MedCrave
Step into the World of Research

Journal of Cardiology & Current Research

Review Article

Open Access

CrossMark

Galectin-3, a new proof of the better outcome of deferred stenting in STEMI patients with high thrombus burden

Abstract

Background: The issue of inevitable microvascular blockade after PPCI, especially if high thrombus burden, raise the idea of deferred stenting "DS". DS refers to the concept of a minimalist immediate mechanical intervention (MIMI) using the simple guide wire or a very small balloon in an emergency to reopen an infarct-related artery in acute STEMI, and to postpone stenting to the following days in stable conditions. Remodeling and myocardial fibrosis are inevitable with subsequent progression to heart failure (HF) if we fail to protect the microvasculature in STEMI. Macrophages secrete Galectin-3, which stimulate additional macrophages, pericytes, myofibroblasts, and fibroblasts and subsequent cellular proliferation and secretion of procollagen I.

Methods: We recruited consecutive 116 STEMI cases with high thrombus burden (grades 4–5). Admission Galectin-3 assessment. Precise timing of onset of chest Pain until Wiring of the blocked artery (PWT). Echocardiography assessment was done during preparation of PPCI, measures of LV systolic function (EF by modified Simpson method and Left Ventricular End Systolic Volume Index "LVESVI"). All cases were prepared with the same antiplatelet, anticoagulant and statin therapies then PPCI was performed as soon as possible, decision to immediate stenting or just wiring to achieve TIMI-3 flow, keep on medical therapy and stent after 48 hours (deferred stenting), was the operator choice. Follow up of the cases for the following 3 months and then the same echocardiographic measures as well as measuring the level of Galectin-3 was repeated. We classified the patients into Group I (Immediate stenting, 78 cases) and Group II (Deferred stenting, 38 cases).

Results: ***After 3 months of follow up,*** there was a highly significant difference between both groups concerning EF, LVESVI and Galectin-3. EF decreased to 44.18±11.32 % in group I while it jumps to 52.89±7.32% in-group II (t=3.05, p<0.001). ***LVESVI;*** it increased to 44.77±11.84 ml^3/m^2 in-group I while in-group II it decreased to 33.26±6.27ml^3/m^2 (t=-3.96, p<0.001). Galactin-3, it was 21.67±6.48 ng/ml in-group I while it was 15.71±3.80 ng/mL in-group II (t=-3.70, p<0.001). The EF after 3 months has a highly significant negative correlation with the level of Galectin-3 after 3 months of follow up (r=-0.82, p<0.001) while it has no significant correlation with the level of admission Galactin-3. LVESVI after 3 months has a highly significant positive correlation with the level of Galaectin-3 after 3 months (r=0.89, p<0.001) while it has no significant correlation with level of admission Galactin-3. The regression analysis confirmed that level of Galactin-3 after 3 months is a strong predictor of recovery of both LVESVI and EF (t=8.13, p<0.001), (t=-5.28, p<0.001).

Conclusion: Admission Galectin-3 level cannot predict the recovery of LV function after PPCI while Galectin-3 after 3 months can do. DS is recommended in STEMI cases with high thrombus burden.

Keywords: Primary PCI, Deferred stenting, Remodeling, Galectin-3

Volume 15 Issue 3 - 2022

Mohammad Gouda, Baher Nabil, Marwa Mohammad Gad

Cardiology Department, Faculty of Medicine, Zagazig University, Egypt

Correspondence: Mohammad Gouda, MD, Faculty of Medicine, Cardiology Department, Assistant Professor of Cardiology, Egypt, Zagazig, Zagazig University, Egypt 44519, Tel +21019693393, Email cardioman77@yahoo.com

Received: May 26, 2022 | **Published:** June 07, 2022

Introduction

It was noticed that many cases of ST-segment elevation myocardial infarction "STEMI" who were treated with Primary PCI "PPCI", did not show the expected recovery of left ventricular "LV" function. The issue of inevitable microvascular blockade after PPCI, especially if high thrombus burden, raise the idea of deferred stenting "DS". DS refers to the concept of a minimalist immediate mechanical intervention (MIMI) using the simple guide wire or a very small balloon in an emergency to reopen an infarct-related artery "IRA" with a thrombolysis in myocardial infarction (TIMI) grade 0 flow in patients with an acute STEMI, and to postpone stenting to the following days in stable conditions.[1] DS may protect the microvasculature if high thrombus burden. Myocardial fibrosis and remodeling occur if functional myocytes are replaced with crosslinked collagen with subsequent progress to heart failure (HF) if we fail to protect the microvasculature in STEMI. Macrophages secrete Galectin-3, which works as an endocrine and paracrine signal to stimulate more macrophages, myofibroblasts, fibroblasts and pericytes. The response to this signal is cellular proliferation and secretion of procollagen I. This protein is then irreversibly crosslinked to form collagen with subsequent cardiac fibrosis.[2]

Mehta angiography thrombus grade Classification:

a) Grade 0: No cine angiographic characteristics of thrombus.

b) Grade 1 lesions show characteristics on angiography like reduced contrast density, irregular lesion contour, haziness, or a smooth convex meniscus at the site of total occlusion, suggestive, but not diagnostic, of thrombus.

©2022 Gouda et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

c) *Grade 2 (Thrombus present, small size): Definite thrombus with greatest dimensions ≤ ½ vessel diameter*

d) *Grade 3 (Thrombus present, moderate size): Definite thrombus but with greatest linear dimension > ½ but <2 vessel diameter.*

e) *Grade 4 (Thrombus present, large size): As in Grade 3 but with the largest ≥2 vessel diameter*

f) *Grade 5: Total occlusion.*

Small thrombus burden (grades 0–3) while large thrombus burden (grades 4–5). Optimal angiographic visualization of thrombus is the first step; however, thrombus is very labile and its grading is better done after crossing the thrombotic lesion with the guide wire. Often, there is no change in thrombus grade, but thrombus grade 5 most commonly is downsized.[3] We aim to confirm the better outcome of deferred stenting in STEMI patients with high thrombus burden.

Patients and methods

We recruited consecutive 116 STEMI cases, eligible for PPCI with and high thrombus burden (grades 4–5). Admission blood samples were taken, to measure Galectin-3 and other cardiac markers; precise timing of onset of chest pain was recorded to calculate the time from onset of chest Pain until Wiring of the blocked artery *(PWT)*. Echocardiography assessment was done during preparation of PPCI, measures of LV systolic function (EF by modified Simpson method and Left Ventricular End Systolic Volume Index "LVESVI"). All cases were prepared with the same antiplatelet, anticoagulant and statin therapies then PPCI was performed as soon as possible, decision to immediate stenting or just wiring to achieve TIMI-3 flow, keep on medical therapy and stent after 48 hours (deferred stenting), was the operator choice. Follow up of the cases for the following 3 months and then the same echocardiographic measures as well as measuring the level of Galectin-3 was repeated. We classified the patients into Group I (*Immediate stenting, 78 cases*) and Group II (*Deferred stenting, 38 cases*). Informed consent was obtained to be eligible for enrollment into the study. The study was done according to the rules of the Local Ethics Committee of Faculty of Medicine, Zagazig University, Egypt.

Statistical analysis: Statistical analysis was conducted, using the mean, standard deviation, independent t test, and chi square by SPSS V 20. Bivariate correlation and Regression analysis was performed to determine the independent predictors of remodeling after 3 months of PPCI. p value<0.05 was considered as statistically significant.

Results: Demographically; we had 116 cases, 66 males (56.9%) and 50 females (43.1%). Age of 55.38±10.03 years old. 54 hypertensive cases (46.6%), 78 diabetic cases (67.2), 76 dyslipidemia cases (65.5%). Cardiogenic shock was diagnosed in 10 cases only (8.6%) and clinical heart failure during the 3 months follow up was diagnosed in 34 cases (29.3%). The target artery harboring the thrombus was LAD in 78 cases (67.2%), RCA in 28 cases (24.1%) and lastly LCX in 10 cases (8.6%). *PWT* was 5.20±1.13 hours. Immediate wiring and stenting were done in 78 cases (67.2%) while the policy of deferred stenting was performed in 38 cases (32.8%). Echocardiographically, the admission EF by modified Simpson was 48.03±6.81% while after 3 months of follow up it was 47.03±10.88%. Admission LVESVI was 38.14±7.11ml^3/m^2 while after 3 months it was 41±11.59 ml^3/m^2. Troponin I level at time of admission ranged from 2.2-28u, mean was 6.45±5.32u. The admission Galactin-3 level ranged from 10.5-19 ng/mL, mean was 15.65±2.05 ng/mL while after 3 months of follow up, Galactin-3 level ranged from 11-35 ng/mL, mean was 19.72±6.34 ng/ml.

On grouping, (Table 1& 2) the age in-group I was 53.67±9.96 years while it was 58.89±9.36 in-group II, this difference was not significant (t=2.71, p>0.05). In-group I, we had 17 males (43.59%) and 22 females (56.41%) while we had 11 males (57.89%) and 8 females (42.11%) in group-II, this difference was not significant (X=0.01, p>0.05). There was 36/78 hypertensive cases in-group I while there was 18/38 hypertensive cases in group-II, This difference was not significant (X=0.008, p>0.05). Concerning DM, we had 56/78 in-group I while we had 22/38 in group-II, this difference was not significant (X=1.12, p>0.05). We had 56/78 dyslipidimic cases in-group I Versus 20/38 in-group II, this difference was not significant (X=2.1, p>0.05). There were 6 cases who developed cardiogenic shock during hospital stay after PPCI in group I versus 4 cases in Group II, this difference was not significant (X=0.13, p>0.05). Regarding the development of clinical heart failure during the 3 months of follow up, we had 34/78 cases in-group I versus No cases in group II, this difference was Highly significant (X=11.72, p<0.001). Concerning PWT, it was 5.28±2.31 hours in-group I while it was 5.04±1.69 hours in-group II, this difference is not significant (t=-0.58, p>0.05).

At admission, EF in-group I was 49.64±5.88% while it was 44.74±7.45% in group II, this represents a highly significant difference (t=-3.85, p<0.001). LVESVI was 36.59±5.29 ml^3/m^2 in-group I while it was 41.32±9.14 ml^3/m^2 in-group II, this is a highly significant difference as well (t=3.52, p<0.001). On contrary, there was no significant difference between both groups concerning the admission level of Galectin-3, it was 15.61±2.23 ng/ml in group I while it was 15.73±1.63ng/ml in group II (t=0.31, p>0.05).

After 3 months of follow up, there was a highly significant difference between both groups concerning EF, LVESVI and Galectin-3. EF decreased to 44.18±11.32 % in group I while it jumps to 52.89±7.32% in-group II (t=3.05, p<0.001). *LVESVI;* it increased to 44.77±11.84 ml^3/m^2 in-group I while in-group II it decreased to 33.26±6.27ml^3/m^2 (t=-3.96, p<0.001). Galactin-3, it was 21.67±6.48 ng/ml in-group I while it was 15.71±3.80 ng/mL in-group II (t=-3.70, p<0.001). There was no significant difference between both groups regarding the coronary artery that harbor the thrombus, as in group I it was as follow, LAD in 48 cases, RCA in 22 cases and LCX in 8 cases while in group II, LAD in 30 cases, RCA in 6 cases and LCX in only 2 case (X=1.76, p>0.05).

Correlation studies: (Table 3) concerning EF after 3 months of follow up, it has a *highly significant negative correlation* with the level of Galaectin-3 after 3 months of follow up (r=-0.82, p<0.001), (Figure 1) PWT (r=-0.77, p<0.001) and with the level of admission troponin (r=-0.54, p<0.001) while it has no significant correlation with age or level of admission Galactin-3. Concerning LVESVI after 3 months of follow up, it has a *highly significant positive correlation* with the level of Galaectin-3 after 3 months of follow up (r=0.89, p<0.001), (Figure 2) PWT (r=0.73, p<0.05) and with the level of admission troponin (r=0.56, p<0.001) while it has no significant correlation with age or level of admission Galactin-3. On performing regression analysis, (Table 4) it was clear that the level of galactin-3 after 3 months of follow up is a strong predictor of recovery of both LVESVI and EF after 3 months of follow up (t=8.13, p<0.001), (-5.28, p<0.001). In addition, PWT is another good predictor of recovery of EF after 3 months of follow up (t=-3.18, p<0.001).

Copyright: ©2022 Gouda et al.

Table 1 Comparative study between both groups concerning study variables

	Group I (78 cases)	Group II (38 cases)	(t)	(*p*)
Age (years)	53.67±9.96	58.89±9.36	2.71	>0.05
PWT (hours)*	5.28±2.31	5.04±1.69	-0.58	>0.05
EF at Admission (%)	49.64±5.88	44.74±7.45	-3.85	<0.001
EF after 3 months (%)	44.18±11.24	52.89±7.23	4.35	<0.001
LVESVI¥ at admission ($ml^3/m^{2)}$	36.59±5.29	41.32±9.14	3.52	<0.001
LVESVI¥ after 3 months ($ml^3/m^{2)}$	44.77±11.76	33.26±6.18	-5.65	<0.001
Galectin-3 at admission (ng/Ml)	15.61±2.23	15.73±1.63	0.31	>0.05
Galectin-3 after 3 months (ng/Ml)	21.67±6.43	15.71±3.75	-5.28	<0.001

* Chest pain to wiring time

¥ Left Ventricular end systolic volume index

Table 2 Comparative study between both groups concerning study categorical variables

	Group I (78 cases)	Group II (38 cases)	X	(*p*)
Gender	34 M 43.59% 44 F 56.41%	22 M 57.89% 16 F 42.11%	0.01	>0.05
Cardiogenic shock during in-hospital stay	6/78 (7.69%)	4/38 (10.53%)	0.13	>0.05
Clinical HF during 3 months of follow up	34/78 (43.59%)	0/38 (0%)	11.72	*<0.001*
Hypertension	36/78 (46.15%)	18/38 (47.37%)	0.008	>0.05
DM	56/78 (71.79%)	22/38 (57.89%)	1.12	>0.05
Dyslipidemia	56/78 (71.79%)	20/38 (52.63%)	2.1	>0.05
Target vessel harboring the thrombus	LAD 48 (61.54%) RCA 22 (28.21%) LCX 8 (10.26%)	LAD 30 (78.95%) RCA 6 (15.79%) LCX 2 (83.1%)	1.76	>0.05

Table 3 Correlation studies of different study variables versus remodeling parameters

Item	Variable	(r)	(*p*)
EF after 3 months of follow up	*Age*	0.07	>0.05
	*PWT**	-0.77	<0.001
	Admission Troponin	-0.54	<0.001
	Admission Galactin-3	0.24	>0.05
	Galactin-3 after 3 months	-0.82	<0.001
LVESVI after 3 months of follow up	*Age*	-0.14	>0.05
	*PWT**	0.73	<0.001
	Admission Troponin	0.56	<0.001
	Admission Galactin-3	-0.22	>0.05
	Galactin-3 after 3 months	0.89	<0.001

PWT*, Time from onset of chest pain to wiring of the thrombus

Table 4 Predictors of remodeling by regression analysis

Item	Variable	R	(t)	(*p*)
EF after 3 months of follow up	*Age*	0.87	-0.003	>0.05
	*PWT**		-3.81	<0.001
	Admission Troponin		-1.74	>0.05
	Admission Galactin-3		-0.41	>0.05
	Galactin-3 after 3 months		-5.28	<0.001
LVESVI after 3 months of follow up	*Age*	0.89	-0.59	>0.05
	*PWT**		1.82	>0.05
	Admission Troponin		-0.42	>0.05
	Admission Galactin-3		0.77	>0.05
	Galactin-3 after 3 months		8.13	<0.001

PWT*, Time from onset of chest pain to wiring of the thrombus

Citation: Gouda M, Nabil B, Gad MM. Galectin-3, a new proof of the better outcome of deferred stenting in STEMI patients with high thrombus burden. *J Cardiol Curr Res.* 2022;15(3):83–87. DOI: 10.15406/jccr.2022.15.00558

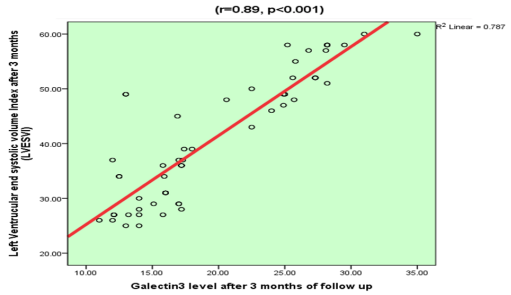

Figure 1: Correlation of Left Ventricular End Systolic Volume Index (LVESVI) after 3 months of primary PCI with Measured Level of Galactin-3 after 3 months of primary PCI

Figure 1 Correlation of Left Ventricular End Systolic Volume Index (LVESVI) after 3 months of primary PCI with Measured Level of Galactin-3 after 3 months of primary PCI.

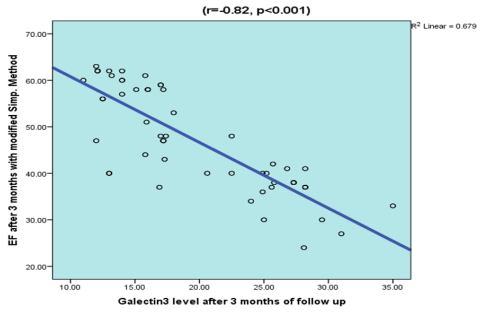

Figure 2: Correlation of Left Ventricular Ejection Fraction (EF) after 3 months of primary PCI with Measured Level of Galactin-3 after 3 months of primary PCI

Figure 2 Correlation of Left Ventricular Ejection Fraction (EF) after 3 months of primary PCI with Measured Level of Galactin-3 after 3 months of primary PCI.

Discussion

No doubt, saving as much as we can of myocardium after STEMI is the holey mission of all cardiology interventionists. It became an embarrassing situation in cath. Lab to all cardiologists when they face an artery with big thrombus burden in a STEMI case. Opening the artery, put a stent or just use the minimalist immediate mechanical intervention (MIMI), and deferred stenting "DS"? Some trials from 2014 up to 2016, using MRI, have shown a high myocardial salvage without microvascular obstruction with DS strategy.[4]

DS is associated with an improvement in angiographic, electrocardiographic, and even clinical outcomes. In PPCI, Intraprocedural flow reduction (slow or no flow) has been reported in many patients in previous studies, and has been regarded as a strong predictor of long-term mortality. Thus, residual thrombosis might best be left to dissolve during subsequent intensive antiplatelet therapy before stent implantation.[5] However, DS strategy still has many disadvantages, as extended hospital stay, increased costs, and risk of bleeding. If proved a better clinical outcome in STEMI cases with high thrombus burden, it may has the priority in such cases. However, we still need more proofs.[4]

According to our work, In the DS group, we had better LVEF, less LVESVI and No cases with heart failure during the 3 months of follow up after PPCI. This actually supports the use of DS strategy in cases of STEMI with high thrombus burden. This agreed with *Tsai et al.*, who concluded that the circulating level of Galectin-3 was higher in STEMI patients with advanced Killip score and severe congestive heart failure.[6] On contrary of our conclusion, *Kelbaek et al.* concluded that routine DS strategy could not be recommended. This is an apparent contradiction, as they add a recommendation if a STEMI case with high thrombus burden that could potentially benefit from this particular strategy.[5]

Galectin-3, proved to be a good marker of remodeling and myocardial fibrosis. It is even well known that if Galectin-3 is >25.9ng/mL, independent of complains, clinical findings, and other laboratory data, it can predicts the high-risk patient who is likely to get rapid heart failure progression, resulting in hospitalization and death. In addition, a doubling in Galectin-3 level over the course of 6 months, whatever the baseline value is, identifies a high-risk patient who deserves additional care management efforts and advanced therapies.[2]

In our study, base line Galectin-3 did not predict the outcome after 3 months of PPCI. There is an apparent contradiction with *Weir et al.*, who concluded that high baseline Galectin-3 is associated with lower LVEF at 24-weeks follow-up, in patients admitted with STEMI and with supra median baseline LVEF (i.e, >49.2%). However, they only included patients with LV dysfunction (LVEF<40%).Therefore, patients with relatively preserved LVEF were not part of their study, whereas the large majority in our work had relatively preserved LVEF and we did not select cases of LV dysfunction alone as a criterion for enrollment. Interestingly, in the study by *Weir et al.*, blood withdrawn after a mean period of 46 h after enrollment while our baseline sampling was done immediately at hospital admission [(7)]. Our results agreed with *Lisowska et al.*, who concluded that admission Galectin-3 concentration did not correlate with the EF value, it may be due the lack of HF symptoms at admission.[8]

This can be explained by the fact that remodeling and activation of macrophages start early after STEMI with subsequent early occurrence of remodeling at the cellular level before gross remodeling occurs. However, this is not enough to raise the level of Galectin-3, especially if the blood samples are withdrawn early after STEMI. This fact is additionally supported by the recent experimental data on animals, showed that Galectin-3 mRNA expression in the infarcted myocardium is increased after permanent left anterior descending coronary artery ligation and reaches its maximum level after 1 week.[9] This was supported by the strong correlation of LV systolic function recovery after 3 months of follow up with *PWT* and admission troponin level, as both of them reflect the rapidity of myocardial reperfusion. All of this emphasis the great value of early restoration of coronary blood flow as early as possible after STEMI and push for rethinking in the pharmaco-invasive method.

We found a significantly lower level of Galectin-3 at the third month of follow up after PPCI in the DS group that signify less remodeling, less fibrosis and was linked with better LVEF, lower LVESVI and less heart failure than the immediate stenting group. This is explained by better microvascular protection and better myocardial protection in DS group. This was in concordance with *van der Velde et al.,* who stated that in post-MI cases, high Galectin-3 was linked to better LVEF than patients with lower levels. This suggests the potential beneficial role of galectin-3 during the first initial period after STEMI, which may reflect an attempt to restore LV function during the process of inflammation and fibrogenesis. It is upregulated to form stiffer collagen in order to prevent LV dilatation and preserve LVEF.[10] Nevertheless, sustained high Galectin-3 levels remain an adverse signal and this was clear in our study as strong negative correlation of LVEF and strong positive correlation of LVESVI with the level of Galectin-3 after 3 months. Furthermore, the level of Galectin-3 after 3

months was the strongest predictor of recovery of LV systolic function with follow up.

Limitations: being a single center study represents the main limitation beside lack of access to cardiac MRI, which is known to be more accurate in calculation of LVEF and LVESVI.

Conclusion and recommendations

We recommend the use of DS strategy in STEMI cases with high thrombus burden (4-5). Lack of predictive power of admission level of Galectin-3 to outcomes after PPCI in these cases.

Acknowlegments

None.

Conflicts of Interset

None.

References

1. Belle L, Motreff P, Mangin L, et al. Comparison of immediate with delayed stenting using the minimalist immediate mechanical intervention approach in acute STEMI. The MIMI study. *Circ Cardiovasc Interv.* 2016;9:e003388.
2. McCullough PA, Olobatoke A, Vanhecke TE. Galectin-3: a novel blood test for the evaluation and management of patients with heart failure. *Rev Cardiovasc Med.* 2011;12(4):200–210.
3. Sianos G, Papafaklis MI, Daemen J, et al. Angiographic stent thrombosis after routine use of drug-eluting stents in STEMI: The importance of thrombus burden. *J Am Coll Cardiol.* 2007;50(7):573–583.
4. Carrick D, Oldroyd KG, McEntegart M, et al. A randomized trial of deferred stenting versus immediate stenting to prevent no- or slow-reflow in acute STEMI (DEFER-STEMI). *J Am Coll Cardiol.* 2014;63:2088–2098.
5. Kelbæk H, Dan Eik Høfsten, Lars Køber, et al. Deferred versus conventional stent implantation in patients with ST-segment elevation myocardial infarction (DANAMI 3-DEFER): an open-label, randomized controlled trial. *Lancet.* 2016;387(10034):2199–206.
6. Tsai TH, PH Sung, LT Chang, et al. Value and level of galectin-3 in acute myocardial infarction patients undergoing primary percutaneous coronary intervention. *J Atherosclerosis Thromb.* 2012;1073e1082.
7. Weir Robin AP, Colin J, Aengus Murphy, et al. Galectin-3 and Cardiac Function in Survivors of Acute Myocardial Infarction. *Circ Heart Fail.* 2013;112.000146.
8. Lisowska A, Małgorzata Knapp, Agnieszka Tyci_nska, 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. *J. Atherosclerosis.* 2016;246:309e317.
9. Meijers C, Rogier vander Velde A, Pascual-Figal DA, et al. Galectin-3 and post-myocardial infarction cardiac remodeling. *Eur J Pharmacol.* 2015.763(Pt A):115–121.
10. 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.