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Increased Galectin-3 Levels Predicts Ventricular Arrhythmic Events Following ST-elevation Myocardial İnfarction

Artmış Galektin-3 Düzeyleri, ST Elevasyonlu Miyokart Enfarktüsünü Takiben Gelişen Ventriküler Aritmik Olayları Öngörür

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Abstract

Objectives: We aimed to determine the association between Galectin-3 (Gal-3) levels and microvolt T-wave alternans (MTWA) and frequent premature ventricular complexes (PVCs) in single-vessel patients with left ventricular ejection fraction (EF) (LVEF) >35%, who presented with ST-elevated myocardial infarction (MI) (STEMI) and were treated with primary percutane-ous coronary intervention (pPCI).

Materials and Methods: A total of 81 patients were included in this cross-sectional study. Blood samples for Gal-3 levels were obtained from all patients at the time of admission. The patients were separated into low and high Gal-3 (≤ and >1.93 ng/dL, respectively) groups. Low-Gal-3 and high-Gal-3 groups were compared with respect to both MTWA and PVC positivity and their association with Gal-3 levels were examined.

Results: When compared to the low-Gal-3 group, left atrial volume (LAV) was higher in the high-Gal-3 patients (55.7±18.0 vs 40.6±13.7 mL, p<0.001). Multivariate analyses revealed that age, LAV and Gal-3 levels were significant independent predictors of PVC positivity (p=0.005, p=0.04, p=0.002, respectively); and Gal-3 was a significant independent predictor of MTWA positivity (p=0.002).

Conclusion: Gal-3 was associated with PVC and MTWA positivity, and was a predictor of arrhythmic events in single-vessel STEMI patients with LVEF >35%.

Key Words: Galectin-3, Microvolt T-wave Alternans, Premature Ventricular Complexes, ST-elevated Myocardial Infarction

Öz

Amaç: Sol ventrikül ejeksiyon fraksiyonu (EF) (LVEF) >%35 ve tek damar tıkanıklığı olan ve primer perkütan koroner girişim (pPCI) ile tedavi edilen ST segment elevasyonlu miyokart enfarktüsü (MI) (STEMI) hastalarında, Galektin-3 (Gal-3) düzeyleri ile mikrovolt T dalga alternans (MTWA) ve sık prematüre ventriküler kompleksler (PVC) arasındaki ilişkiyi belirlemeyi amaçladık.

Gereç ve Yöntem: Bu kesitsel çalışmaya toplam 81 hasta dahil edildi. Başvuru anında tüm has talardan Gal-3 düzeyleri için kan örnekleri alındı. Hastalar düşük ve yüksek Gal-3 (sırasıyla ≤ ve > 1,93 ng/dL) gruplarına ayrıldı. Düşük Gal-3 ve yüksek Gal-3 grupları hem MTWA hem de PVC pozitifliği açısından karşılaştırılmış ve Gal-3 düzeyleri ile ilişkisi incelenmiştir.

Bulgular: Düşük Gal-3 grubu ile karşılaştırıldığında, yüksek Gal-3 hastalarında sol atriyal hacim (LAV) daha yüksekti (55,7±18,0'a karşı 40,6±13,7 mL, p<0,001). Çok değişkenli analizler yaş, LAV ve Gal-3 düzeylerinin PVC pozitifliğinin anlamlı bağımsız prediktörleri olduğunu (sırasıyla p=0,005, p=0,04, p=0,002); ve Gal-3'ün, MTWA pozitifliğinin anlamlı bir bağımsız prediktörü olduğunu gösterdi (p=0,002).

Sonuç: Gal-3, PVC ve MTWA pozitifliği ile ilişkiliydi ve LVEF >%35 olan tek damarlı STE-MI hastalarında aritmik olayların bir prediktörü idi.

Anahtar Kelimeler: Galectin-3, Mikrovolt T Dalgası Değişim Testi, Ventriküler Erken Atımlar, ST-yükselmeli Miyokart Enfarktüsü

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Introduction

Despite the recent advances patients with ST-elevation myocardial infarction (MI) (STEMI) are still at significant early and late stage risk for cardiovascular adverse events (1,2). Although modern reperfusion therapies have been developed, adverse left ventricular remodeling (aLVR) is still common and a predictor of arrhythmic events following STEMI (3). Implantable cardioverter defibrillator (ICD) is recommended for the primary prevention of sudden cardiac death in patients with heart failure only if their left ventricular ejection fraction (EF) (LVEF) is <35%, and this practice is known to reduce cardiac mortality (4). However, many studies report that a significant proportion of cardiac arrests occurring outside the hospital is accompanied by EF >35% (5).

Microvolt T-wave alternans (MTWA) is defined by fluctuations of T-wave amplitude and morphology in the electrocardiography (ECG) trace. Positive MTWA is shown to be a significant and strong predictor of mortality due to arrhythmic events and all causes among ischemic cardiomyopathy patients (6). Premature ventricular complexes (PVCs) are common findings following MI; and patients with post-MI >10 PVCs/h upon Holter monitoring are at high risk of sudden cardiac death (7).

Galectin-3 (Gal-3) is a new biomarker with a regulatory role in fibrogenesis, tissue repair and inflammation (8). Myocardial fibrosis and aLVR are associated with increased levels of Gal-3 and arrhythmic event development. Increased levels of Gal-3 among hypertensive patients are reported to be associated with ambulatory ECG-based MTWA positivity (9).

Although guidelines recommend ICD as the primary prevention in patients with LVEF <35% following MI, no clear recommendation is present on how to prevent development of arrhythmic events and sudden cardiac deaths among patients with LVEF >35%. The aim of our study was to determine if Gal-3 levels are associated with MTWA positivity and frequent PVCs, known to predict arrhythmic events, among single-vessel patients with LVEF >35%, presented at the hospital with acute STEMI for the first time and underwent pPCI.

Materials and Methods

Study Population

The single-vessel acute STEMI patients successfully treated with pPCI from March 2019 through November 2019 were included in this prospective study. STEMI was defined according to current guidelines (10) and 141 STEMI patients were initially identified. Patients with a LVEF ≤35%, patients with severe valvular diseases, co-existing cancers, connective tissue diseases and cirrhosis were excluded. Patients who were not suitable or indicated for PCI and/or who did not have Gal-3 data at time of admission were also excluded. Consequently, the final study population consisted of 81 patients. In our study, Gal-3 median level was determined as 1.93 ng/dL. The patients grouped based on Gal-3 median level: low- (n=40) and high-Gal-3 (n=41) (≤ and >1.93 ng/dL, respectively) groups (11).

The study was approved by the Muğla University Ethics Committee (decision no: 02/07/2019-E24474).

Patients and Laboratory Measurements

Data about patient demographics, comorbidities, clinical and physical examination findings were recorded at the time of admission. Blood was sampled for routine biochemistry at the time of admission and within 48 h after pPCI for Gal-3 levels. Serum Gal-3 level was measured in duplicate, using a commercially available immunosorbent assay (Human Gal-3 platinum ELİSA BMS279/BMS279/4TEN). The intra-observer variability in the measurements of Gal-3 was also assessed and all of the mean intra-assay coefficients of variance were found to be less than 7.5%.

At 24 h to 72 h after revascularization, a transthoracic echocardiography was performed using a Vivid S5 probe 3S-RS (GE Healthcare). All patients treated according to the current STEMI guidelines (10) and angiographic data were recorded.

Ambulatory ECG-based MTWA

The analyses of MTWA were carried out from 12-channel records of the ambulatory Holter monitoring (DMS 300-7 Holter Reader; DSM, Stateline, Nevada, USA). The recordings were obtained for 24 hours in all patients and control participants. Before automatic analysis of tapes using the Holter program (CardioScan12.0 DM software; DSM), we performed the measurements of TWA at maximum heart rates less than 120 beats/min. MARS PC Software (SPSS INC., Chicago, Illinois, USA) was used to identify the possible TWA periods according to the modified moving average algorithm. Data were edited manually when it was observed to be unsuitable due to noise or artifacts. The highest TWA value observed in either one of the channels was considered the maximum TWA value. TWA greater than or equal to 65 microV was considered positive in this study.

Premature Ventricular Complexes (PVCs)

More than 10 PVCs per hour during a 24-hour rhythm Holter examinations in ischemic heart patients was considered positive as it was reported to be associated with increased arrhythmic events.

Statistical Analysis

Statistical analyses were carried out using SPSS software version 20 (SPSS Inc., Chicago, Illinois, USA). Chi-square (x^2), Student's t-test, and Mann-Whitney U tests were used where

appropriate. We evaluated the levels of possible factors (age, male, hyperlipidemia, Diabetes Mellitus, hypertension, anterior MI, LVEF, peak troponin level, LAV, and Gal-3 class) by univariable analyses, and factor found to be significant predictors were evaluated by multivariable logistic regression to determine independent predictors of TWA and PVCs.

Results

This study includes 81 consecutive patients with LVEF >35%, who presented at our emergency polyclinic with STEMI and had a single vessel stent placement via pPCI. Of 81 patients with STEMI, 39 had left anterior descending artery obstructive coronary artery disease, 28 had right coronary artery disease, and 14 had left circumflex artery disease. A total of 12 bare-metal stents and 70 drug-eluting stents were used to treat obstructive coronary artery lesions. TIMI grade flow 3 could be established in all patients.

The mean age of low-Gal-3 patients was 51.7±11.3 years and 90% of the participants were males, whereas the corresponding values were 50.5±12.3 years and 80.5% within in high-Gal-3 group (Table 1). No statistically significant difference was observed between the low- and high-Gal-3 groups with respect to diabetes, hypertension and hyperlipidemia history, and blood levels of creatinine, hematocrit and cardiac enzymes. As the only statistically significant difference between two Gal-3 groups was that LAV was higher in high-Gal-3 patients (55.7±18 vs 40.6±13.7 mL, p<0.001).

Table 1: Baseline characteristics of study population

	Low Galectin-3 level (n=40)	High Galectin-3 level (n=41)	p
Age, years	51.7±11.3	50.5±12.3	0.653
Male, n (%)	36 (90.0%)	33 (80.5%)	0.228
Smoking, n (%)	16 (40.0%)	25 (61.0%)	0.059
Diabetes Mellitus, n (%)	5 (12.5%)	4 (9.8%)	0.694
Hypertension, n (%)	9 (22.5%)	12 (29.3%)	0.487
Hyperlipidemia, n (%)	5 (12.5%)	4 (9.8%)	0.694
Family history, n (%)	7 (17.5%)	9 (22.0%)	0.615
Anterior MI, n (%)	15 (37.5)	22 (53.7)	0.144
LVEF (%)	52.9±6.6	53.8±7.9	0.601
HDL, mg/dL	39.5±10.9	40.6±10.4	0.638
LDL, mg/dL	118.2±35.7	124.1±33.9	0.479
Trigliserid, mg/dL	186.0±161.2	136.4±89.7	0.089
Glucose, mg/dL	150.8±76.2	135.4±41.7	0.268
Creatinine, mg/dL	0.87±0.19	0.89±0.2	0.694
Hematocrit, %	43.4±6.6	44.4±5.1	0.422
Peak CK-MB, mg/dL	78.3±88.5	114.0±126.2	0.138
Peak troponin, ng/dL	7.78±9.94	8.5±9.4	0.751
Left atrial volume, mL	40.6±13.7	55.7±18.0	<0.001

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, LVEF: Left ventricular ejection fraction, MI: Myocardial infarction, CK-MB: Creatine kinase-myocardial band, n: Number

Table 2: Multivariable Logistic Regression analysis for T-wave and Premature Ventricular Camplexes positivity

	Univariable analysis CI 95%	p	Multivariable analysis OR (CI 95%)*	p
First model¶				
Age, years	1.006-1.100	**0.026**	1.083 (1.023-1.140)	**0.005**
Male, yes	0.410-10.457	0.384	-	
Hyperlipidemia, yes	0.087-14.437	0.929	-	
Diabetes Mellitus, yes	0.021-3.065	0.283	-	
Hypertension, yes	0.249-4.807	0.906	-	
Anterior MI	0.113-1.923	0.291	-	
LVEF, %	0.912-1.045	0.492	-	
Peak troponin, ng/dL	0.902-1.039	0.373	-	
Left atrial volume, mL	1.017-1.085	**0.003**	1.042 (1.002-1.083)	**0.040**
Galectin class	2.825-40.156	**<0.001**	10.576 (2.295-48.726)	
Second Model†				
Age, years	0.937- 1.019	0.282	-	**0.002**
Male, yes	0.914-1.010	0.118	-	
Hyperlipidemia, yes	0.063-3.153	0.419	-	
Diabetes Mellitus, yes	0.466-22.745	0.234	-	
Hypertension, yes	0.128-1.944	0.316	-	
Anterior MI	0.430-4.441	0.587	-	
LVEF, %	1.000-1.150	**0.051**	1.071 (0.995-1.153)	0.066
Peak troponin, ng/dL	0.965-1.087	0.435	-	
Left atrial volume, mL	0.971-1.045	0.689	-	
Galectin class	2.177-20.420	**0.001**	6.734 (2.149-21.101)	**0.002**

LVEF: Left ventricular ejection fraction, OR: Odds ratio, CI: Confidence interval, MI: Myocardial infarction
¶ The first model was constructed to determine PVC presence independent predictors. Nagelkerke R square of the first model was 44.1%.
† The second model was constructed to determine independent predictorsof MTWA positivitiy . Nagelkerke R square of the second model was 26.4%.
* Odds ratios for continuous variables defined as per unit increase.
Important p values are shown as bold.

Predictors of PVCs

Univariable logistic regression analysis showed significant relationships between the presence of PVCs and LAV, age, and high Gal-3 group were detected (p=0.003, p=0.026, p<0.001, respectively) (Table 2).

Multivariable logistic regression revealed that age, increased LAV and high Gal-3 group were significant and independent factors in predicting PVC positivity [Odds ratio (OR) (95% confidence interval (CI)): 1.083 (1.023-1.140), p=0.005; OR (95%CI): 1.042 (1.002-1.083), p=0.04; OR (95%CI): 10.576 (2.295-48.726), p=0.002, respectively] (Table 2). The strongest predictor among these was high Gal-3 group (Table 2).

Predictors of MTWA

The univariable logistic regression model for MTWA positivity yielded that LVEF and high Gal-3 group were the statistically significant independent variables (p=0.05, p=0.001, respectively); while only high Gal-3 was a significant predictor of MTWA positivity [OR (95%CI): 6.734 (2.149-21.101), p=0.002] on multivariable logistic regression (Table 2).

Galectin-3 and Arrhythmic Events

The predictive value of Gal-3 levels on arrhythmic events is presented in Figure 1. Among the MTWA positive patients, the T-wave positive cases were 12.5% in low-and 48.4% in high-Gal-3 subgroups (p<0.001) (Figure 1). Regarding PVC positivity, 7.5% low-Gal-3 patients were PVC positive, while it was 46.3% in high-Gal-3 group (p<0.001) (Figure 1). Furthermore, in a receiver-operating characteristic curve analysis, Gal-3 cut-off ≥3.44 ng/dL had AUC of 0.867 for distinguishing MTWA positivity with a 81.8% sensitivity and 83.0% specificity (Figure 2).

Discussion

This study showed that Gal-3 levels of STEMI patients are independently related to PVC and MTWA positivity that can predict arrhythmic mortalities. LAV is observed to be higher in high-Gal-3 group compared to the low-Gal-3 patients. Independent predictors for ECG-based MTWA positivity were found to be age, LAV, and Gal-3, of which, Gal-3 was the strongest. The only independent predictor of PVC positivity was also Gal-3.

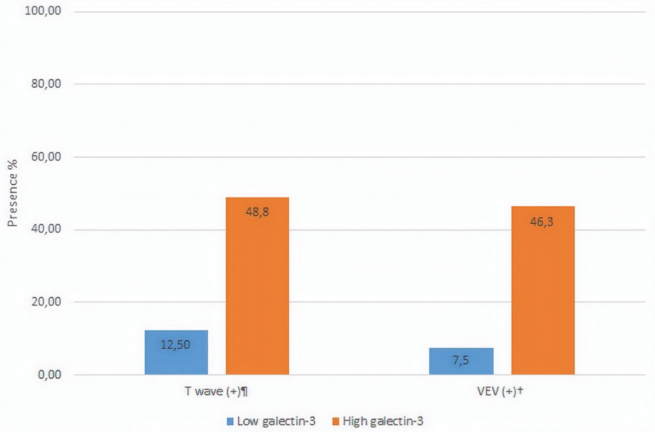

Figure 1: The effect of Galectin-3 level on sudden cardiac death markers.
¶ p<0.001, † p<0.001

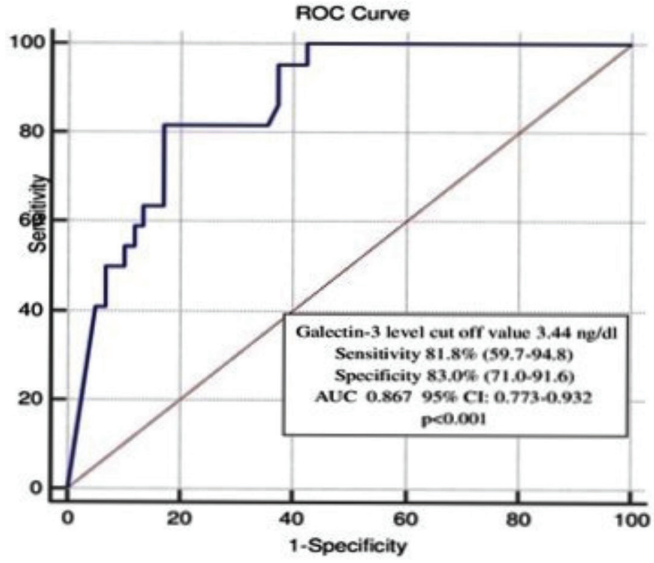

Figure 2: ROC curve showing the distinguishing of the Galectin-3 level for the MTWA positivity

ROC: Receiver operating characteristic curve, MTWA: Microvolt T-wave alternans, AUC: Area under curve, CI: Confidence interval

In STEMI cases, heart failure and arrhythmic events are the most significant causes of mortality, and aLVR has a significant role in this process (12). aLVR occurs rapidly after STEMI and progressive post-infarction re-modelling is the most significant predictor of poor clinical outcomes (12-14). Fibrotic tissue in the heart forms a substrate for ventricular arrhythmias which leads to formation of ventricular tachycardia/ventricular fibrillation (15-17).

Many studies have demonstrated that myocardial fibrosis, detected by late gadolinium enhancement (LGE) in cardiovascular magnetic resonance (CMR), is strongly associated with ventricular arrhythmia/arrhythmic events (18-21). A large meta-analysis study has shown that detection of ventricular fibrosis via LGE-CMR is a strong predictor of ventricular arrhythmia/arrhythmic events among both ischemic and non-ischemic cardiomyopathy patients, especially for those with LVEF ≤30% (20). Another study reported that the presence of midwall LGE showing myocardial fibrosis in CMR, in patients with dilated cardiomyopathy with LVEF ≥40%, was associated with increased risk of sudden cardiac death and that this patient group may benefit from ICD implantation (21).

Ambulatory ECG-based MTWA reflects a temporal dispersion in intra-cardiac repolarization that may contribute to re-entrant

arrhythmias. Although MTWA is often used as a predictor of arrhythmia development and sudden death in patients with low LVEF, some studies also reported that it was a predictor of sudden cardiac death and total mortality in patients with preserved LVEF as well (22,23). In a study with 1037 normal LVEF patients who were recommended an exercise stress test on the basis of clinical assessments, MTWA was determined to be a predictor of mortality (24).

Post-MI PVCs which often develop through infarct scar, are common among patients with LV dysfunction (25). In patients with structural heart disease, PVC increases the risk of mortality and patients with >10 PVCs per hour are considered to have a marker for increased risk of sudden cardiac death (10).

Gal-3 has a central role in development of fibrosis in heart and kidneys and tissue re-modelling (26,27). In recent studies, Gal-3 is reported as a potent prognostic marker for major adverse cardiovascular events in heart failure patients (28,29). Moreover, de Boer et al. (30) reported that Gal-3 is an independent predictor of cardiovascular mortality in the general population. In another study, patients with obstructive sleep apnea syndrome were shown to present with a significant association between Gal-3 levels and coronary atherosclerosis (31).

Increased levels of Gal-3 are shown to be predictive of atrial fibrillation (AF) development in patients with both preserved and impaired left ventricular function (32,11). The largest of these studies, ARIC study also found that increased Gal-3 levels were associated with increased AF risk (33). In another study, high Gal-3 levels were associated with new-onset AF at higher rates among patients treated for the first time with MI and treated with pPCI (34). A study in hypertensive patients also reported that elevated levels of Gal-3 were associated with MTWA positivity (35).

The role of Gal-3 has been assessed in relation to post-MI outcomes (33-36). In patients with anterior STEMI treated with pPCI, high Gal-3 levels in early acute phase (within 48 hours) were found to be associated with 6-month aLVR (36) and was also reported to be a strong independent predictor of long-term outcomes (37).

We demonstrated here that increased levels of Gal-3 were associated with both PVCs and MTWA positivity, known predictors of arrhythmic events. The association was thought to be due to the relationship of aLVR and myocardial fibrosis with Gal-3 levels following STEMI. LAV values were higher in the high-Gal-3 group. Following cardiac ischemia, re-modelling and left atrium enlargement process, led by the profibrotic mediator Gal-3 in the left atrium as well as in the left ventricle, eventually play a role in the development of heart failure. This mechanism may explain the relationship between high Gal-3 level and LAV observed in our study. The relationship between increased Gal-3 levels and increased LAV was not explored directly in this study but it can explain the relationship between Gal-3 levels and AF, observed in prior studies.

Study Limitations

There are some limitations of this study. First of all, the single-center, non-randomized nature of the study may have led to subject selection bias. Second, the post-STEMI serial changes in the Gal-3 levels circulating in the blood were not evaluated, resulting in an inability to identify the best time for peak value measurement of Gal-3 following STEMI. Third, CMR imaging that is a good indicator of myocardial fibrosis was not performed in our patients. Fourth, we included single-vessel patients and patients with EF >35%, which makes the results unsuitable for gener-alization to all STEMI patients. Finally, the most important limitation of our study is that we did not follow the patients for a long period of time, and therefore could not observe the development of arrhythmic events and sudden cardiac death.

Conclusion

Gal-3 levels at the time of admission of patients presenting with STEMI and treated via pPCI are significantly related to PVC and MTWA positivity that are predictors of arrhythmic events. This relationship can be used for risk classifications in this patient group.

Ethics

Ethics Committee Approval: This study was approved by Muğla Sıtkı Koçman University Rectorate Building, Dean's Office of Faculty of Medicine Clinical Researches Ethics Committee (no: 72855364-050.01.04-E.24474).

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.B., H.P., Concept: İ.B., Design: İ.B., H.P., Data Collection or Processing: İ.B., H.P., Analysis or Interpretation: İ.B., Literature Search: İ.B., H.P., Writing: İ.B.

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. McManus DD, Gore J, Yarzebski J, et al. Recent trensds in the incidence,treatment,and outcomes of patients with STEMI and NSTEMI.Am J Med. 2011;124:40-47.

2. Jerberg T, Johanson P, Held C, et al. Association between adoption of evidence-based treatment and survival for patients with St-elevation myocardial infarction. JAMA. 2011;305:1677-1684.
3. Bolognese L, Neskovic AN, Parodi G, et al. Left ventricular remodelling after primary coronary angioplasty: patterns of left ventricular dilation and long-term prognostic implications. Circulation. 2002;106:2351-2357.
4. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, et al. 2015 ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. Eur Heart J. 2015;36:2793-2867.
5. Stecker EC, Vickers C, Waltz J, et al. Population-based analysis of sudden cardiac death with and without left ventricular systolic dysfunction: two-year findings from the Oregon Sudden Unexpected Death Study. J Am Coll Cardiol. 2006;47:1161-1166.
6. Chow T, Kereiakes DJ, Bartone C, et al. Prognostic utility of microvolt T-wave alternans in risk stratification of patients with ischemic cardiomyopathy. J Am Coll Cardiol. 2006;47:1820-1827.
7. Maggioni AP, Zuanetti G, Franzosi MG, et al. Prevalence and prognostic significance of ventricular arrhythmias after acute myocardial infarction in the fibrinolytic era. GISSI-2 results. Circulation. 1993;87:312-322.
8. Dumic J, Dabelic S, Flogel M. Galectin-3:an open-ended story. Biochim Biophys Acta. 2006;1760:616-635.
9. Pusuroglu H, Akgul O, Erturk M, et al. Assessment of relationship between galectin-3 and ambulatory ECG-based microvolt T-wave alternans in sustained systodiastolic hypertension patients. Blood Press Monit. 2016;21:265-270.
10. Ibanez B, James S, Agewall S, et al. ESC Scientific Document Group. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J. 2018;39:119-177.
11. Szadkowska I, Wlazel RN, Migala M, et al. The association between galectin-3 and clinical parameters in patients with first acute myocardial infarction treated with primary percutaneous coronary angioplasty. Cardiol J. 2013;20,6:577-582.
12. Cohn JN, Ferrari R, Sharpe N. Cardiac remodelling-concepts and clinical implications:a consensus paper from an international forum on cardiac remodelling. Behalf of an International Forum on Cardiac Remodelling. J Am Coll Cardiol. 2000;35:569-582.
13. Altara R, Manca M, Sabra R, et al. Temporal cardiac remodelling post-myocardial infarction. Dynamics and prognostic implications in personalized medicine. Heart Fail Rev. 2015:21;25-47.
14. Mann DL, Bristow MR. Mechanisms and models in heart failure: the biomechanical model and beyond. Circulation. 2005:111;2837-2849.
15. Bello D, Fieno DS, Kim RJ, et al. Infarct morphology identifies patients with substrate for sustained ventricular tachycardia. J Am Coll Cardiol. 2005:45;1104-1108.
16. Wu TJ, Ong JJ, Hwang C, et al. Characteristics of wave fronts during ventricular fibrillation in human hearts with dilated cardiomyopathy: role of increased fibrosis in the generation of reentry. J Am Coll Cardiol. 1998:32;187-196.
17. Bogun FM, Desjardins B, Good E, et al. Delayed-enhanced magnetic resonance imaging in nonischemiccardiomypotathy: utility for identifying the ventricular arrhythmia substrate. J Am Coll Cardiol. 2009:53;1138-1145.
18. Schmidt A, Azevedo CF, Cheng A, et al. Infarct tissue heterogeneity by magnetic resonance imaging identifies enhanced cardiac arrhythmias susceptibility in patients with left ventricular dysfunction. 2007:115;2006-2014.
19. Perez-David E, Arenal A, Rubio-Guivernau JL, et al. Noninvasive identification of ventricular tachycardia-related conduction channel using contrast-enhanced magnetic resonance imaging in patients with chronic myocardial infarction:comparison of signal intensity scar mapping and endocardial voltage mapping. J Am Coll Cardiol. 2011:57;184-194.
20. Disertori M, Rigoni M, Pace N, et al. Myocardial fibrosis assessment by LGE is a powerful predictor of ventricular tachyarrhythmias is ischemic and nonischemic LV dysfunction:a meta-analysis. JACC Cardiovascular Imaging. 2016:9;1056-1058.
21. Halliday BP, Gulati A, Ali A, et al. Association between midwall late gadolinium enhancement and sudden cardiac death in patients with dilated cardiomyopathy and mild and moderate left ventricular systolic dysfunction. Circulation. 2017:135;2106-2115.
22. Rosenbaum DS, Jackson LE, Smith JM, et al. Electrical alternans and vulnerability to ventricular arrhythmias. N Eng J Med. 1994;330:235-241.
23. Hohnloser SH, Ikeda T, Bloomfield DM, et al.T-wave alternans negative coronary patients with low ejection and benefit from defibrillator implantation. Lancet. 2003:362;125-126.
24. Nieminen T, Lehtimäki T, Viik J, et al. T wave alternans predicts mortality in a population undergoing a clinically indicated exercise test. Eur Heart J. 2007:28;2332-2337.
25. Bogun F, Crawford T, Chalfoun N, et al. Relationship of frequent postinfarctionprematüre ventricular complexes to the reentry circuit of scar-related ventricular tachycardia. Heart Rhythm. 2008:3;367-374.
26. Sharma UC, Pokharel S, van Brakel TJ, et al. Galectin-3 marks activated macrophages in failure-prone hypertrophied hearts and contributes to cardiac dysfunction. Circulation. 2004;110:3121-3128.
27. Liu YH, D'Ambrosio M, Liao TD, et al. N-acetyl-aspartyl-lysyl-proline prevents cardiac remodelling and dysfunction induced by galectin-3,a mammalian adhesion/growth-regulatory lectin. Am J Physiol Heart Circ Physiol. 2009;296:H404-H412.
28. Lok DJ, van Der Meer P, de la Porte PW, et al. Prognostic value of galectin-3, a novel marker of fibrosis,in patients with chronic heart failure:data from the DEAL-Hf study.Clin Res Cardiol. 2010;99:323-328.
29. de Boer RA, Lok DJ, Jaarsma T, et al. Predictive value of plasma galectin-3 levels in heart failure with reduced and preserved ejection. Ann Med. 2011;43:60-68.
30. de Boer RA, van Velduisen DJ, Gansevoort RT, et al. The fibrosis marker galectin-3 and outcome in the general population. J Intern Med. 2012;272:55-64.
31. Pusuroglu H, Somuncu U, Bolat I, et al. Galectin-3 is associated with coronary plaque burden and obstructive sleep apnoea syndrome severity. Kardiol Pol. 2017;75:351-359.
32. Fashanu OE, Norby FL, Aguilar D, et al. Galectin-3 and incidence of atrial fibrillation: The Atherosclerosis Risk in Communities (ARIC) study. Am Heart J. 2017;192:19-25.
33. Perea RJ, Morales-Ruiz M, Ortiz-Perez JT, et al. Utility of galectin-3 in predicting post-infarct remodelling after acute myocardial infarction based on extracellular volume fraction mapping. Int J Cardiol. 2016;223:458-464.
34. Weir RA, Petrie CJ, Murphy CA, et al. Galectin-3 and cardiac function in survivors of acute myocardial infarction. Cir Heart Fail. 2013;6:492-498.
35. Van Der Velde AR, Lexis CP, Meijers WC, et al. Galectin-3 and sST2 in prediction of left ventricular ejection fraction after myocardial infarction. Clin Chim Acta. 2016;452:50-57.
36. Di Tano G, Ceretta G, De Maria R, et al. Galectin-3 predicts left ventricular remodelling after anterior-wall myocardial infarction treated by primary percutaneous coronary intervention. Heart. 2017;103:71-77.
37. Di Tano G, Caretta G, De Maria R, et al. Galectin-3 and outcomes after anterior-wall myocardial infarction treated by primary percutaneous coronary intervention. Biomark Med. 2018;12:21-26.