Association of galectin-3 and soluble ST2 with in-hospital and one-year outcomes in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

Authors: Agata Tymińska, Agnieszka Kapłon-Cieślicka, Krzysztof Ozierański, Monika Budnik, Anna Wancerz, Piotr Sypień, Michał Peller, Jakub Maksym, Paweł Balsam, Grzegorz Opolski, Krzysztof J. Filipiak

Article type: Original article

Received: September 7, 2019.

Accepted: October 23, 2019.

Published online: October 23, 2019.

ISSN: 1897-9483
Title: Association of galectin-3 and soluble ST2 with in-hospital and one-year outcomes in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention.

Running title: Gal-3 and sST2 in myocardial infarction

Agata Tymińska¹, Agnieszka Kapłon-Cieślicka¹, Krzysztof Ozierański¹, Monika Budnik¹, Anna Wancerz¹, Piotr Sypień¹, Michał Peller¹, Jakub Maksym¹, Paweł Balsam¹, Grzegorz Opolski¹, Krzysztof J Filipiak¹

¹ 1st Department of Cardiology, Medical University of Warsaw, Warsaw, Poland

Key words: biomarkers, heart failure, hospitalization, independent predictor, prognosis

Category of manuscript: Original Article (Clinical Investigation)

Conflict of interest: none declared

Correspondence to:
Agnieszka Kapłon-Cieślicka, MD, PhD
1st Department of Cardiology, Medical University of Warsaw,
ul. Banacha 1a, 02-097 Warszawa, Poland,
tel. +48 22 599 29 58,
email: agnieszka.kaplon@gmail.com
What’s new?

Despite modern reperfusion strategies, myocardial infarction leads to deleterious processes resulting in left ventricular remodelling (LVR) and heart failure (HF). Galectin-3 (Gal-3) and soluble ST-2 (sST2) are involved in LVR as a result of inflammation and fibrosis. There is an evidence of a prognostic value of both biomarkers in predicting outcomes in HF patients. However, studies evaluating the role of Gal-3 and sST2 in patients after ST-segment elevation myocardial infarction (STEMI) are insufficient. The study aimed to investigate the association of Gal-3 and sST2 with prognosis in patients with STEMI treated with primary percutaneous coronary intervention. We also established new cut-offs for Gal-3 and sST2 (based on Youden index) for prediction of the primary endpoint occurrence. The results of the study suggest that both biomarkers may play an important role in cardiovascular risk stratification after STEMI, although Gal-3 may be considered preferable.

Abstract

**Introduction:** Galectin-3 (Gal-3) and soluble ST-2 (sST2) have known prognostic value in already diagnosed heart failure (HF). **Objectives:** To investigate the association of Gal-3 and sST2 with prognosis in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (pPCI). **Patients and Methods:** The analysis was based on data collected in a prospective observational BIOSTRAT (Biomarkers for Risk Stratification After STEMI; NCT03735719) study. Analysis included 117 patients with first-time STEMI treated with pPCI. Serum for Gal-3 and sST2 was sampled 72-96 hours after STEMI admission. The patients were followed for the primary endpoint (cardiovascular (CV) death or HF hospitalization at one year). **Results:** Both biomarkers correlated significantly with NT-proBNP; Gal-3 correlated with older age. Data on the primary endpoint were available for 104 patients (89%). At one-year observation, 9 patients...
(8.7%) reached the primary endpoint. In univariate Cox proportional hazards regression analysis, both Gal-3 and sST2 as continuous variables, as well as their newly-established cut-offs (≥9.57 ng/mL for Gal-3 and ≥45.99 ng/mL for sST2, based on Youden index) were predictors of the primary endpoint, and of HF hospitalizations alone. Gal-3 also predicted CV death. After adjustment for age and NT-proBNP, Gal-3 and sST2 remained predictors of the primary endpoint in multivariate models. **Conclusions:** In patients with first-time STEMI treated with pPCI, baseline Gal-3 and sST2 predicted the composite of CV death and HF hospitalization at one year. Both biomarkers may play an important role in CV risk stratification after STEMI, although Gal-3 may be considered preferable.

**Introduction**

Despite modern reperfusion strategies and evidence-based pharmacotherapy, acute myocardial infarction (AMI) causes pathological left ventricular remodelling (LVR), development of heart failure (HF) and therefore leads to adverse cardiovascular (CV) outcomes [1-4]. AMI represents the major cause of HF [1, 5-7]. According to a Polish nationwide database of acute coronary syndromes (AMI-PL database), HF is one of the most frequent causes of recurrent hospitalization in patients after AMI in one-year follow-up [8], indicating a need for an intensification of secondary prevention programmes (including cardiac rehabilitation, smoking cessation and improvement of risk stratification) [3, 4, 9]. Therefore, it is important to explore new sensitive and specific biomarkers that could help identify patients at risk of developing HF and adverse CV outcomes after AMI.

Galectin-3 (Gal-3) and soluble interleukin-1 receptor-like 1 (sST2) are promising biomarkers involved in LVR, resulting from inflammatory processes and fibrosis [10-14]. There is evidence for a high prognostic value of both biomarkers in predicting outcomes in
patients with chronic and acute HF [15]. Biomarkers of myocardial fibrosis (including sST2 and Gal-3) were recommended as useful tools for additional risk stratification in the American guidelines for the management of HF [16].

However, studies evaluating the role of Gal-3 and sST2 and their relationship with adverse outcomes in patients after AMI are insufficient. Therefore, we aimed to evaluate the association of Gal-3 and sST2 in patients with first-time ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) with in-hospital and one-year CV outcomes.

**Patients and Methods**

**Study population**

The analysis was based on data collected in a prospective observational BIOSTRAT (Biomarkers for Risk Stratification After STEMI; NCT03735719) study. The BIOSTRAT study included 117 consecutive Caucasian subjects with first-time STEMI treated with primary PCI in the 1st Chair and Department of Cardiology, Medical University of Warsaw from October 2014 to April 2017. STEMI was diagnosed in accordance with the applicable guidelines [17]. Main inclusion criteria were age ≥18 years and first-time STEMI treated with primary PCI. Main exclusion criteria were previous AMI, pre-existing HF (history of LV ejection fraction (LVEF) <50% or diagnosed HF with preserved LVEF), severe renal dysfunction (plasma creatinine level >220 mmol/L (≈2.5 mg/dL), and/or creatinine clearance <30 mL/min), severe liver disease, chronic inflammatory disease, current neoplastic disease, and life expectancy <1 year.

Informed written consent was obtained from each study participant. The trial protocol complied with the Declaration of Helsinki and was approved by the local ethics committee of the Medical University of Warsaw.
Baseline tests and measurements

Routine laboratory parameters, including complete blood count, glycemia, lipid profile, electrolytes, serum creatinine, and biomarkers such as cardiac troponin I (cTnI), creatine kinase myocardial band (CK-MB), high-sensitive C-reactive protein (hs-CRP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were measured using standard methods in the hospital laboratory. N-terminal B-type natriuretic peptide (NT-proBNP) concentration was measured using the Roche Elecsys® 1010 analyzer (Roche Diagnostics, Mannheim, Germany). High-sensitivity C-reactive protein (hs-CRP) concentration was assessed using Cobas Integra 800 (Roche Diagnostics).

The highest concentrations of cTnI, NT-proBNP and hs-CRP were subsequently included in the analyses.

Electrocardiogram, transthoracic echocardiogram and clinical examination were performed in each patient during index hospitalization. Demographic data, details on previous and current pharmacotherapy, clinical and angiographic characteristics, and medical history were also prospectively gathered.

Gal-3 and sST2 measurements

Additionally, blood samples were collected from all recruited subjects for further measurements of serum concentrations of Gal-3 and sST2. To avoid the potential impact of PCI on biomarker concentration, we sampled blood after 72-96 hours after hospital admission, as per previous studies [18, 19]. Serum was prepared from blood samples by allowing the blood to clot for 60 min, followed by centrifugation at 3500 rpm for 15 min. Serum samples were then stored at -80 °C. Measurements were performed after all patients had entered the study. Serum concentrations of Gal-3 were measured using Human Galectin-3
Quantikine ELISA Kit® (BIOKOM, Janki, Poland), and plasma sST2 - using Presage ST2 Assay (Genloxa Sp. z o. o., Puck, Poland).

**Study endpoints**

Patients were followed for 12 months. The primary endpoint was combined of CV death or hospitalization for HF during one-year follow-up. CV death was defined as deaths related to AMI, HF, sudden cardiac death or stroke. Hospitalization for HF was considered as hospitalization with a primary diagnosis of HF supported by evidence of clinical signs of HF (rales, peripheral edema), pulmonary congestion on a chest radiograph, or a need for the use of intravenous diuretics.

Secondary endpoints concerned in-hospital outcomes including 1) total length of index hospitalization, 2) length of stay in intensive cardiac care unit during index hospitalization, 3) in-hospital death; and events that occurred in one-year follow-up including 4) CV death, 5) hospitalization for HF, and 6) MI.

**Statistical analysis**

For a between-group comparison, we used a Fisher exact test and a Mann–Whitney test for categorical and continuous variables, respectively. Categorical data were presented as numbers and percentages of patients. Normally distributed continuous data were expressed as mean values with a standard deviation, while non-normally distributed continuous data were presented as median with an interquartile range. Pearson’s and Spearman’s correlation coefficients were used for parametric and nonparametric variables, respectively. The Cox proportional hazards regression model was performed to identify predictors of the primary endpoint. Receiver operating characteristic (ROC) curves were plotted for baseline Gal-3 and sST2 in relation to the primary endpoint. In addition, Youden's J statistic was performed to
determine the optimal biomarker cut-off point for the prediction of the primary endpoint. A \( P \)-value of less than 0.05 was considered significant. All tests were two-tailed. SPSS software, version 22 (IBM SPSS Statistics 22, New York, United States) was used for analysis.

Results

Baseline characteristics

A total of 117 consecutive first-time STEMI patients were included to the study. The study group’s median age was 61.0 years (interquartile range [IQR]: 50.5 to 67.0 years) and 70% were men. Median baseline LVEF was 48% (IQR: 41.0-53.0). Median Gal-3 and sST2 concentrations were: 7.1 ng/mL (IQR: 5.6-8.8) and 23.4 ng/mL (IQR: 18.0-32.0), respectively.

Correlation analysis with baseline parameters

We also performed correlation analysis of baseline Gal-3 and sST2 concentrations with clinical parameters (table 1). A significant correlation was found between Gal-3 and sST2 levels. Both, Gal-3 and sST2 correlated positively with stay in intensive cardiac care unit, NT-proBNP and hs-CRP and inversely with glomerular filtration rate. Gal-3 correlated positively with age, Killip class, as well as TIMI (The Thrombolysis in Myocardial Infarction) and GRACE (The Global Registry of Acute Coronary Events) scores. sST2 correlated negatively with sodium level on admission and inversely with baseline and final TIMI Coronary Grade Flow. There was non-significant correlation between sT2 and age.

One-year follow-up

Data on survival was available for all patients (5 out of 117 patients (4.3%) died). Thirteen patients were lost to follow-up in terms of hospitalization for HF leaving 104
patients (89%) for the composite primary endpoint analyses at one-year. During one-year follow-up 9 patients (8.7%) reached the primary endpoint (three died due to CV causes and 6 were hospitalized for HF). Among CV causes of death, HF-related death occurred in two patients and AMI-related death in one patient (including one patient who died during index hospitalization after recruitment).

Patients who experienced the primary endpoint during follow-up had higher levels of baseline Gal-3 and sST2 (for sST2 non-significant). Baseline characteristics of patients who reached and who did not reach the primary endpoint at one year are presented in Table S1 (supplementary material online).

**Comparison of baseline characteristics, laboratory findings, clinical presentations, in-hospital and one-year outcomes in patients with high and low Gal-3 and sST2 levels**

ROC analysis revealed the area under the curve (AUC) for Gal-3 and sST2 (for prediction of the primary endpoint) was 0.85 and 0.64, respectively (Figure 1). Gal-3 concentration of ≥9.57 ng/mL had a sensitivity of 41%, a specificity of 91%, a negative predictive value of 92%, and a positive predictive value of 36% for prediction of the primary endpoint at follow-up (Youden's index). sST2 concentration of ≥45.99 ng/mL had a sensitivity of 44%, a specificity of 97%, a negative predictive value of 95%, and a positive predictive value of 57% for prediction of the primary endpoint at follow-up (Youden's index).

Baseline characteristics, laboratory findings, clinical presentations, in-hospital and one-year outcomes of patients with high and low Gal-3 and sST2 levels depending on established cut-offs are presented in Tables 2 and 3. Twenty-four patients (20.5%) had baseline Gal-3 levels equal to or above the upper limit of the established cut-off value of 9.57 ng/mL. Eight patients (6.8%) had baseline sST2 levels equal to or above the upper limit of the
established cut-off value of 45.99 ng/mL. Higher concentrations of both biomarkers (above the cut-offs) were associated with a longer hospital stay (including a longer stay in intensive cardiac care unit) and more frequent occurrence of the primary endpoint. Patients with a Gal-3 level above the cut-off also experienced CV death more frequently.

**Predictors of the primary endpoint**

In the univariate Cox proportional hazards regression analysis, both baseline Gal-3 and sST2 (as continuous variables, as well as their newly-established cut-offs) were predictors of the primary endpoint (CV death or HF hospitalization), and of HF hospitalizations (Table 4). Furthermore, in contrast to sST2, Gal-3 predicted CV death.

Gal-3 and sST2 remained significant predictors of the primary endpoint even after adjustment for age and NT-proBNP in multivariate analyses (Figure 2, Table 5).

**Discussion**

In our study, concentrations of both Gal-3 and sST2 were higher in those with worse clinical presentation at baseline. Both Gal-3 and sST2 were associated with unfavorable in-hospital outcomes and were independent predictors of CV death or hospitalization for HF in one-year follow-up (when regarded as continuous variables). However, if the newly-established cut-offs of both biomarkers were included in one multivariate model (together with age), only Gal-3 remained an independent predictor of the primary endpoint. Moreover, Gal-3 also predicted CV death alone. Furthermore, there was no difference in sST2 concentration between those who did and did not reach the primary endpoint during follow-up. Therefore, Gal-3 might be preferable to ST2 in risk stratification after STEMI.

In our study there was a small number of events, but the results are in line with recent study assessing the same composite endpoint in patients with a first anterior STEMI treated with pPCI. In this study 20 out of 103 patients (19.4%) died or were admitted for HF within 6
months follow-up. Gal-3, measured within 48 h after STEMI, significantly predicted the composite endpoint after adjustment for age, gender, renal and ventricular function, troponin and NT-proBNP [20].

Gal-3 plays an important role in various biological processes, but the most acknowledged role of Gal-3 is participation in fibrosis [10, 21, 22]. Gal-3 is produced by activated macrophages that stimulate inflammation and proliferation of myofibroblasts and collagen deposition [10]. In experimental data, Sanchez-Mas et al. observed that Gal-3 increases in myocardium after AMI with the maximum concentration achieved in the infarcted area during the first week, with a gradual decrease in the following weeks. It appears that the increase in concentration of Gal-3 in the early phase after myocardial infarction contributes to the activation of repair functions in the damaged zone in order to maintain the geometry and function of the heart [23]. However, in longer perspective, chronic activation leads to tissue fibrosis and accelerates adverse LVR [23].

The ST2 molecule is a soluble glycoprotein belonging to the interleukin-1 receptor family, and is secreted by inflammatory cells, cardiomyocytes and endothelium [11]. ST2 has two clinically relevant isoforms - transmembrane (ST2L, ST2 ligand) and soluble (sST2, soluble ST2) circulating in the bloodstream [11, 24]. The balance between these two forms of ST2 guarantees an appropriate biological effect. Elevated sST2 triggers myocardial fibrosis [11, 24]. In an experimental study, sST2 concentrations increased steadily after AMI with maximum expression at first day [11].

It is also known that Gal-3 and IL-33 / ST2 pathways are involved in the pathogenesis of atherosclerosis, in which the inflammatory substrate is one of the main causes of instability of atherosclerotic plaques [24, 25]. Tsai et al. showed that Gal-3 levels were significantly higher in AMI patients than in healthy controls [26]. In our study, we observed lower median Gal-3 concentrations (7.1 ng/mL) in patients following first-time AMI than was reported
previously by Szadkowska et al. and van der Velde et al. (13.0 and 13.4 ng/mL, respectively) [27, 28]. However, these differences can be explained by more restrictive exclusion criteria related to potential fibrosis processes (i.e. exclusion of patients with neoplasms, advanced chronic kidney disease, previous HF) in our study. We also only enrolled patients with STEMI, excluding patients with non-STEMI. In addition, it has also previously been shown that elevated Gal-3 and sST2 concentrations were observed in patients with hypertension, diabetes, prior AMI, and prior HF, factors which may bias the biomarkers’ measurements between studies [19, 29].

The first studies on Gal-3 and sST2 were in the field of HF and showed that higher levels of circulating Gal-3 and sST2 were associated with worse prognosis in those patients [15, 29, 30]. The American Heart Association recommendations have even considered Gal-3 and sST2 to be valuable prognostic markers in acute and chronic HF (class IIb recommendations, level of evidence B) [16]. The FDA approved threshold values of 17.8 ng/mL for Gal-3 and 35.0 ng/mL for sST2 for additional risk stratification in patients with chronic and acute HF [28]. However, there is still a need to assess the clinical utility and specific cut-offs of both biomarkers to help clinicians conduct better risk stratification in patients with AMI but without previous HF. Only few studies have described the impact of Gal-3 and sST2 on outcomes after AMI.

Sub-analysis of the PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) trial showed that Gal-3 concentrations above median value of 16.7 μg/L, measured within 7 days after acute coronary syndrome (100 patients after AMI or unstable angina), were associated with a significantly higher risk of HF development in a two-year observation [19]. In our study, the cut-off Gal-3 level for the primary endpoint occurrence was equal to or above 9.57 ng/mL. This Gal-3 threshold was associated with a worse clinical condition during index hospitalization, as well
as a higher rate of unfavorable outcomes during index hospitalization and follow-up.

Similarly, the study performed by Tsai et al. (196 patients with first-time STEMI) revealed that a Gal-3 level equal to or above 7.67 ng/mL was the most powerful predictor of death and development of HF in a 30-day post-infarction period [26]. Moreover, this association was observed regardless of the severity of coronary artery lesions, LVEF and serum creatinine [26]. Of note, in our study patients with higher Gal-3 concentrations had higher risk in GRACE and TIMI scores, which identify high-risk patients after MI.

In our study median sST2 concentration in the study group was 23.4 ng/mL, while in Jenkins et al. study (1401 patients after AMI) the median sST2 value was 48.7 ng/mL. However, their study relied on heterogeneous diagnoses - 79% of patients had non-STEMI. Increased concentrations of sST2 were associated with an increased risk of death and HF development during 5 years of follow-up, independently of other prognostic factors [29]. Liu et al. showed that sST2 concentrations above 58.7 ng/mL have highest specificity in predicting either MACEs (defined as the composite of all-cause death, HF, and non-fatal AMI) or mortality at one-year after STEMI [31]. In our study, the cut-off sST2 value of 45.99 ng/mL identified patients at high risk of the primary endpoint.

Another analysis based on BIOSTRAT study assessed the association of Gal-3 and sST2 and changes in their concentrations after one year with the development of HF which showed that baseline Gal-3 and sST2 concentrations have higher clinical value than measurements obtained after one year [32].

In the CORONA study, Gal-3 was not correlated with worse prognosis after adjusting for NT-proBNP in older patients with ischemic chronic HF, hence Gal-3 may have limited the application of risk stratification in older patients [33]. However, our study showed that this does not apply to patients after STEMI. Gal-3 (but not sST2) correlated with age but both Gal-3 and sST2 were independent predictors of the primary endpoint even after adjusting for
In our study, there was no association between sST2 and Gal-3 concentrations and maximum troponin I. An explanation for this is that these biomarkers are involved in distinct pathophysiological pathways than that which are already known. AMI provokes an inflammatory response with the migration of a multitude of cells and regulators into the infarcted and non-infarcted areas. This process initiates reparative changes in the early phase after AMI [2]. This could be the reason of higher values of hs-CRP in both groups of sST-2 and Gal-3 upper cut-offs values. However, chronic activation of these processes leads to tissue fibrosis, adverse LVR and development of HF. Szadkowska et al. found that elevated Gal-3 (>16 ng/mL) concentrations during hospitalization in patients after AMI were associated with a higher risk of developing HF and atrial fibrillation [27]. In our study, patients with higher levels of Gal-3 and sST2 were more likely to have a higher Killip class on admission, and more frequently required diuretics intravenously during hospitalization and orally at discharge. Consequently, elevated Gal-3 and sST2 concentrations were associated with increased risk of combined endpoint – CV death and HF hospitalization, as well as the risk of HF hospitalization itself.

Therefore, it may be concluded that increased levels of Gal-3 and sST2 after AMI reflect myocardial damage and may help in the early identification of patients at higher risk of HF development. It may have important implications for post-discharge follow-up and stresses the need for therapies which impact adverse cardiac remodeling, such as angiotensin-converting enzyme inhibitors, aldosterone receptor blockers or mineralocorticoid receptor antagonists. There are several studies showing the potential advantageous influence of renin-angiotensin-aldosterone antagonists, as well as genetic therapies on the reduction of biomarker levels [34-38]. Other mediators of inflammatory processes (i.e. leukotrienes) have recently been intensively studied for their role in coronary artery disease. Further studies will
show if novel anti-inflammatory strategies added to conventional therapy will reduce cardiovascular risk [39].

Limitations

The main limitations of our study relate to the small sample size and relatively short follow-up which translated into a small number of events. Additionally, 13 patients (11.1% of the 117 patients) were lost to follow-up in terms of hospitalization for HF. Therefore, in order to maintain an adequate events per predictor variable (EPV) value, we were not able to include more potentially significant variables in the Cox proportional hazards regression model [28]. Moreover, a certain proportion of data (including NT-proBNP concentrations) for some of the patients was missing (as indicated in tables). Still, given the correlation of both Gal-3 and sST2 with NT-proBNP, as well as the fact that NT-proBNP concentration predicted the primary endpoint, we decided it was important to include NT-proBNP in our multivariate models. However, we also performed a separate multivariate analysis including age and both of the studied biomarkers (Gal-3 and sST2), but not NT-proBNP. Gal-3 and sST2 remained significant predictors of the primary endpoint in all those models.

Further studies with longer follow-up are still needed to determine the predictive value and clinical utility of serum levels of sST2 and Gal-3 in AMI patients.

Conclusion

In patients with first-time STEMI treated with primary PCI, Gal-3 and sST2 predicted CV death or hospitalization for HF at one year. Concentrations of both biomarkers above the established cut-offs (≥9.57 ng/mL for Gal-3 and ≥45.99 ng/mL for ST-2) were associated with worse clinical presentation at baseline, as well as adverse in-hospital and one-year
outcomes. Assessment of these two biomarkers of inflammation and fibrosis may play an important role in CV risk stratification after AMI, however, Gal-3 may be considered more preferable option.

**Contribution statement:**

All authors made substantial contributions to the concept and design of the study. AT, AKC, KO, MB, AW, PS, JM researched data, conducted data interpretation. AT, KO and MP performed statistical analysis. AT, KO and AKC wrote manuscript. All authors reviewed the manuscript and approved its final version.

**Acknowledgements:**

The BIOSTRAT study is supported by two Grants from Medical University of Warsaw. AT received 1WR/NM2/14 grant and AW received 1WR/NM4/16.

**Funding**

The source of funding of the BIOSTRAT study were two Grants from Medical University of Warsaw (grant number: 1WR/NM2/14 and 1WR/NM4/16).

**Ethics committee:**

The decision number of the ethics committee: KB/97/2014.

**References:**

1. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology
2. Sutton MG, Sharpe N. Left ventricular remodeling after myocardial infarction: pathophysiology and therapy. Circulation. 2000; 101: 2981-2988.

3. Trzeciak P, Gierlotka M, Poloński L, Gąsior M. Treatment and outcomes of patients under 40 years of age with acute myocardial infarction in Poland in 2009-2013: an analysis from the PL-ACS registry. Pol Arch Intern Med. 2017; 127: 666-673.

4. Karwowski J, Gierlotka M, Gąsior M, et al. Relationship between infarct artery location, acute total coronary occlusion, and mortality in STEMI and NSTEMI patients. Pol Arch Intern Med. 2017; 127: 401-411.

5. Kapłon-Cieślicka A, Tymińska A, Peller M, et al. Diagnosis, Clinical Course, and 1-Year Outcome in Patients Hospitalized for Heart Failure With Preserved Ejection Fraction (from the Polish Cohort of the European Society of Cardiology Heart Failure Long-Term Registry). Am J Cardiol. 2016; 118: 535-542.

6. Tymińska A, Kapłon-Cieślicka A, Ozierański K, et al. Anemia at Hospital Admission and Its Relation to Outcomes in Patients With Heart Failure (from the Polish Cohort of 2 European Society of Cardiology Heart Failure Registries). Am J Cardiol. 2017; 119: 2021-2029.

7. Balsam P, Ozierański K, Kapłon-Cieślicka A, et al. Differences in clinical characteristics and 1-year outcomes of hospitalized patients with heart failure in ESC-HF Pilot and ESC-HF-LT registries. Pol Arch Intern Med. 2019; 129: 106-116.

8. Gierlotka M, Zdrojewski T, Wojtyniak B, et al. Incidence, treatment, in-hospital mortality and one-year outcomes of acute myocardial infarction in Poland in 2009-2012-nationwide AMI-PL database. Kardiol Pol. 2015; 73: 142-158.
9. Ozierański K, Witkowska A, Wojtyniak B, et al. Smoking ban in public places and myocardial infarction hospitalizations in a European country with high cardiovascular risk: insights from the Polish nationwide AMI-PL database. Pol Arch Intern Med. 2019; 129: 386-391.

10. Meijers WC, van der Velde AR, Pascual-Figal DA, Boer RA. Galectin-3 and post-myocardial infarction cardiac remodeling. Eur. J. Pharmacol. 2015; 763: 115–121.

11. Weinberg EO, Shimpo M, De Keulenaer GW, et al. Expression and regulation of ST2, an interleukin-1 receptor family member, in cardiomyocytes and myocardial infarction. Circulation. 2002; 106: 2961-2966.

12. Tomaniak M, Sygitowicz G, Filipiak KJ, et al. Dysregulations of miRNAs and galectin-3 may underlie left ventricular dilatation in patients with systolic heart failure. Kardiol Pol. 2018; 76: 1012-1014.

13. Sygitowicz G, Tomaniak M, Filipiak KJ, et al. Galectin-3 in Patients with Acute Heart Failure: Preliminary Report on First Polish Experience. Adv Clin Exp Med. 2016; 25: 617-623.

14. Wiśniowska-Śmiałek S, Dziewięcka E, Holcman K, et al. Kinetics of selected serum markers of fibrosis in patients with dilated cardiomyopathy and different grades of diastolic dysfunction of the left ventricle. Cardiol J. 2018 Nov 28. [Epub ahead of print]

15. Bayes-Genis A, de Antonio M, Vila J, et al. Head-to-head comparison of 2 myocardial fibrosis biomarkers for long-term heart failure risk stratification: ST2 versus galectin-3. J Am Coll Cardiol. 2014; 63: 158-166.

16. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical
17. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012; 33: 2569-2619.

18. Di Tano G, Caretta 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.

19. Grandin EW, Jarolim P, Murphy SA, et al. Galectin-3 and the development of heart failure after acute coronary syndrome: pilot experience from PROVE IT-TIMI 22. Clin Chem. 2012; 58: 267-273.

20. 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.

21. Yang RY, Rabinovich GA, Liu FT. Galectins: structure, function and therapeutic potential. Expert Rev Mol Med. 2008; 10: e17.

22. Ho JE, Liu C, Lyass A, et al. Galectin-3, a marker of cardiac fibrosis, predicts incident heart failure in the community. J Am Coll Cardiol. 2012; 60: 1249-1256.

23. Sanchez-Mas J, Lax A, Asensio-Lopez MC, et al. Galectin-3 expression in cardiac remodeling after myocardial infarction. Int. J. Cardiol. 2014; 172: e98–e101.

24. Kakkar R, Lee RT. The IL-33/ST2 pathway: Therapeutic target and novel biomarker. Nat. Rev. Drug Discov. 2008; 7: 827–840.

25. Papaspyridonos M, McNeill E, de Bono JP, 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: 433-440.
26. Tsai TH, Sung PH, Chang LT, et al. Value and level of galectin-3 in acute myocardial infarction patients undergoing primary percutaneous coronary intervention. J Atheroscler Thromb. 2012; 19: 1073-1082.

27. Szadkowska I, Wlazeł 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: 577-582.

28. 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.

29. Jenkins WS, Roger VL, Jaffe AS, et al. Prognostic value of soluble ST2 after myocardial infarction: A community perspective. Am J Med 2017; 130: 1112.e9-1112.e15.

30. van der Velde AR, Gulstad L, Ueland T, et al. Prognostic value of changes in galectin-3 levels over time in patients with heart failure: data from CORONA and COACH. Circ Heart Fail. 2013; 6: 219-226.

31. Liu X, Hu Y, Huang W, et al. Soluble ST2 for Prediction of Clinical Outcomes in Patients with ST-Segment Elevation Myocardial Infarction Receiving Primary PCI. Int Heart J. 2019; 60: 19-26.

32. Tymińska A, Kapłon-Cieślicka A, Ozierański K, et al. Association of Galectin-3 and Soluble ST2, and Their Changes, with Echocardiographic Parameters and Development of Heart Failure after ST-Segment Elevation Myocardial Infarction. Disease Markers 2019 Oct 10

33. Gulstad L, Ueland T, Kjekshus J, et al. The predictive value of galectin-3 for mortality and cardiovascular events in the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA). Am Heart J. 2012; 164: 878-883.
34. Yu L, Ruifrok WP, Meissner M, et al. Genetic and Pharmacological Inhibition of Galectin-3 Prevents Cardiac Remodeling by Interfering With Myocardial Fibrogenesis. Circ Heart Fail. 2013; 6: 107-117.

35. Anand IS, Rector TS, Kuskowski M, et al. Baseline and serial measurements of galectin-3 in patients with heart failure: relationship to prognosis and effect of treatment with valsartan in the Val-HeFT. Eur J Heart Fail. 2013; 15: 511-518.

36. Lax A, Sanchez-Mas J, Asensio-Lopez MC, et al. Mineralocorticoid receptor antagonists modulate galectin-3 and interleukin-33/ST2 signaling in left ventricular systolic dysfunction after acute myocardial infarction. JACC Heart Fail. 2015; 3: 50-58.

37. Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and Cox regression. Am J Epidemiol 2007; 165: 710-718.

38. Xia J, Qu Y, Yin C, Xu D. Preliminary study of beta-blocker therapy on modulation of interleukin-33/ST2 signaling during ventricular remodeling after acute myocardial infarction. Cardiol J. 2017; 24: 188-194.

39. Stodółkiewicz E, Rewerska B, Rzeszutko M, et al. Leukotriene biosynthesis in coronary artery disease. Results of the Leukotrienes and Thromboxane In Myocardial Infarction (LTIMI) study. Pol Arch Intern Med. 2018; 128: 43-51.
Figure 1A. Receiver operating characteristic (ROC) curve for Gal-3 concentration in relation to the primary endpoint.

Gal-3 – galectin-3
Figure 1B. Receiver operating characteristic (ROC) curve for sST2 concentration in relation to the primary endpoint.

sST2 - soluble interleukin-1 receptor-like 1
Figure 2 A, B and C. Forest plot of multivariate analyses of predictors of the primary endpoint. CI - confidence interval, Gal-3 – galectin-3, HR - hazard ratio, NT-proBNP - N-terminal pro-brain natriuretic peptide, sST2 - soluble interleukin-1 receptor-like 1, yrs - years.
Table 1. Clinical correlates of Gal-3 and sST2 in patients with ST-segment elevation myocardial infarction treated with primary coronary intervention.

| Variable                          | Baseline Gal-3 | Baseline sST2 |
|-----------------------------------|----------------|---------------|
|                                   | Rho | p-value | Rho | p-value |
| **Baseline characteristics**      |     |         |     |         |
| Age, years                        | 0.38 | <0.001 | 0.09 | 0.32 |
| BMI, kg/m²                        | 0.14 | 0.15 | 0.01 | 0.93 |
| **Clinical status, laboratory and angiographic findings on admission** |     |         |     |         |
| Killip class                      | 0.20 | **0.03** | 0.10 | 0.27 |
| Hemoglobin, g/dl                  | -0.26 | **0.004** | -0.14 | 0.12 |
| hs-CRP, mg/dL                     | 0.18 | 0.05 | 0.19 | **0.047** |
| Troponin I, ng/mL                 | -0.45 | 0.64 | 0.03 | 0.74 |
|                  | NT-proBNP, pg/mL | 0.36 | 0.001 | 0.38 | <0.001 |
|------------------|------------------|------|-------|------|--------|
| Gal-3, ng/mL     |                  |      |       | 0.48 | 0.04   |
| sST2, ng/mL      | 0.48             | 0.04 |       |      |        |
| eGFR, ml/min/1.73m² | -0.30           | 0.001| -0.11 | 0.23 |
| Serum sodium, mmol/L | -0.09           | 0.36 | -0.20 | 0.03 |
| Total cholesterol, mg/dL | -0.23           | 0.01 | -0.24 | 0.01 |
| LDL, mg/dL       | -0.12            | 0.07 | -0.19 | 0.059|
| TIMI score       | 0.34             | <0.001| 0.12  | 0.19  |
| GRACE score      | 0.38             | <0.001| 0.10  | 0.26  |
| Baseline TIMI Grade Flow | 0.10           | 0.31 | -0.16 | 0.04  |
| Final TIMI Grade Flow | -0.05           | 0.63 | -0.16 | 0.045 |

**Echocardiographic and laboratory findings at discharge**

|                  |                  |       |       |       |        |
|------------------|------------------|------|-------|------|--------|
| Hemoglobin, g/dl | -0.19            | 0.05 | -0.03 | 0.78 |
| Serum creatinine, mg/dl | 0.13           | 0.18 | 0.19  | 0.054|
| eGFR, mL/min/1.73m² | -0.36           | <0.001| -0.24 | 0.01  |

**Outcomes**

|                  |                  |       |       |       |        |
|------------------|------------------|------|-------|------|--------|
| Hospitalization length, days | 0.18           | 0.055| 0.35  | <0.001|
| Time in ICCU, days     | 0.35            | <0.001| 0.45  | <0.001|

BMI – body mass index, eGFR – estimated glomerular filtration rate, Gal-3 – galectin-3, GRACE - The Global Registry of Acute Coronary Events, hs-CRP – high-sensitive C-reactive protein, ICCU – intensive cardiac care unit, LDL - low density lipoprotein, NT-proBNP - N-terminal pro-brain natriuretic peptide, sST2- soluble interleukin-1 receptor-like 1, TIMI - The Thrombolysis in Myocardial Infarction
Table 2. Baseline characteristics and clinical course of index hospitalization of patients with ST-segment elevation myocardial infarction treated with primary coronary intervention with reference to baseline Gal-3 and sST2 cut-offs.

| Variable                  | n=117 | sST2 < 45.99 ng/mL (n=109) | sST2 ≥ 45.99 ng/mL (n=8) | p-value | Gal-3 < 9.57 ng/mL (n=93) | Gal-3 ≥ 9.57 ng/mL (n=24) | p-value |
|---------------------------|-------|---------------------------|--------------------------|---------|--------------------------|---------------------------|---------|
| Baseline characteristics  |       |                           |                           |         |                           |                           |         |
| Age, years                |       | 60.0 (50.5-67.0)          | 69.5 (51.0-78.8)          | 0.19    | 59.0 (50.0-64.5)          | 66.5 (55.3-78.8)          | 0.01    |
| Male gender               |       | 70.6%; 77/109             | 62.5%; 5/8               | 0.69    | 75.3%; 70/93             | 50.0%; 12/24              | 0.02    |
| BMI, kg/m²                |       | 28.4 (24.6-30.5); n=98    | 33.3 (29.3-34.7); n=7    | 0.07    | 28.1 (24.4-30.4); n=87   | 30.0 (28.6-33.7); n=18    | 0.02    |
| Moderate valve disease    |       | 3.7%; 4/109               | 12.5%; 1/8               | 0.30    | 3.2%; 3/93               | 8.3%; 2/24                | 0.27    |
| Hypertension              |       | 59.6%; 65/109             | 75.0%; 6/8               | 0.48    | 59.1%; 55/93             | 66.7%; 16/24              | 0.64    |
| Condition                        | Incidence | Comparison | p-Value |
|---------------------------------|-----------|------------|---------|
| Atrial fibrillation             | 2.8%; 3/109 | 25.0%; 2/8 | 0.04    |
| Diabetes                        | 19.3%; 21/109 | 25.0%; 2/8 | 0.66    |
| Chronic kidney disease          | 13.8%; 15/109 | 62.5%; 5/8 | 0.04    |
| COPD                            | 3.7%; 4/109  | 37.5%; 3/8 | 0.01    |
| Prior stroke or TIA             | 3.7%; 4/109  | 25.0%; 2/8 | 0.054   |
| Peripheral artery disease       | 3.7%; 4/109  | 37.5%; 3/8 | 0.01    |
| Current or former smoking       | 73.4%; 80/109 | 75.0%; 6/8 | 1.00    |

| Clinical status and laboratory findings on admission |
|-----------------------------------------------------|
| Heart rate, b.p.m.                                  | 80.0 (70.0-90.0) | 90.0 (71.0-98.8) | 0.24    |
| SBP, mmHg                                           | 130.0 (120.0-141.0) | 142.5 (120.0-168.5) | 0.18    |
| DBP, mmHg                                           | 77.0 (70.0-90.0) | 83.0 (62.5-94.8) | 0.52    |
| Intraavenous diuretics                             | 30.3%; 33/109 | 75.0%; 6/8 | 0.02    |
| Killip class                                       | 1 (1-2) | 2 (1-3) | 0.01    |
| TIMI score                                         | 3 (2-5) | 5 (3-7) | 0.02    |
| GRACE score                                        | 110 (95-127) | 135 (100.0-171) | 0.17    |

| Laboratory findings on admission                   |
|----------------------------------------------------|
| Hemoglobin, g/dl                                   | 14.3 (13.5-15.6) | 13.2 (12.2-13.8) | 0.02    |
| hs-CRP peak, mg/dL                                 | 3.2 (1.7-7.4); n=104 | 91.6 (3.2-208.0) | 0.01    |
| Troponin I peak, ng/L                              | 31.91 (3.73-82.31); n=105 | 40.04 (16.92-102.07) | 0.37    |
| CK-MB peak, U/L                                    | 74.55 (12.68-178.68); n=108 | 116.00 (48.25-428.20) | 0.26    |
| NT-proBNP peak, pg/mL                              | 886.0 (329.0-1945.0); n=75 | 7194.0 (2343.3-14701.5) | <0.001  |
| Serum creatinine, mg/dL                            | 0.93 (0.86-1.06) | 1.15 (0.87-1.31) | 0.12    |
| Variable                              | Value                  | p-value | Reference Range         | p-value | Reference Range         | p-value | Reference Range         | p-value | Reference Range         |
|---------------------------------------|------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|---------|-------------------------|
| eGFR, ml/min/1.73m²                   | 92.8 (64.2-117.9)      | 0.30    | 84.3 (58.1-107.9)       | 0.03    | 96.3 (68.8-117.9)       | 0.06    | 74.1 (58.4-102.2)       |         |                         |
| Serum sodium, mmol/L                 | 140.0 (138.4-141.9)    |         | 138.5 (135.4-139.8)     | 0.03    | 140.0 (137.9-142.0)     | 0.34    | 139.5 (138.7-141.2)     |         |                         |
| Serum potassium, mmol/L              | 3.9 (3.6-4.2)          | 0.53    | 4.0 (3.7-4.3)           | 0.34    | 3.97 (3.6-4.18)         | 0.76    | 3.94 (3.5-4.38)         |         |                         |
| Total cholesterol, mg/dL             | 187.0 (162.0-223.0); n=105 | 0.002   | 145.5 (121.3-162.8)     | 0.004   | 188.0 (163.8-226.5); n=90 |         | 153.0 (140.0-188.0); n=23 |         |                         |
| LDL, mg/dL                           | 113.0 (84.0-145.0); n=95 | 0.01    | 77.0 (61.8-95.3)        | 0.03    | 115.5 (85.0-148.0); n=80 |         | 84.0 (75.0-121.0); n=23 |         |                         |
| HDL, mg/dL                           | 44.5 (34.3-52.0); n=104 | 0.78    | 43.5 (15.5-58.8)        | 0.34    | 45.0 (35.0-53.5); n=89  |         | 40.0 (33.0-50.0); n=23  |         |                         |
| Triglycerides, mg/dL                 | 136.0 (93.0-177.0); n=103 | 0.67    | 103.0 (85.5-227.3)      | 0.63    | 135.5 (91.3-181.3); n=88 |         | 134.0 (91.0-157.0); n=23 |         |                         |

Angiographic characteristics

| Location                        | p-value |
|---------------------------------|---------|
| Right coronary artery          | 0.50    |
| Left anterior descending artery| 0.65    |
| Circumflex artery              | 1.00    |

Extent of CAD

| Disease                      | p-value |
|------------------------------|---------|
| One-vessel disease           | 0.49    |
| Two-vessel disease           | 0.31    |
| Three-vessel disease         | 1.00    |

TIMI Grade Flow

| Flow  | p-value |
|-------|---------|
| Baseline   | 0.35    |
| Final       | 0.52    |

Stent implantation

| Stent type         | p-value |
|--------------------|---------|
| 1-stent            | 0.81    |
| 2 or more stents   | 0.80    |
| Complete revascularization | 0.26  |
| Ejection fraction, % | 48 (42-53) | 38 (29-49) | **0.03** | 48 (41-54) | 46 (35-51) | **0.15** |
|---------------------|------------|------------|----------|------------|------------|----------|
| LVEDD, mm | 4.8 (4.5-5.2); n=108 | 5.3 (4.5-5.4) | 0.19 | 4.8 (4.5-5.2); n=92 | 5.0 (4.3-5.4) | 0.62 |
| LVEDV, ml | 104 (80-127) | 130 (65-131) | 0.99 | 105 (79-124) | 112 (74-131) | 0.86 |
| LVESV, ml | 53 (40-70) | 86 (32-95) | 0.46 | 53 (41-70) | 59 (34-92) | 0.77 |
| LVH * | 32.6%; 31/95 | 50.0%; 3/6 | 0.40 | 28.6%; 24/84 | 58.8%; 10/17 | **0.02** |
| LA dimension, mm | 3.8 (3.5-4.2); n=108 | 4.1 (3.6-5.2) | 0.18 | 3.8 (3.5-4.2); n=92 | 4.1 (3.6-4.2) | 0.08 |

**Clinical status and laboratory findings at discharge**

| Heart rate, b.p.m. | 70.0 (64.0-76.0); n=108 | 80.0 (72.8-84.5) | **0.01** | 70.0 (64.0-80.0); n=23 | 71.0 (67.0-80.0); n=23 | 0.43 |
|--------------------|--------------------------|------------------|----------|--------------------------|--------------------------|----------|
| SBP, mmHg | 120.0 (110.0-130.8); n=108 | 132.0 (103.8-138.8) | 0.55 | 120.0 (110.0-130.0); n=23 | 130.0 (105.0-141.0); n=23 | 0.41 |
| DBP, mmHg | 73.5 (60.0-80.0); n=108 | 80.0 (65.5-80.00) | 0.64 | 75.0 (62.5-80.0); n=86 | 70.0 (60.0-80.00); n=23 | 0.49 |
| Hemoglobin, g/dl | 13.7 (12.6-14.7); n=99 | 12.9 (11.0-14.5) | 0.17 | 14.0 (12.7-14.8); n=86 | 12.9 (11.5-14.2); n=21 | **0.01** |
| Serum creatinine, mg/dl | 0.93 (0.81-1.10); n=97 | 1.24 (0.83-1.45) | 0.054 | 0.95 (0.81-1.05); n=84 | 0.93 (0.81-1.25); n=21 | 0.42 |
| eGFR, mL/min/1.73m² | 91.36 (74.75-120.25); n=97 | 57.14 (37.94-121.55) | 0.10 | 92.59 (78.17-112.06); n=84 | 65.07 (54.60-106.38); n=21 | **0.01** |
| Serum sodium, mmol/L | 141.3 (139.5-143.3); n=97 | 140.8 (137.3-142.9) | 0.47 | 141.0 (139.5-143.3); n=84 | 141.6 (139.4-143.0); n=21 | 0.64 |
| Serum potassium, mmol/L | 4.4 (4.1-4.6); n=97 | 4.6 (4.1-5.0) | 0.34 | 4.45 (4.19-4.69); n=84 | 4.3 (4.1-4.7); n=21 | 0.34 |

**Pharmacotherapy at hospital discharge**

| ASA | 100%; 108/108 | 100%; 8/8 | 1.00 | 100%; 93/93 | 100%; 23/23 | 1.00 |
| Clopidogrel | 88.0%; 95/108 | 87.5%; 7/8 | 1.00 | 89.2%; 83/93 | 82.6%; 19/23 | 0.47 |
| Ticagrelor | 12.0%; 13/108 | 12.5%; 1/8 | 1.00 | 10.8%; 10/93 | 17.4%; 4/23 | 0.47 |
| Drug                        | Use               | 6.5%; 7/108 | 25.0%; 2/8 | 0.12 | 6.5%; 6/93 | 13.0%; 3/23 | 0.38 |
|-----------------------------|-------------------|-------------|------------|------|------------|-------------|------|
| Anticoagulants              |                   |             |            |      |            |             |      |
| Loop diuretics              |                   | 22.2%; 24/108 | 62.5%; 5/8 | 0.02 | 19.4%; 18/93 | 47.8%; 11/23 | 0.01 |
| ACE-I                       |                   | 96.3%; 104/108 | 100%; 8/8 | 1.00 | 95.7%; 89/93 | 100%; 23/23 | 0.58 |
| ARB                         |                   | 5.6%; 6/108 | 12.5%; 1/8 | 0.40 | 6.5%; 6/93 | 4.3%; 1/23 | 1.00 |
| β-blocker                   |                   | 93.5%; 101/108 | 100%; 8/8 | 1.00 | 93.5%; 87/93 | 95.7%; 22/23 | 1.00 |
| Aldosterone antagonist      |                   | 34.3%; 37/108 | 12.5%; 1/8 | 0.27 | 34.4%; 32/93 | 26.1%; 6/23 | 0.62 |
| Ivabradine                  |                   | 1.9%; 2/108 | 0.0%; 0/8 | 1.00 | 2.2%; 2/93 | 0.0%; 0/23 | 1.00 |
| Statin                      |                   | 96.3%; 104/108 | 87.5%; 7/8 | 0.31 | 95.7%; 89/93 | 95.7%; 22/23 | 1.00 |

ACE-I - angiotensin-converting-enzyme inhibitor, ARB - angiotensin II receptor blocker, ASA – acetylsalicylic acid, BMI – body mass index, CAD - coronary artery disease, CK-MB - creatine kinase-muscle/brain, COPD – chronic obstructive pulmonary disease, DBP – diastolic blood pressure, eGFR – estimated glomerular filtration rate, Gal-3 – galectin-3, GRACE - The Global Registry of Acute Coronary Events, HDL - high density lipoprotein, hs-CRP – high-sensitive C-reactive protein, LA – left atrium, LDL - low density lipoprotein, LVEDD – left ventricular end diastolic diameter, LVEDV - left ventricular end-diastolic volume, LVESV - left ventricular end-systolic volume, LVH – left ventricular hypertrophy, n – number, NT-proBNP - N-terminal pro-brain natriuretic peptide, SBP – systolic blood pressure, sST2- soluble interleukin-1 receptor-like 1, TIA – transient ischemic attack, TIMI - The Thrombolysis in Myocardial Infarction

*LVH was based on left ventricular mass index (LVMI): LVMI >95 g/m2 for female, LVMI >115 g/m2 for male

** in patients who survived to hospital discharge
Table 3. In-hospital and one-year outcomes of patients with ST-segment elevation myocardial infarction treated with primary coronary intervention with reference to baseline Gal-3 and sST2 cut-offs.

| Variable                             | sST2 < 45.99 ng/mL (n=109) | sST2 ≥ 45.99 ng/mL (n=8) | p-value | Gal-3 < 9.57 ng/mL (n=93) | Gal-3 ≥ 9.57 ng/mL (n=24) | p-value |
|--------------------------------------|-----------------------------|---------------------------|---------|----------------------------|----------------------------|---------|
| **In-hospital outcomes**             |                             |                           |         |                            |                            |         |
| Hospitalization length, days         | 8.0 (7.0-10.0)              | 15.5 (12.3-24.8)          | **<0.001** | 8.0 (6.5-10.0)             | 9.5 (7.3-13.8)             | **0.03** |
| Time in ICCU, days                   | 4.0 (3.0-5.0)               | 11.0 (7.5-17.0)           | **<0.001** | 3.0 (3.0-5.0)              | 5.5 (4.3-10.8)             | **<0.001** |
| Death during hospitalization         | 0.9%; 1/109                 | 0.0%; 0/8                 | **1.00** | 0.0%; 0/93                 | 4.2%; 1/24                 | **0.21** |
| **One-year outcomes**                |                             |                           |         |                            |                            |         |
| CV death or HF hospitalization       | 5.2%; 5/97                  | 57.1%; 4/7                | **0.001** | 2.4%; 2/83                 | 33.3%; 7/21                | **<0.001** |
CV - cardiovascular, Gal-3 – galectin-3, HF - heart failure, ICCU – intensive cardiac care unit, MI – myocardial infarction, n – number, sST2- soluble interleukin-1 receptor-like 1

| Variable               | HR (95% CI)           | p-value |
|------------------------|-----------------------|---------|
| Age, per 10 years      | 1.97 (1.02-3.71)      | 0.04    |
| NT-proBNP, per 1000 pg/mL | 1.14 (1.04-1.25)    | 0.01    |
| Gal-3, per 1 ng/mL     | 1.34 (1.17-1.54)      | <0.001  |
| Gal-3 ≥ 9.57 ng/mL     | 15.94 (3.31-76.82)    | 0.001   |
| sST2, per 10 ng/mL    | 1.63 (1.22-2.16)      | 0.001   |
| sST2 ≥ 45.99 ng/mL    | 12.62 (3.37-47.20)    | <0.001  |

CI - confidence interval, Gal-3 – galectin-3, HR – hazard ratio, NT-proBNP - N-terminal pro-brain natriuretic peptide, sST2- soluble interleukin-1 receptor-like 1
### Table 5. Predictors of the primary endpoint in multivariate analyses.

| Variable                        | HR   | 95% CI       | p-value |
|---------------------------------|------|--------------|---------|
| Age, per 10 years               | 1.22 | 0.74 – 2.16  | 0.44    |
| Gal-3 ≥ 9.57 ng/mL              | 8.65 | 1.45 – 51.70 | 0.02    |
| sST2 ≥ 45.99 ng/mL             | 3.15 | 0.72 – 13.81 | 0.13    |
| Age, per 10 years               | 1.22 | 0.66 – 2.16  | 0.62    |
| Gal-3 ≥ 9.57 ng/mL              | 14.51| 1.46 – 143.95| 0.02    |
| NT-proBNP, per 1000 pg/mL      | 1.05 | 0.94 - 1.25  | 0.36    |
| Age, per 10 years               | 1.34 | 0.74 – 2.59  | 0.36    |
| sST2 ≥ 45.99 ng/mL | 11.79 | 1.52 – 91.26 | **0.02** |
|-------------------|-------|-------------|---------|
| NT-proBNP, per 1000 pg/mL | 0.99 | 0.85 - 1.16 | 0.95 |

CI - confidence interval, Gal-3 – galectin-3, HR - hazard ratio, NT-proBNP - N-terminal pro-brain natriuretic peptide, sST2- soluble interleukin-1 receptor-like 1