ORIGINAL ARTICLE

The relationship between galectin-3 and SYNTAX Score I in patients with non-ST-segment elevation myocardial infarction

ST-segment yükselmesiz miyokart enfarktüsü hastalarında galektin-3 ile SYNTAX Skoru I arasındaki ilişki

Alaa Quisi, M.D.,[1] Gökhan Alıcı, M.D.,[2] Ömer Genç, M.D.,[3] Hazar Harbalıoğlu, M.D.,[4] İbrahim Halil Kurt, M.D.[3]

[1]Department of Cardiology, Medline Hospital, Adana, Turkey; [2]Department of Cardiology, Okmeydanı Training and Research Hospital, İstanbul, Turkey; [3]Department of Cardiology, Adana City Training and Research Hospital, Adana, Turkey; [4]Department of Cardiology, Düzce Atatürk State Hospital, Düzce, Turkey

ABSTRACT

Objective: The expression of galectin-3 has been found to be increased in human atherosclerotic lesions, suggesting a role in atherogenesis. However, there is a lack of data regarding an association between galectin-3 and the extent, severity, and complexity of coronary artery disease (CAD). The aim of this study was to investigate the relationship between galectin-3 and SYNTAX Score I in patients with non-ST-segment elevation myocardial infarction (NSTEMI).

Methods: This study included a total of 95 consecutive patients who were diagnosed with NSTEMI and underwent coronary angiography. The baseline galectin-3 level of each patient was measured. The SYNTAX Score I of each patient was calculated using the online calculator (www.syntaxscore.com). The study population was divided into 2 groups: SYNTAX Score I ≤22 group (n=55) and SYNTAX Score I >22 group (n=40).

Results: The galectin-3 level was significantly higher in the SYNTAX Score I >22 group than in the SYNTAX Score I ≤22 group (22.1±8.3 ng/mL vs. 13.5±7.7 ng/mL; p<0.001). Forward stepwise logistic regression analysis demonstrated that galectin-3 (odds ratio [OR]: 1.195, 95% confidence interval [CI]: 1.097–1.302; p<0.001), left ventricular ejection fraction (OR: 0.941, 95% CI: 0.888–0.997; p=0.040), and platelet count (OR: 1.013, 95% CI: 1.003–1.024; p=0.014) were independently associated with intermediate and high SYNTAX scores. ROC analysis provided a cut-off value of 14.0 ng/mL for galectin-3 to predict an intermediate or high SYNTAX Score I with 75.0% sensitivity and 51.0% specificity (p<0.001).

Conclusion: In patients with NSTEMI, galectin-3 was associated with the extent, severity, and complexity of CAD as assessed by the SYNTAX Score I.

ÖZET

Amaç: İnsanlarda yapılan çalışmalarda aterosklerotik lezyonlarda galektin-3 ekspresyonunun artmış olduğu bildirilmiştir. Bu bulgu galektin-3'ün aterojenezdeki rolünü düşündürmektedir. Bununla birlikte, galektin-3 ile koroner arter hastalığının şiddeti ve karmaşıklığı arasındaki ilişki hakkında veri eksikliği vardır. Bu çalışmada ST-segment yükselmesiz miyokart enfarktüslü (STYzME) hastalarda galektin-3 ile SYNTAX Skoru I arasındaki ilişki araştırıldı.

Yöntemler: Bu çalışmaya STYzME tanısı konan ve koroner anjiyografi uygulanan toplam 95 ardışık hasta alındı. Her hastanın başlangıç galektin-3 düzeyi ölçüldü. Her hastanın SYNTAX Skoru I çevrimiçi skor hesaplayıcısı (www.syntaxscore.com) kullanılarak hesaplandı. Çalışma popülasyonu iki gruba ayrıldı: SYNTAX Skoru I ≤22 olan grup (n=55) ve SYNTAX Skoru I >22 olan grup (n=40).

Bulgular: Galektin-3, SYNTAX Skoru I >22 olan grupta SYNTAX Skoru I ≤22 olan gruba göre anlamlı olarak daha yüksekti (22.1±8.3 ve 13.5±7.7, p<0.001). Lojistik regresyon analizinde, galektin-3'ün (odds oranı [OO]=1.195, %95 güven aralığı [GA]: 1.097–1.302, p<0.001), sol ventrikül ejeksiyon fraksiyonunun (OO=0.941, %95 GA: 0.888–0.997, p=0.040) ve trombosit sayısının (OO=1.013, %95 GA: 1.003–1.024, p=0.014) orta ve yüksek SYNTAX Skoru I ile ilişkili olan bağımsız değişkenlerin olduğu gösterildi. ROC analizinde orta ve yüksek SYNTAX Skoru I'i tahmin etmede galektin-3 için 14.0 ng/mL kestirim değeri %75.0 hassasiyet ve %51.0 özgüllük ile anlamlı bulundu (p<0.001).

Sonuç: Galektin-3, NSTEMI hastalarında SYNTAX Skoru I ile değerlendirilen koroner arter hastalığının ciddiyeti ve karmaşıklığı ile ilişkilidir.

Received: February 09, 2020 *Accepted:* May 09, 2020

Correspondence: Dr. Alaa Quisi. Medline Hastanesi, Kardiyoloji Bilim Dalı, 01170 Adana, Turkey.
Tel: +90 322 - 455 25 50 e-mail: dr.quisi@hotmail.com

Galectin-3 is a beta-galactoside-binding lectin coded by a single gene (LGALS3) and is located on chromosome 14.[1] This lectin is widely expressed in human tissues, including immune cells, epithelial cells, endothelial cells, and sensory neurons. Previous studies have demonstrated the pivotal role of galectin-3 in cardiovascular remodeling,[2–4] as well as in various biological activities, including cell growth, apoptosis,[5] pre-mRNA splicing, differentiation, transformation, angiogenesis, inflammation, and fibrosis.[6] The pathophysiology of atherosclerosis involves the formation of an atherosclerotic plaque, subsequent local immune-inflammation, including endothelial dysfunction, leukocyte migration, extracellular matrix degradation, and platelet activation, and ultimately an acute thrombosis of an erosive or ruptured coronary plaque resulting in acute coronary syndrome.[7] The expression of galectin-3 has been found to be elevated in human atherosclerotic lesions, suggesting a role in atherogenesis.[8,9]

The SYNTAX Score I tool is used to assess the extent, severity, and complexity of coronary artery disease (CAD), as well as to determine the optimal treatment for patients undergoing coronary angiography. A higher SYNTAX score indicates a complex condition, a greater risk of major adverse cardiovascular events, and a bigger therapeutic challenge.[10,11] The objective of the present study was to investigate the relationship between galectin-3 and the SYNTAX Score I result in patients with non-ST-segment elevation myocardial infarction (NSTEMI).

METHODS

Study population and design

This single-center, cross-sectional study included a total of 95 consecutive patients who were diagnosed with NSTEMI and underwent coronary angiography between July and December 2018. The diagnosis of NSTEMI was made according to the European Society of Cardiology guideline for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation.[12] Patients <18 or >80 years of age, with a history of coronary artery bypass graft, left ventricular ejection fraction (LVEF) ≤40%, severe heart valve disease, atrial fibrillation, obstructive sleep apnea, acute or chronic infectious or inflammatory disease, malignancy, severe kidney disease (glomerular filtration rate [GFR] <30 mL/min/1.73 m^2), or chronic liver disease were excluded. All of the patients received optimal medical therapy consistent with the European Society of Cardiology guidelines for the management of acute myocardial infarction.[12] The GFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. The principles of the Declaration of Helsinki were observed throughout this research. This study was approved by the Çukurova University Faculty of Medicine Ethics Committee (no. 39, date: 06.07.2018). Each participant provided written, informed consent.

Abbreviations:

CAD	*Coronary artery disease*
CI	*Confidence interval*
CRP	*C-reactive protein*
cTnT	*Cardiac troponin T*
GFR	*Glomerular filtration rate*
LVEF	*Left ventricular ejection fraction*
NLR	*Neutrophil-to-lymphocyte ratio*
OR	*Odds ratio*
NSTEMI	*Non-ST-segment elevation myocardial infarction*
ROC	*Receiver operating characteristic*
SYNTAX	*Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery*

Cardiovascular risk factors

Patients who had previously used an oral antidiabetic and/or insulin therapy and those with a fasting blood glucose level, measured at least twice, of ≥126 mg/dL were considered diabetic.[13] Patients who had used antihypertensive therapy and those with an office blood pressure, measured at least twice, of ≥140/90 mmHg were considered hypertensive.[14] The presence of hyperlipidemia was defined as a measurement of total cholesterol of >200 mg/dL or low-density lipoprotein cholesterol of >100 mg/dL or when the patient had used lipid-lowering medication, consistent with the National Cholesterol Education Program Adult Treatment Panel III guideline.[15] Patients who used tobacco products at the time of admission to the hospital and those who had quit smoking within the past month were considered smokers.

Biochemical measurements

Two peripheral venous blood samples were collected from each patient on admission. One blood sample was used for standard biochemistry tests. The second blood sample was centrifuged, frozen at -80°C and used for galectin-3 measurements. The C-reactive protein (CRP) level was measured using a commercial kit and the Aeroset system (Abbott Laboratories, Inc., Abbott Park, IL, USA). The cardiac troponin

T (cTnT) concentration was measured with highly sensitive cardiac troponin T reagents on an Elecsys 2010 analyzer (Roche Diagnostics, Basel, Switzerland). The analytical measurement range of the assay was 3 to 10,000 pg/mL. The plasma concentration of galectin-3 was measured using a chemiluminescent microparticle immunoassay on an Architect i2000 SR device (Abbott Laboratories, Inc., Abbott Park, IL, USA) in ethylenediaminetetraacetic acid anticoagulated plasma. The Architect galectin-3 assay has a limit of detection of 1.1 ng/mL and a limit of quantitation of 4.0 ng/mL. The inter-assay coefficients of variation were 5.2%, 3.3%, and 2.3% at a mean galectin-3 level of 8.8 ng/mL, 19.2 ng/mL, and 72.0 ng/mL, respectively.

Transthoracic echocardiography

Each patient underwent transthoracic echocardiography using a 3.5-MHz transducer while at rest in the left lateral decubitus position. All of the measurements were performed according to the criteria provided in the American Society of Echocardiography guidelines. LVEF was calculated using the modified Simpson method.[16]

SYNTAX Score I measurements

The SYNTAX Score I value for each patient was calculated using the online calculator (www.syntaxscore.com). A low SYNTAX Score I result was defined as ≤22, an intermediate score was defined as 23–32, and a high score was defined as ≥33.[17] The study population was divided into 2 groups: the SYNTAX Score I ≤22 group (n=55) and the SYNTAX Score I >22 group (n=40).

Statistical analysis

Data analyses were performed using the IBM SPSS Statistics for Windows, Version 22.0 software package (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as the mean±SD or median (minimum-maximum). Categorical variables were expressed as a number (percentage). Normal distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. A chi-squared test was used to compare categorical variables. An independent samples t-test or the Mann-Whitney U test was used to compare continuous variables, depending on whether statistical assumptions were fulfilled or not. Correlation between variables was assessed using the Pearson product-moment correlation test or the Spearman rank correlation test, as appropriate. Pearson's correlation coefficient was expressed as (r) and Spearman's correlation coefficient was expressed as (rho). All of the significant parameters (p<0.25) in the univariate analysis were selected for the multivariable model and forward stepwise logistic regression analysis was used to determine the independent predictors of intermediate and high SYNTAX Score I results. The odds ratio (OR) and 95% confidence interval (CI) of each independent variable were calculated. A receiver operating characteristic (ROC) curve analysis was performed to identify the optimal cut-off level of galectin-3 to predict an intermediate or high SYNTAX Score I value. The area under the curve was calculated as a measure of the accuracy of the test. A 2-tailed p value of <0.05 was considered significant.

RESULTS

This study included a total of 95 consecutive NSTEMI patients (80 male and 15 female patients; mean age: 55.3±9.6 years). The SYNTAX Score I ≤22 group included 55 patients (45 male; mean age: 54.2±9.9 years) and the SYNTAX Score I >22 group included 40 patients (35 male; mean age: 56.7±9.2 years). The baseline characteristics of the study groups are shown in Table 1.

The level of galectin-3 was significantly higher in the SYNTAX Score I >22 group than in the SYNTAX Score I ≤22 group (22.1±8.3 vs. 13.5±7.7; p<0.001). The LVEF was significantly lower in the SYNTAX Score I >22 group than in the SYNTAX Score I ≤22 group (52.4±10.8 vs. 59.1±7.3; p<0.001).

Age (r=0.222; p=0.031), LVEF (r=-0.240; p=0.022) and SYNTAX Score I (rho=0.759; p<0.001) were significantly associated with galectin-3. There was a strong correlation between the SYNTAX Score I result and the galectin-3 level (Fig. 1).

Independent predictors of intermediate and high SYNTAX Score I results are shown in Table 2.

All of the significant parameters in the univariate analysis, including age, diabetes mellitus, hyperlipidemia, hemoglobin level, platelet count, triglyceride level, galectin-3 level, and LVEF were selected for the multivariable model, and forward stepwise logistic regression analysis was used to determine the

Table 1. Baseline characteristics of the study groups

Variable	SYNTAX score I ≤22 (n=55)	SYNTAX score I >22 (n=40)	*p*-value*
Age (years)	54.2±9.9	56.7±9.2	0.210
Gender, (male), n (%)	45 (81.8)	35 (87.5)	0.453
BMI (kg/m^2)	28.0 (22.5–40.8)	26.7 (19.4–34.9)	0.335
DM, n (%)	23 (41.8)	12 (30.0)	0.238
HT, n (%)	20 (36.4)	16 (40.0)	0.718
HPL, n (%)	14 (25.5)	4 (10.0)	0.058
Smoker, n (%)	29 (52.7)	20 (50.0)	0.793
Family history of CAD, n (%)	27 (49.1)	20 (50.0)	0.930
Hemoglobin (mmol/L)	8.9 (6.3–10.5)	8.8 (5.2–10.9)	0.223
Leukocyte count, x10^3/uL	10.3±3.3	10.8±2.6	0.335
Platelet count, x10^3/uL	241.9±65.2	276.3±154.8	0.142
Neutrophil count, x10^3/uL	6.5±2.6	7.1±2.6	0.282
Lymphocyte count, x10^3/uL	3.0±1.4	2.9±1.2	0.808
NLR	2.3 (0.8–6.0)	2.6 (0.8–6.2)	0.497
GFR (mL/min per 1.73 m^2)	97.0 (55.0–139.5)	96.0 (44.0–138.8)	0.678
Triglyceride (mmol/L)	1.9 (0.8–8.9)	1.5 (0.5–5.5)	0.082
Total cholesterol (mmol/L)	5.2±1.2	5.1±1.0	0.669
HDL cholesterol (mmol/L)	1.0±0.3	0.9±0.2	0.658
LDL cholesterol (mmol/L)	3.6±1.3	3.7±0.9	0.662
cTnT (pg/mL)	92.0 (6.0–4629.0)	166.0 (6.0–5309.0)	0.678
CRP (nmol/L)	28.6 (3.8–733.3)	30.5 (1.0–1342.9)	0.895
Galectin-3 (ng/mL)	13.5±7.7	22.1±8.3	<0.001
LVEF (%)	59.1±7.3	52.4±10.8	<0.001

Data are presented as mean±SD, median (min-max) or number (%).
*The p value was calculated using an independent samples t-test or the Mann-Whitney U test for continuous variables and a chi-squared test for categorical variables. A p value <0.05 was considered significant.
BMI: Body mass index; CAD: Coronary artery disease; CRP: C-reactive protein; cTnT: Cardiac troponin T; DM: Diabetes mellitus; GFR: Glomerular filtration rate; HDL: High-density lipoprotein; HPL: Hyperlipidemia; HT: Hypertension; LDL: Low-density lipoprotein; LVEF: Left ventricular ejection fraction; NLR: Neutrophil-to-lymphocyte ratio.

Table 2. Independent predictors of intermediate or high SYNTAX Score I result

Variable	Odds ratio	95% Confidence interval	*p*-value*
Galectin-3 (ng/mL)	1.195	1.097–1.302	<0.001
Left ventricular ejection fraction (%)	0.941	0.888–0.997	0.040
Platelet count, x10^3/uL	1.013	1.003–1.024	0.014

*A p value <0.05 was considered significant.

independent predictors of intermediate and high SYNTAX Score I values. The analysis demonstrated that galectin-3 (OR: 1.195, 95% CI: 1.097–1.302; p<0.001), LVEF (OR: 0.941, 95% CI: 0.888–0.997; p=0.040), and platelet count (OR: 1.013, 95% CI: 1.003–1.024; p=0.014) were independently associated with intermediate and high SYNTAX Score I results.

The ROC curve analysis provided a cut-off value of 14.0 ng/mL for galectin-3 to predict an intermediate or high SYNTAX score with 75.0% sensitivity and 51.0% specificity, with an area under the curve

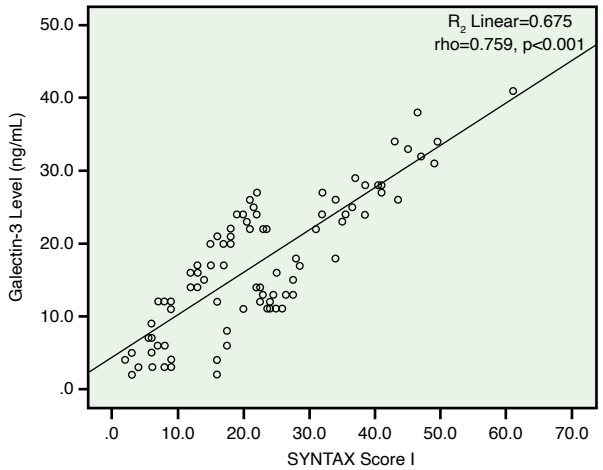

Figure 1. The correlation between galectin-3 and SYNTAX Score I results.

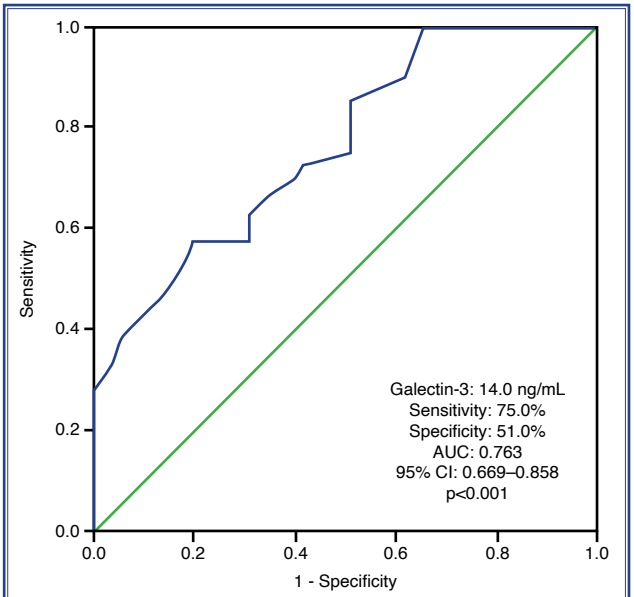

Figure 2. The receiver operating characteristic curve analysis of galectin-3 for predicting intermediate to high SYNTAX Score I results. AUC: Area under the curve; CI: Confidence interval.

of 0.763 (95% CI: 0.669–0.858; p<0.001). The ROC curve analysis of galectin-3 for predicting an intermediate or high SYNTAX Score I result is shown in Figure 2.

DISCUSSION

The major findings of the current study include (1) NSTEMI patients with intermediate and high SYNTAX Score I results had significantly higher galectin-3 levels, and (2) galectin-3 was an independent predictor of intermediate and high SYNTAX scores in these patients. To the best of our knowledge, this is the first study in the literature to report a relationship between the galectin-3 level and the extent, severity, and complexity of CAD in patients with NSTEMI.

The potential underlying pathophysiological mechanism of these findings may be inflammation, which underlies all of the phases of atherosclerosis, including atherosclerotic plaque development, progression, and plaque rupture.[18] Several studies have investigated the immune-inflammatory mediators that may be involved in this cascade.[19–23] Recent studies have demonstrated that galectin-3, which interferes with cell adhesion, proliferation, differentiation, and angiogenesis,[24,25] played a key role in both acute and chronic inflammatory responses, including atherosclerosis.[26,27] Nachtigal et al.[28] demonstrated that galectin-3 was up-regulated in human atherosclerotic lesions. Additionally, Papaspyridonos et al.[29] found that galectin-3 enhanced inflammation by inducing the expression of several pro-inflammatory molecules in plaque pathology. Moreover, plaque foam cells and activated macrophages may secrete galectin-3, a potent chemoattractant for monocytes and macrophages.[30] Thus, galectin-3 enhances the recruitment of these cells into the vascular wall.[25] Furthermore, it has been reported that inactivation of the galectin-3 gene reduced inflammation and subsequently decreased atherosclerotic lesions in mice.[31] All of these findings support the hypothesis that galectin-3 accelerates atherogenesis by enhancing inflammation.

Zuin et al.[32] demonstrated that the neutrophil-to-lymphocyte ratio (NLR) was significantly associated with the SYNTAX score and 1-year cardiovascular mortality in patients with acute myocardial infarction. Kurtul et al.[33] also revealed that the NLR was significantly associated with the SYNTAX score in patients with NSTEMI. In contrast, Demir et al.[34] reported a weak positive correlation between the NLR and SYNTAX score (p=0.05). Cagdas et al.[35] reported that inflammatory status, reflected by the decreased albumin level, increased CRP level, and higher CRP-to-albumin ratio, was closely related to severe CAD, which was determined using the SYNTAX Score I and SYNTAX Score II. In our study, inflammatory indicators, including NLR and CRP levels, were higher in the SYNTAX Score I >22 group than in the SYNTAX Score I ≤22 group. How-

ever, the difference between study groups was not significant.

Galectin-3 has been widely investigated in several clinical conditions, including heart failure,[1,36–38] and coronary artery ectasia.[39] De Boer et al.[40] examined a potential relationship between LVEF and the predictive value of plasma galectin-3. There was a statistically significant interaction between a depressed LVEF (≤40%) and preserved LVEF (>40%) and the predictive value of galectin-3 level (p=0.047). Tang et al.[41] reported no relationship between galectin-3 and LVEF. Ansari et al.[42] demonstrated a significant association between galectin-3 and LVEF in heart failure with preserved ejection fraction patients. In our study, LVEF was significantly associated with galectin-3. Also, LVEF was an independent predictor of intermediate and high SYNTAX scores. Aciksari et al.[39] recently reported that galectin-3 was significantly elevated in patients with isolated coronary artery ectasia, indicating that galectin-3 may be involved in the pathogenesis of this entity.

In our study, cardiovascular risk factors such as hypertension, hyperlipidemia, diabetes mellitus, smoking, and a family history of CAD were not significantly different between the study groups. Cagdas et al.[35] reported similar findings regarding hypertension hyperlipidemia, and smoking status. However, the prevalence of diabetes mellitus was significantly higher in patients with severe CAD.

Galectin-3 elevation reflects cardiac inflammation and fibrosis It was logical to hypothesize that it would be independently associated with post-myocardial infarction outcomes. Recent studies have evaluated the prognostic role of galectin-3 in patients with acute myocardial infarction.[43–45] Tsai et al.[43] demonstrated that galectin-3 levels were higher among patients with myocardial infarction, and that galectin-3 was associated with 30-day mortality and heart failure after myocardial infarction. Lisowska et al.[44] reported that galectin-3 was associated with more severe CAD in patients with ischemic heart disease and was an independent predictor of death after myocardial infarction. Asleh et al.[45] observed that galectin-3 was an independent predictor of mortality and heart failure post myocardial infarction. All of these findings suggest a role for the measurement of galectin-3 in risk stratification post myocardial infarction.

In the present study, the galectin-3 level was significantly higher in patients with more extensive and more severe CAD. Therefore, it is plausible that galectin-3 may interfere with the development and progression of atherosclerotic CAD. Several studies have reported that patients with 3-vessel disease had higher levels of galectin-3 than patients with 1- or 2-vessel disease.[46,47] Our findings are in agreement with these reports.

Limitations

Our study has several limitations. First, it should be noted that our results are based on a single-center study of a relatively small number of patients. A multi-center study with more patients could have more significant results. Second, our data were obtained from patients with NSTEMI. Thus, our results may not apply for patients with stable CAD. Also, the present study did not determine the mechanism of action of galectin-3 in atherogenesis; further studies are needed. Finally, this was a cross-sectional study and there was no long-term follow-up of the patients. Therefore, we could not provide any prognostic data in terms of cardiovascular events.

Conclusion

In patients with NSTEMI, the level of galectin-3 was associated with the extent, severity, and complexity of CAD as assessed by the SYNTAX Score I.

Funding: This research did not receive any specific grant from any funding agency.

Ethical statement: This study was approved by the Çukurova University Faculty of Medicine Ethics Committee (no. 39, date: 06.07.2018).

Peer-review: Externally peer-reviewed.

Conflict-of-interest: None.

Authorship contributions: Concept: A.Q., G.A., H.H., I.H.K.; Design: A.Q., G.A., I.H.K.; Supervision: G.A., Ö.G., H.H.; Materials: A.Q., I.H.K.; Data: A.Q., G.A., Ö.G., H.H.; Analysis: A.Q., Ö.G.; Literature search: G.A., Ö.G., H.H.; Writing: A.Q.; Critical revision: A.Q., I.H.K.

REFERENCES

1. Dong R, Zhang M, Hu Q, Zheng S, Soh A, Zheng Y, et al. Galectin-3 as a novel biomarker for disease diagnosis and a target for therapy (Review). Int J Mol Med 2018;41:599–614.
2. Rieth AJ, Jung C, Gall H, Rolf A, Mitrovic V, Hamm CW, et al. Association of galectin-3 with changes in left ventricular

function in recent-onset dilated cardiomyopathy. Biomarkers 2019;24:652–8. [CrossRef]
3. Tang Z, Zeng L, Lin Y, Han Z, Gu J, Wang C, et al. Circulating Galectin-3 is Associated With Left Atrial Appendage Remodelling and Thrombus Formation in Patients With Atrial Fibrillation. Heart Lung Circ 2019;28:923–31. [CrossRef]
4. Meijers WC, van der Velde AR, Pascual-Figal DA, de Boer RA. Galectin-3 and post-myocardial infarction cardiac remodeling. Eur J Pharmacol 2015;763:115–21. [CrossRef]
5. Liu FT, Patterson RJ, Wang JL. Intracellular functions of galectins. Biochim Biophys Acta 2002;1572:263–73. [CrossRef]
6. Suthahar N, Meijers WC, Sillje HHW, Ho JE, Liu FT, de Boer RA. Galectin-3 Activation and Inhibition in Heart Failure and Cardiovascular Disease: An Update. Theranostics 2018;8:593–609. [CrossRef]
7. Libby P, Buring JE, Badimon L, Hansson GK, Deanfield J, Bittencourt MS, et al. Atherosclerosis. Nat Rev Dis Primers 2019;5:56. [CrossRef]
8. Ozturk D, Celik O, Satilmis S, Aslan S, Erturk M, Cakmak HA, et al. Association between serum galectin-3 levels and coronary atherosclerosis and plaque burden/structure in patients with type 2 diabetes mellitus. Coron Artery Dis 2015;26:396–401. [CrossRef]
9. Aksan G, Gedikli O, Keskin K, Nar G, Inci S, Yildiz SS, et al. Is galectin-3 a biomarker, a player-or both-in the presence of coronary atherosclerosis? J Investig Med 2016;64:764–70.
10. Capodanno D, Di Salvo ME, Cincotta G, Miano M, Tamburino C, Tamburino C. Usefulness of the SYNTAX score for predicting clinical outcome after percutaneous coronary intervention of unprotected left main coronary artery disease. Circ Cardiovasc Interv 2009;2:302–8. [CrossRef]
11. Safarian H, Alidoosti M, Shafiee A, Salarifar M, Poorhosseini H, Nematipour E. The SYNTAX Score Can Predict Major Adverse Cardiac Events Following Percutaneous Coronary Intervention. Heart Views 2014;15:99–105. [CrossRef]
12. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2016;37:267–315. [CrossRef]
13. Expert Committee on the D, Classification of Diabetes M. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;26 Suppl 1:S5–20. [CrossRef]
14. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021–104.
15. National Cholesterol Education Program Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143–421. [CrossRef]
16. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28:1–39 e14. [CrossRef]
17. Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961–72. [CrossRef]
18. Libby P, Ridker PM, Hansson GK, Leducq Transatlantic Network on A. Inflammation in atherosclerosis: from pathophysiology to practice. J Am Coll Cardiol 2009;54:2129–38. [CrossRef]
19. Zernecke A, Weber C. Inflammatory mediators in atherosclerotic vascular disease. Basic Res Cardiol 2005;100:93–101.
20. Ilhan F, Kalkanli ST. Atherosclerosis and the role of immune cells. World J Clin Cases 2015;3:345–52. [CrossRef]
21. Hansson GK, Hermansson A. The immune system in atherosclerosis. Nat Immunol 2011;12:204–12. [CrossRef]
22. Raggi P, Genest J, Giles JT, Rayner KJ, Dwivedi G, Beanlands RS, et al. Role of inflammation in the pathogenesis of atherosclerosis and therapeutic interventions. Atherosclerosis 2018;276:98–108. [CrossRef]
23. Back M, Yurdagul A Jr, Tabas I, Öörni K, Kovanen PT. Inflammation and its resolution in atherosclerosis: mediators and therapeutic opportunities. Nat Rev Cardiol 2019;16:389–406.
24. Dumic J, Dabelic S, Flogel M. Galectin-3: an open-ended story. Biochim Biophys Acta 2006;1760:616–35. [CrossRef]
25. Al-Ansari S, Zeebregts CJ, Slart RH, Peppelenbosch M, Tio RA. Galectins in atherosclerotic disease. Trends Cardiovasc Med 2009;19:164–9. [CrossRef]
26. Uno K, Nicholls SJ. Biomarkers of inflammation and oxidative stress in atherosclerosis. Biomark Med 2010;4:361–73.
27. Henderson NC, Sethi T. The regulation of inflammation by galectin-3. Immunol Rev 2009;230:160–71. [CrossRef]
28. Nachtigal M, Al-Assaad Z, Mayer EP, Kim K, Monsigny M. Galectin-3 expression in human atherosclerotic lesions. Am J Pathol 1998;152:1199–208.
29. Papaspyridonos M, McNeill E, de Bono JP, Smith A, Burnand KG, Channon KM, et al. Galectin-3 is an amplifier of inflammation in atherosclerotic plaque progression through macrophage activation and monocyte chemoattraction. Arterioscler Thromb Vasc Biol 2008;28:433–40. [CrossRef]
30. Sano H, Hsu DK, Yu L, Apgar JR, Kuwabara I, Yamanaka T, et al. Human galectin-3 is a novel chemoattractant for monocytes and macrophages. J Immunol 2000;165:2156–64. [CrossRef]
31. Nachtigal M, Ghaffar A, Mayer EP. Galectin-3 gene inactivation reduces atherosclerotic lesions and adventitial inflammation in ApoE-deficient mice. Am J Pathol 2008;172:247–55.
32. Zuin M, Rigatelli G, Picariello C, dell'Avvocata F, Marcantoni L, Pastore G, et al. Correlation and prognostic role of

neutrophil to lymphocyte ratio and SYNTAX score in patients with acute myocardial infarction treated with percutaneous coronary intervention: A six-year experience. Cardiovasc Revasc Med 2017;18:565–71. [CrossRef]

33. Kurtul S, Sarli B, Baktir AO, Demirbas M, Saglam H, Dogan Y, et al. Neutrophil to lymphocyte ratio predicts SYNTAX score in patients with non-ST segment elevation myocardial infarction. Int Heart J 2015;56:18–21. [CrossRef]
34. Demir K, Avci A, Altunkeser BB, Yilmaz A, Keles F, Ersecgin A. The relation between neutrophil-to-lymphocyte ratio and coronary chronic total occlusions. BMC Cardiovasc Disord 2014;14:130. [CrossRef]
35. Cagdas M, Rencuzogullari I, Karakoyun S, Karabag Y, Yesin M, Artac I, et al. Assessment of Relationship Between C-Reactive Protein to Albumin Ratio and Coronary Artery Disease Severity in Patients With Acute Coronary Syndrome. Angiology 2019;70:361–8. [CrossRef]
36. Besler C, Lang D, Urban D, Rommel KP, von Roeder M, Fengler K, et al. Plasma and Cardiac Galectin-3 in Patients With Heart Failure Reflects Both Inflammation and Fibrosis: Implications for Its Use as a Biomarker. Circ Heart Fail 2017;10:e003804. [CrossRef]
37. Zhong X, Qian X, Chen G, Song X. The role of galectin-3 in heart failure and cardiovascular disease. Clin Exp Pharmacol Physiol 2019;46:197–203. [CrossRef]
38. Gocer H, Gunday M, Unal M. Plasma galectin-3 as a biomarker for clinical staging of heart failure: a cross-sectional evaluation of 100 cases. Clin Ter 2019;170:e267–e71.
39. Aciksari G, Uygun T, Atici A, Aciksari K, Toprak AE, Onur I, et al. Association between galectin-3 levels and isolated coronary artery ectasia. Cardiovasc J Afr 2020;31:1–6. [CrossRef]
40. de Boer RA, Lok DJ, Jaarsma T, van der Meer P, Voors AA, Hillege HL, et al. Predictive value of plasma galectin-3 levels in heart failure with reduced and preserved ejection fraction. Ann Med 2011;43:60–8. [CrossRef]
41. Tang WH, Shrestha K, Shao Z, Borowski AG, Troughton RW, Thomas JD, et al. Usefulness of plasma galectin-3 levels in systolic heart failure to predict renal insufficiency and survival. Am J Cardiol 2011;108:385–90. [CrossRef]
42. Ansari U, Behnes M, Hoffmann J, Natale M, Fastner C, El-Battrawy I, et al. Galectin-3 Reflects the Echocardiographic Grades of Left Ventricular Diastolic Dysfunction. Ann Lab Med 2018;38:306–15. [CrossRef]
43. Tsai TH, Sung PH, Chang LT, Sun CK, Yeh KH, Chung SY, et al. Value and level of galectin-3 in acute myocardial infarction patients undergoing primary percutaneous coronary intervention. J Atheroscler Thromb 2012;19:1073–82. [CrossRef]
44. Lisowska A, Knapp M, Tycinska A, Motybel E, Kaminski K, Swiecki P, et al. Predictive value of Galectin-3 for the occurrence of coronary artery disease and prognosis after myocardial infarction and its association with carotid IMT values in these patients: A mid-term prospective cohort study. Atherosclerosis 2016;246:309–17. [CrossRef]
45. Asleh R, Enriquez-Sarano M, Jaffe AS, Manemann SM, Weston SA, Jiang R, et al. Galectin-3 Levels and Outcomes After Myocardial Infarction: A Population-Based Study. J Am Coll Cardiol 2019;73:2286–95. [CrossRef]
46. Falcone C, Lucibello S, Mazzucchelli I, Bozzini S, D'Angelo A, Schirinzi S, et al. Galectin-3 plasma levels and coronary artery disease: a new possible biomarker of acute coronary syndrome. Int J Immunopathol Pharmacol 2011;24:905–13.
47. Sanchez-Mas J, Lax A, Asensio-Lopez MC, Fernandez-Del Palacio MJ, Caballero L, Garrido IP, et al. Galectin-3 expression in cardiac remodeling after myocardial infarction. Int J Cardiol 2014;172:e98–e101. [CrossRef]

Keywords: Atherosclerosis; galectin-3; myocardial infarction; SYNTAX score.

Anahtar sözcükler: Ateroskleroz; galektin-3; miyokart enfarktüsü; SYNTAX skoru.