sci 2015;31(1):159-63. (PMID:25878635).
9. Karakas MS, Korucuk N, Tosun V, Altekin RE, Koç F, Ozbek SC, et al. Red cell distribution width and neutrophil-to-lymphocyte ratio predict left ventricular dysfunction in acute anterior ST-segment elevation myocardial infarction. J Saudi Heart Assoc 2016 Jul;28(3):152-8. (PMID:27358532).
10. Muhammed Suliman MA, Bahnacy Juma AA, Ali Ahmadhani AA, Pathare AV, Alkindi SS, Uwe Werner F. Predictive value of neutrophil to lymphocyte ratio in outcomes of patients with acute coronary syndrome. Arch Med Res 2010;41(8):618-22. (PMID:21199731).
11. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol 2008 15;102(6):653-7. (PMID:18773982).
12. Cho KH, Jeong MH, Ahmed K, et al. Value of early risk stratification using hemoglobin level and neutrophil-to-lymphocyte ratio in patients with ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention. Am J Cardiol.2011;107(6):849-56. (PMID:21247535).
13. Carbone F, Nencioni A, Mach F, Vuilleumier N, Montecucco F. Pathophysiological role of neutrophils in acute myocardial infarction. Thromb Haemost 2013;110(3):501–514. (PMID:23740239).
14. Sarma J, Laan CA, Alam S, Jha A, Fox KA, Dransfield I. Increased platelet binding to circulating monocytes in acute coronary syndromes. Circulation 2002;105(18):2166-71. (PMID:11994250).
15. Avanzas P, Quiles J, Lopez de Sa E, et al. Neutrophil count and infarct size in patients with acute myocardial infarction. Int J Cardiol 2004;97(1):155-6. (PMID:15336829).
16. Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. N Engl J Med. 2003;348(2):138-50. (PMID:12519925).
17. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 2005 Apr 21;352(16):1685-95. (PMID:15843671).
18. Zakynthinos E, Pappa N. Inflammatory biomarkers in coronary artery disease. J Cardiol 2009 Jun;53(3):317-33. (PMID:19472372).
19. Yndestad A, Damås JK, Oie E, Ueland T, Gullestad L, Aukrust P. Systemic inflammation in heart failure--the whys and wherefores. Heart Fail Rev. 2006;11(1):83-92.(PMID:16819581).
20. Taleb S. Inflammation in atherosclerosis. Arch Cardiovasc Dis 2016 Aug 29. pii: S1875-2136(16)30112-7. (PMID:27595467).

21. Altun B, Turkon H, Tasolar H, et al. The relationship between high-sensitive troponin T, neutrophil lymphocyte ratio and SYNTAX Score. Scand J Clin Lab Invest 2014;74(2):108-15. (PMID:24304492).

22. Kurtul S, Sarli B, Baktir AO, et al. Neutrophil to lymphocyte ratio predicts SYNTAX score in patients with non-ST segment elevation myocardial infarction. Int Heart J 2015;56(1):18-21. (PMID:25742940).

23. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non-st-elevation acutecoronary syndromes: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014 Dec 23;64(24):e139-228. (PMID:25260718).

24. Tulgar YK, Cakar S, Tulgar S, Dalkilic O, Cakiroglu B, Uyanik BS. The effect of smoking on neutrophil/lymphocyte and platelet/lymphocyte ratio and platelet ındices: a retrospective study. Eur Rev Med Pharmacol Sci 2016 Jul;20(14):3112-8. (PMID:27460742).