ISSN 2786-6661
eISSN 2786-667X

**UDC 616.12-008.46-005.4-036.1:616.379-008.64-056.25]:616-008.9:577.115**
**https://doi.org/10.32345/USMYJ.4(158).2025.116-126**

Received: September 02, 2025
Accepted: November 22, 2025

# The role of galectin-3 in lipid metabolism disorders in patients with chronic heart failure of ischemic origin and concomitant metabolic pathology

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***Abstract:*** *Chronic heart failure of ischaemic origin remains a leading cause of morbidity and mortality, and its course is significantly aggravated by concomitant metabolic pathology (type 2 diabetes mellitus and obesity). The role of galectin-3 in the mechanisms of direct participation in lipid metabolism disorders in this vulnerable cohort of patients remains insufficiently studied, which justifies the relevance of the study. The aim of the work was to study the role of galectin-3 as a potential diagnostic and prognostic marker of lipid metabolism disorders in patients with chronic heart failure of ischemic origin against the background of concomitant metabolic pathology. The study examined 225 patients with chronic heart failure with coronary artery disease, who were divided into four groups based on the presence of a combined course of diabetes mellitus and obesity (n=75), type 2 diabetes mellitus (n=50), obesity (n=50), isolated course of coronary artery disease (n=50), and 30 practically healthy individuals who were included in the control group. A biochemical study of lipid metabolism indicators was carried out, including total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, very low-density lipoprotein cholesterol and atherogenic index, as well as determination of serum galectin-3 levels by enzyme-linked immunosorbent assay. The results showed that the concentration of galectin-3 in the blood serum significantly increases in proportion to the degree of metabolic burden, reaching the highest values in patients with a combination of chronic heart failure, type 2 diabetes mellitus, and obesity, which was more than twice as high compared to patients without concomitant metabolic pathology ($p<0.05$). In the same group, the most pronounced deterioration of the lipid profile was found: low-density lipoprotein cholesterol increased by 99.2% compared to the group without metabolic pathology, and the atherogenic coefficient increased by 300.9% ($p<0.001$). At the same time, a significant decrease in antiatherogenic high-density lipoprotein cholesterol was recorded. Correlation analysis confirmed that serum galectin-3 has close links with dyslipidemic processes, and the strength of the correlation depends on the comorbid status. The strongest direct correlations with proatherogenic fractions, such as triglycerides and low-density lipoprotein cholesterol, were found in patients with comorbid obesity. These associations indicate that galectin-3 is actively involved in the mechanisms of dyslipidaemia and reflects a triglyceride-dependent aspect of the disorders, closely related to insulin resistance and chronic inflammation. The study also showed that even in patients without comorbid metabolic pathology, a statistically significant association of galectin-3 with total cholesterol and triglycerides persists, which emphasises its role as a marker of fundamental inflammation and fibrosis, independent of external metabolic factors. Thus, the results obtained expand the understanding of the role of galectin-3 as a key mediator integrating inflammatory, fibrotic, and dyslipidemic processes, providing*

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eISSN 2786-667X

*a strong rationale for including galectin-3 in cardiometabolic risk stratification strategies and the search for new therapeutic targets in patients with chronic heart failure.*

**Keywords:** Heart failure, Coronary Disease, Lipid metabolism, Galectin-3, Obesity, Diabetes Mellitus Type 2, Coronary Artery Disease.

## Introduction

Chronic heart failure (CHF) caused by coronary artery disease (CAD) has remained one of the leading causes of morbidity, hospitalisation and mortality worldwide for many decades, despite significant advances in treatment. The importance of the problem increases many times over in the context of comorbidity, namely when CHF is combined with metabolic pathology, in particular type 2 diabetes mellitus (T2DM) and obesity [1]. This concomitant pathology not only complicates the clinical course and worsens the prognosis of CHF, but also significantly modifies its pathogenesis, largely due to lipid metabolism disorders and the development of dyslipidaemia [2].

In recent years, researchers have focused their attention on galectin-3, a multifunctional β-galactoside-binding lectin that is a key mediator of inflammation and fibrosis [3]. Galectin-3 is expressed by activated macrophages and fibroblasts and plays a critical role in the processes of adverse remodelling, myocardial fibrosis and the progression of CHF, regardless of its ejection fraction [4]. Recent studies show that galectin-3 is not only a marker of myocardial damage, but also has the ability to actively influence metabolic dysregulation [3, 5].

Despite significant evidence of the association of galectin-3 with overall metabolic risk and cardiac fibrosis, the mechanisms of its direct involvement in lipid metabolism disorders in an extremely vulnerable cohort of patients — those with ischaemic CHF and concomitant metabolic pathology – remain poorly understood. Understanding this interaction is crucial, as dyslipidaemia is a powerful modified risk factor that exacerbates atherogenesis and the progression of CAD, and galectin-3 may act as a common link connecting inflammatory, fibrotic and metabolic disorders.

## Aim

The aim of this study is to investigate the role of galectin-3 as a potential diagnostic and prognostic marker of lipid metabolism disorders in patients with chronic heart failure of ischaemic origin against the background of concomitant metabolic pathology.

## Materials and methods

According to the study design, 225 patients undergoing inpatient treatment in the cardiology department of Kharkiv City Hospital No. 27 were divided into groups as follows: Group 1 included patients with CHF against the background of CAD with concomitant T2DM and obesity (n=75), Group 2 included patients with ischaemic CHF with T2DM (n=50), Group 3 included patients with CHF against the background of CAD with concomitant obesity (n=50), the comparison group (Group 4) consisted of patients with CHF and CAD without comorbid metabolic pathology (n=50). The control group included 30 practically healthy individuals. The groups of examinees were comparable in terms of age (63.44±2.06; 64.47±1.88; 60.59±2.43 and 63.27±1.72 years, respectively) and gender.

The diagnosis of CAD was verified in accordance with current international and national clinical protocols: the standards of the European Society of Cardiology (ESC) and the Unified Clinical Protocol of the Ministry of Health of Ukraine "Stable Ischemic Heart Disease" (Order No. 2857 of 23 December 2021). The presence of CHF was determined according to the classification of the Working Group on Heart Failure of the Association of Cardiologists of Ukraine, and its functional class was assessed according to the NYHA (New York Heart Association) criteria. T2DM was diagnosed based on the Unified Clinical Protocol of the Ministry of Health of Ukraine "Diabetes mellitus" (Order No. 1300 of 24 July 2024). To

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eISSN 2786-667X

diagnose abdominal obesity, anthropometric indicators of waist and hip circumference and body mass index (BMI) were determined using the following formula:

$$BMI = m / h^2,$$

where

BMI – body mass index (kg/m$^2$);
m – body weight (kg);
h – height (m).

The inclusion criteria were age over 18 years, CAD with signs of CHF with or without excess body weight, grade 1-3 obesity, type 2 diabetes mellitus, and voluntary written consent to participate in the study.

Exclusion criteria were based on the need to minimise the influence of extraneous factors on the assessment of biomarkers and cardiometabolic status. Pregnant women were not included in the study, nor were patients with acute infectious and autoimmune diseases, diffuse connective tissue diseases, oncological diseases, diseases of the pituitary gland and hypothalamus, chronic renal failure with a GFR of less than 35 ml/min/1.73 m$^2$, symptomatic hypertension, acute coronary syndrome and acute cerebrovascular accident within the last 6 months, exacerbation of chronic or acute inflammatory diseases; patients with a history of alcohol abuse or mental illness; patients who were likely to violate the study protocol and individuals who are not citizens of Ukraine.

Biochemical testing included determination of total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) levels, which were performed using the peroxidase method with the Cholesterol Liquicolor reagent kit from Human (Germany) in heparin-stabilised blood serum. Triglyceride (TG) levels were determined by an enzymatic colorimetric method using the Triglycerides 105 GPO reagent kit from Human (Germany). The atherogenicity coefficient (AC) was calculated using the Klimov A.M. formula:

$$AC = (TC – HDL\text{-}C)/HDL\text{-}C$$

The level of very low-density lipoprotein cholesterol (VLDL-C) was calculated using the following formula:

$$VLDL\text{-}C = TG/2.2 \times 0.45, (mmol/L)$$

Low-density lipoprotein cholesterol (LDL-C) levels were determined using the Friedwald formula:

$$LDL\text{-}C = TC – (VLDL\text{-}C + HDL\text{-}C), (mmol/L)$$

The level of galectin-3 in blood serum was determined by immunoenzymatic method. For quantitative measurement, a commercial Human Galectin-3 ELISA Kit (eBioscience, Austria) was used. The study was conducted on a Labline–90 immunoenzymatic analyser (Austria Lab Technologies, Austria) at the biochemical department of the Central Research Laboratory of Kharkiv National Medical University.

Statistical analysis was performed using parametric statistics methods with the use of Microsoft Excel 2010 software. The normality of the distribution of quantitative data was checked using the Kolmogorov–Smirnov criterion. If normal distribution was confirmed, the data were presented as M±m (mean ± standard error of the mean). The comparison of mean values was performed using Fisher's criterion (F). Spearman's rank correlation coefficient (r) was used to assess the correlation between samples. The difference was considered statistically significant at $p<0.05$.

The study was approved by the Ethics and Bioethics Committee of the Kharkiv National Medical University (protocol №2, dated 12.10.2022). All procedures were performed in accordance with the written informed consent of the participants. The study fully complies with the international standards of bioethics established in the Helsinki Declaration («Ethical Principles for Medical Research Involving Human Subjects») and the Universal Declaration on Bioethics and Human Rights (UNESCO).

Results. Analysis of lipid metabolism indicators and galectin-3 levels in patients in the study groups revealed significant differences that correlate with the deterioration of the metabolic status of patients. The data obtained, illustrating the dynamics of metabolic parameters and serum galectin-3 levels, are presented in Table 1.

While analysing lipid metabolism indicators, we found a significant increase in TC (by 19.1%; 18.3%; 21.2% and 72.3%) and TG (by

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**Table 1.** Analysis of lipid metabolism indicators and serum galectin-3 levels in patients in the study groups

| Parameter, Units Measurement | Patients with CHF | | | | |
|---|---|---|---|---|---|
| | CAD + T2DM + obesity (n=75) | CAD + T2DM (n=50) | CAD + obesity (n=50) | CAD without metabolic pathology (n=50) | Control group (n=30) |
| | 1 | 2 | 3 | 4 | 5 |
| TC, mmol/l | 6.41±0.08 | 5.38±0.07 | 5.42±0.11 | 5.29±0.09 | 3.72±0.11 |
| | | $P_{1-2}$ <0.05<br>$P_{2-3}$ >0.05<br>$P_{2-4}$ >0.05<br>$P_{2-5}$ <0.05 | $P_{1-3}$ <0.05<br>$P_{3-4}$ >0.05<br>$P_{3-5}$ <0.05 | $P_{1-4}$ <0.05<br>$P_{4-5}$ <0.05 | $P_{1-5}$ <0.05 |
| TG, mmol/l | 2.84±0.07 | 1.81±0.08 | 1.91±0.09 | 1.44±0.05 | 1.31±0.03 |
| | | $P_{1-2}$ <0.05<br>$P_{2-3}$ >0.05<br>$P_{2-4}$ <0.05<br>$P_{2-5}$ <0.05 | $P_{1-3}$ <0.05<br>$P_{3-4}$ <0.05<br>$P_{3-5}$ <0.05 | $P_{1-4}$ <0.05<br>$P_{4-5}$ <0.05 | $P_{1-5}$ <0.01 |
| HDL-C, mmol/l | 1.15±0.03 | 1.77±0.04 | 1.74±0.03 | 2.47±0.07 | 2.86±0.05 |
| | | $P_{1-2}$ <0.05<br>$P_{2-3}$ >0.05<br>$P_{2-4}$ <0.05<br>$P_{2-5}$ <0.05 | $P_{1-3}$ <0.05<br>$P_{3-4}$ <0.05<br>$P_{3-5}$ <0.05 | $P_{1-4}$ <0.05<br>$P_{4-5}$ <0.05 | $P_{1-5}$ <0.01 |
| LDL-C, mmol/l | 4.68±0.05 | 2.74±0.04 | 2.94±0.06 | 2.35±0.04 | 0.82±0.03 |
| | | $P_{1-2}$ <0.05<br>$P_{2-3}$ >0.05<br>$P_{2-4}$ <0.05<br>$P_{2-5}$ <0.05 | $P_{1-3}$ <0.05<br>$P_{3-4}$ <0.05<br>$P_{3-5}$ <0.05 | $P_{1-4}$ <0.05<br>$P_{4-5}$ <0.05 | $P_{1-5}$ <0.01 |
| VLDL-C, mmol/l | 0.58±0,05 | 0.37±0.04 | 0.39±0.03 | 0.30±0.04 | 0.16±0.04 |
| | | $P_{1-2}$ <0.05<br>$P_{2-3}$ >0.05<br>$P_{2-4}$ <0.05<br>$P_{2-5}$ <0.05 | $P_{1-3}$ <0.05<br>$P_{3-4}$ <0.05<br>$P_{3-5}$ <0.05 | $P_{1-4}$ <0.05<br>$P_{4-5}$ <0.05 | $P_{1-5}$ <0.01 |
| AC | 4.57±0.04 | 2.04±0.05 | 2.15±0.07 | 1.14±0.06 | 0.51±0.04 |
| | | $P_{1-2}$ <0.05<br>$P_{2-3}$ >0.05<br>$P_{2-4}$ <0.05<br>$P_{2-5}$ <0.05 | $P_{1-3}$ <0.05<br>$P_{3-4}$ <0.05<br>$P_{3-5}$ <0.05 | $P_{1-4}$ <0.001<br>$P_{4-5}$ <0.05 | $P_{1-5}$ <0.001 |
| Galectin-3, ng/ml | 29.66±1.37 | 27.14±1.63 | 20.22±1.87 | 14.54±1.48 | 10.07±1.02 |
| | | $P_{1-2}$ > 0.05<br>$P_{2-3}$ <0.05<br>$P_{2-4}$ <0.05<br>$P_{2-5}$ <0.01 | $P_{1-3}$ <0.05<br>$P_{3-4}$ <0.05<br>$P_{3-5}$ <0.05 | $P_{1-4}$ <0.05<br>$P_{4-5}$ <0.05 | $P_{1-5}$ <0.01 |

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eISSN 2786-667X

56.9%; 48.7%; 97.2% and 116.8%), LDL-C (by 70.8%; 59.2%; 99.2% and 407.7%), VLDL-C (by 56.8%; 58.7%; 93.3% and 262.5%), AC (by 124.0%; 112.6%; 300.9% and 796.1%), as well as a decrease in HDL-C (by 35.0%; 33.9%; 53.4% and 59.8%) in patients with CHF against a background of CAD combined with T2DM and obesity, compared with patients with CAD and T2DM, CAD and obesity, CAD without concomitant metabolic pathology ($p<0.05$) and with individuals from the control group ($p<0.001$), respectively.

It should be noted that no lipid profile parameters showed significant changes between patients with CAD and concomitant T2DM and patients with CAD and obesity ($p>0.05$). These results can be explained by common mechanisms of insulin resistance (IR) in both obese patients and patients with T2DM which is a key mechanism of dyslipidaemia. Systemic inflammation also has a significant impact, affecting lipid metabolism and contributing to the progression of atherosclerosis.

Among patients with CAD and concomitant T2DM, there was a significant increase in LDL levels by 30.9% compared to the control group ($p<0.05$). Compared to the comparison group (with isolated CAD) and the control group, the indicators changed as follows: there was an increase in TG concentrations by 20.4% and 27.6%, LDL-C by 50.7% and 70.1%, VLDL-C by 18.9% and 56.8%, AC by 44.1% and 75%, and a decrease in HDL-C by 28.3% and 38.1%, respectively ($p<0.05$).

Patients with CHF against the background of CAD with concomitant obesity also showed a significant increase in TG levels by 24.6% and 31.4%, LDL-C by 54.1% and 72.1%, VLDL-C by 23.1% and 59%, AC by 54.4% and 76.3%, as well as a decrease in HDL-C concentration by 29.6% and 39.2% compared to patients with isolated CAD and healthy volunteers from the control group, respectively ($p<0.05$).

Serum galectin-3 showed significant differences in the form of concentration increase in the main study group (group 1) by 8.5%, 31.8%, and 51% compared to groups 2, 3, and 4, respectively ($p<0.05$) and by 66.1% compared to the control group ($p<0.01$). Such changes in this indicator are likely due to the fact that in patients with obesity and T2DM, chronic low-level inflammation is a key pathogenetic factor. It should also be noted that this lectin is actively involved in the processes of fibrogenesis, stimulating the activation of fibroblasts and enhancing collagen synthesis. In patients with concomitant T2DM and obesity, this profibrotic effect is further enhanced by the accumulation of advanced glycation end products, which have a direct damaging effect on cardiac and vascular structures.

A correlation analysis was performed to establish the presence and nature of relationships between serum galectin-3 levels and lipid metabolism indicators.

**Table 2.** Relationships between galectin-3 levels and lipid metabolism indicators in patients with chronic heart failure against a background of coronary artery disease with concomitant obesity and type 2 diabetes mellitus ($r_{crit}=0.34$)

| Parameter, units | r | p |
|---|---|---|
| TC, mmol/l | 0.42 | <0.05 |
| TG, mmol/l | 0.51 | <0.05 |
| HDL-C, mmol/l | -0.35 | <0.05 |
| LDL-C, mmol/L | 0.56 | <0.05 |
| VLDL-C, mmol/l | 0.59 | <0.05 |
| AC | 0.22 | >0.05 |

Thus, in a group of patients with CAD against the background of concomitant T2DM and obesity, moderate direct correlations were found between galectin-3 concentration and TC level ($r=0.42$; $p<0.05$), LDL-C ($r=0.56$; $p<0.05$), VLDL-C ($r=0.59$; $p<0.05$) TG ($r=0.51$; $p<0.05$) and an inverse relationship with HDL-C ($r= -0.35$; $p<0.05$), indicating an increase in atherogenic fractions of the lipid profile in response to galectinemia, along with a decrease in antiatherogenic components of the lipid profile. The correlation with the atherogenicity coefficient was not statistically significant ($r=0.22$; $p>0.05$). The data are presented in Table 2. These results confirm that galectin-3 not only reflects fibrotic changes but is also actively

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eISSN 2786-667X

involved in the mechanisms of dyslipidaemia, making it a key biomarker of cardiometabolic risk in this cohort of patients.

The results of the correlation analysis presented in Table 3 allowed us to identify statistically and clinically significant associations between galectin-3 levels and key indicators of lipid metabolism in patients with CAD against the background of T2DM.

**Table 3.** Correlations between galectin-3 levels and lipid metabolism indicators in patients with chronic heart failure against a background of coronary artery disease with concomitant type 2 diabetes mellitus ($r_{crit}$=0.34)

| Parameter, units | r | p |
|---|---|---|
| TC, mmol/l | 0.42 | <0.05 |
| TG, mmol/l | 0.61 | <0.05 |
| HDL-C, mmol/l | -0.19 | >0.05 |
| LDL-C, mmol/L | 0.30 | >0.05 |
| VLDL-C, mmol/l | 0.26 | >0.05 |
| AC | 0.31 | >0.05 |

In this group of patients, statistically significant direct correlations were found between serum galectin-3 concentration and two main proatherogenic indicators. A strong direct correlation (r=0.61; p<0.05) with TG levels was established, emphasising the close relationship between the fibrosis biomarker and TG metabolism disorders characteristic of insulin resistance and T2DM. A moderate direct correlation (r=0.42; p<0.05) with TC was also determined, indicating the clinical significance of the association of serum galectin-3 with total lipidemia. For the remaining indicators, the correlations were statistically insignificant (p>0.05). Therefore, the data obtained suggest that in the context of metabolic pathology galectin-3 primarily reflects the TG-dependent aspect of dyslipidaemia, which is closely associated with chronic inflammation and insulin resistance.

In the group of patients with CHF against the background of CAD with concomitant obesity, strong statistically significant associations were found between serum galectin-3 levels and TG (r=0.76; p<0.05), LDL-C (r=0.69; p<0.05) and

**Table 4.** Correlations between galectin-3 levels and lipid metabolism indicators in patients with chronic heart failure against a background of coronary artery disease with concomitant obesity ($r_{crit}$=0.34)

| Parameter | r | p |
|---|---|---|
| TC, mmol/l | 0.46 | <0.05 |
| TG, mmol/l | 0.76 | <0.05 |
| HDL-C, mmol/l | -0.28 | >0.05 |
| LDL-C, mmol/L | 0.69 | <0.05 |
| VLDL-C, mmol/l | 0.27 | >0.05 |
| AC | 0.26 | >0.05 |

a moderate direct correlation with TC (r=0.46; p<0.05). At the same time, HDL-C (r=-0.28; p>0.05), VLDL-C (r=0.27; p>0.05) and AC (r=0.26; p>0.05) had weak correlations that did not reach statistical significance. In this cohort of patients, the presence of strong and moderate associations with key proatherogenic cholesterol fractions emphasises that serum galectin-3 is a powerful biomarker that integrates inflammatory, fibrotic and dyslipidaemic processes characteristic of the comorbidity of heart failure and obesity, signalling a high cardiometabolic risk.

The results of the correlation analysis demonstrate that even in the absence of concomitant metabolic pathology, serum galectin-3 levels in patients with heart failure of ischemic origin maintain statistically significant associations with major proatherogenic fractions (Table 5).

**Table 5.** Correlations between galectin-3 levels and lipid metabolism indicators in patients with chronic heart failure against a background of coronary artery disease without concomitant metabolic pathology ($r_{crit}$=0.34)

| Parameter, units | r | p |
|---|---|---|
| TC, mmol/l | 0.38 | <0.05 |
| TG, mmol/l | 0.43 | <0.05 |
| HDL-C, mmol/l | -0.28 | >0.05 |
| LDL-C, mmol/L | 0.26 | >0.05 |
| VLDL-C, mmol/l | 0.27 | >0.05 |
| AC | 0.32 | >0.05 |

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eISSN 2786-667X

A weak direct correlation was established with TG levels ($r=0.43$; $p<0.05$) and TC ($r=0.38$; $p<0.05$). The results obtained prove that serum galectin-3 is closely associated with TG metabolism disorders regardless of the presence of obesity or T2DM and indicate a significant relationship between the studied indicator and general lipid dysregulation in this group of patients. The remaining indicators did not show statistically significant correlations ($p>0.05$). The results indicate that in a group of patients with CAD without concomitant metabolic pathology, serum galectin-3 likely acts as a marker of fundamental inflammation and fibrosis, which partially overlaps with basic dyslipidaemia, but is not as closely associated with specific proatherogenic fractions as in groups with pronounced metabolic disorders.

**Discussion**

The study, aimed at investigating the relationship between serum galectin-3 and lipid metabolism parameters in patients with CHF against the background of CAD with concomitant metabolic pathology, confirmed the hypothesis about the integrative role of this biomarker in the cardiometabolic continuum. Our results demonstrate that the concentration of serum galectin-3 increases significantly in proportion to the degree of metabolic burden, which is consistent with most current studies. In their study on mouse models, Du XJ et al. found that galectin-3 has a direct effect on the transcription of genes associated with lipid metabolism and influences its disruption at the cellular level [7]. Taking into account the study by Du XJ et al. is fundamental, and lipidomics, which allows detecting profound changes at the cellular level, prevailed among the research methods, while our clinical indicators are an integral assessment of systemic lipid metabolism, it should be noted that the pathophysiological mechanisms of galectin-3 in fibrogenesis and lipid metabolism are universal.

In turn, Storman M et al. considered galectin-3 as a biomarker, particularly in the presence of other established factors such as age, body weight, and abdominal obesity. This confirms our concept that this lectin is an integrative marker of comorbidity of CHF and obesity [8].

Lin D et al. in their work associate an increase in serum galectin-3 with the presence or risk of T2DM, which is a key link in the cardiometabolic continuum, and also prove that lipids and galectin-3 should be assessed together for better prediction of metabolic risk, which once again confirms the importance of galectin-3 not only as a marker of fibrosis, but also as an integrative biomarker that plays a key role in the early stages of cardiometabolic dysfunction, including the development of T2DM [9]. This further substantiates its significance as a prognostic marker for assessing the risk of dyslipidaemia in patients with CHF burdened by metabolic pathology.

Some researchers like Schmitt et al. [10] and Lorenzo-Almorós A et al. [11] argue that higher serum galectin-3 levels are associated with a higher prevalence of prediabetes, T2DM, and other cardiovascular risk factors and comorbidities. The authors also believe that this lectin is cross-linked with impaired systolic and diastolic function in patients with T2DM and reduced systolic function in prediabetes, and is prospectively associated with systolic dysfunction and cardiovascular and all-cause mortality in T2DM. This is fully consistent with our results and confirms the role of galectin-3 as a link between metabolic disorders and myocardial damage. The study by Schmitt et al. also states that N-terminal pro B-type natriuretic peptide (NT-proBNP) was superior to galectin-3 for assessing reduced systolic and diastolic function and had higher prognostic value for mortality. At the same time, galectin-3 was not associated with cardiac function in patients with euglycaemia. This proves that serum galectin-3 is activated specifically by metabolic dysfunction and is a marker of metabolically dependent fibrosis in a cohort of patients with cardiometabolic pathology, and not just hydrodynamic stress, which is measured by NT-proBNP.

At the same time, a study by Ianos RD et al. showed that measuring galectin-3 concentrations in patients with CHF with preserved and moderately reduced ejection fraction can provide a deeper understanding of the severity of heart failure, especially in patients with T2DM, which fully coincides with our statements [12]. Jiang J et

ISSN 2786-6661
eISSN 2786-667X

al also considered galectin-3 was an independent predictor of heart failure with preserved ejection fraction [13].

Khadeja Bi et al. also reveals galectin-3 as a marker for the diagnosis of CHF (at 8 ng/ml, sensitivity 92%, specificity 71%), which also confirms our hypothesis of using serum galectin-3 in CHF risk stratification [2].

The clinical correlations we found between high serum galectin-3 levels and proatherogenic lipid fractions in patients with comorbid T2DM and obesity have also been confirmed in experimental studies. The researches established the role of galectin-3 as an important regulatory factor in myocardial remodelling induced by disturbances in glucose-lipid metabolism [14, 15]. The authors demonstrated that galectin-3 activity promotes fibrosis, apoptosis, and cardiomyocyte hypertrophy by inhibiting the activity of the Akt signalling pathway, thus acting as a key molecular link that converts systemic metabolic disorders into direct myocardial damage and remodelling.

Thus, the study is fully consistent with the results of current scientific advances and provides important clinical confirmation of the fundamental mechanisms identified in experimental and cohort studies in recent years.

Our study expands the current understanding of the role of galectin-3 from a simple marker of fibrosis to a key link integrating inflammation, dyslipidaemia, and CHF progression in T2DM and obesity. The data obtained provide a strong rationale for including galectin-3 in strategies for stratifying cardiometabolic risk.

**Conclusions**

1. The study confirmed the integrative role of galectin-3 as a potential diagnostic and prognostic marker of lipid metabolism disorders in patients with chronic heart failure of ischaemic origin against the background of concomitant metabolic pathology. The established links between serum galectin-3 and proatherogenic lipid fractions indicate that this biomarker is a key link connecting inflammatory, fibrotic, and metabolic disorders.

2. Patients with chronic heart failure and comorbid metabolic disorders such as type 2 diabetes mellitus and obesity show a significant deterioration in their lipid profile, manifested by an increase in proatherogenic fractions – total cholesterol (by 21.2%), triglycerides (by 97.2%) and low-density lipoprotein cholesterol (by 99.2%) and a decrease in antiatherogenic high-density lipoprotein cholesterol (by 53.4%), as well as the highest concentrations of serum galectin-3 (29.66±1.37 ng/ml vs. 14.54±1.48 ng/ml) were recorded in patients with metabolic syndrome with a combination of chronic heart failure, type 2 diabetes mellitus and obesity, compared to patients without metabolic pathology. This confirms that galectin-3 not only reflects fibrosis induced by heart failure, but is also actively activated by metabolic dysfunction and acts as a key link connecting chronic low-level inflammation, dyslipidaemia and fibrogenesis processes.

3. Correlation analysis confirmed that serum galectin-3 is an integrating biomarker closely associated with dyslipidaemic processes, with the strength of this association depending on the degree of metabolic burden. In patients with chronic heart failure of ischaemic origin against a background of concomitant obesity, galectin-3 showed the strongest direct correlations with proatherogenic fractions, namely triglycerides ($r=0.76$; $p<0.05$) and low-density lipoprotein cholesterol ($r=0.69$; $p<0.05$). In the group with a combination of type 2 diabetes mellitus and obesity, moderate direct correlations were also found with low-density lipoprotein cholesterol ($r=0.56$; $p<0.05$) and triglycerides ($r=0.51$; $p<0.05$), as well as an inverse correlation with antiatherogenic high-density lipoprotein cholesterol ($r=-0.35$; $p<0.05$). At the same time, even in the absence of metabolic pathology, a weaker but statistically significant correlation between galectin-3 and total cholesterol ($r=0.38$; $p<0.05$) and triglycerides ($r=0.43$; $p<0.05$) persists. Thus, serum galectin-3 acts as a key mediator linking inflammatory and profibrotic processes with metabolic dysfunction, while particularly sensitively reflecting the triglyceride-dependent aspect of dyslipidaemia, which is a direct consequence of insulin resistance.

Prospects for further research. Currently, it is extremely important to conduct long-term prospective studies to assess the extent to which

ISSN 2786-6661
eISSN 2786-667X

galectin-3 levels correlate with the risk of acute cardiovascular events (myocardial infarction, stroke) and overall/cardiovascular mortality in metabolically burdened patients.

**Funding**

This study did not receive external funding.

**Conflict of interest**

None

**Consent to publication**

All procedures related to patient examination and use of the data obtained were carried out in accordance with the principles of biomedical ethics and international standards. Each study participant provided voluntary, informed, and written consent to participate in the study, as well as to the subsequent publication and use of anonymised scientific results. The study was conducted in accordance with the Helsinki Declaration and the recommendations of the Committee on Publication Ethics (COPE). The author confirms that the publication does not contain any personal data that could identify patients.

**AI Disclosure**

The author used ChatGPT (OpenAI, San Francisco, CA, USA) for language editing of the English text. The authors reviewed and verified all AI-generated content to ensure accuracy and integrity.

**Author Contributions (CRediT taxonomy)**

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eISSN 2786-667X

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# Роль галектину-3 у порушеннях ліпідного обміну у хворих з хронічною серцевою недостатністю ішемічного та супутньою метаболічною патологією

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***Анотація.*** *Хронічна серцева недостатність ішемічного генезу залишається провідною причиною захворюваності та смертності, при цьому її перебіг значно обтяжується супутньою метаболічною патологією (цукровим діабетом 2 типу та ожирінням). Роль галектину-3 у механізмах безпосередньої участі в порушеннях ліпідного обміну в цій вразливій когорті пацієнтів залишається недостатньо вивченою, що обґрунтовує актуальність дослідження. Метою роботи було вивчення ролі галектину-3 як потенційного діагностичного та прогностичного маркера порушень ліпідного обміну у пацієнтів із хронічною серцевою недостатністю ішемічного генезу на тлі супутньої метаболічної патології. У дослідженні було обстежено 225 хворих на хронічну серцеву недостатність при ІХС, яких було розподілено на чотири групи, виходячи з наявності поєднаного перебігу цукрового діабету та ожиріння (n=75), цукрового діабету 2 типу (n=50), ожиріння (n=50), ізольованого перебігу ІХС (n=50) та 30 практично здорових осіб, які увійшли до контрольної групи. Проводилось біохімічне дослідження показників ліпідного обміну, включаючи загальний холестерин, тригліцериди, холестерин ліпопротеїнів високої щільності, холестерин ліпопротеїнів низької щільності, холестерин ліпопротеїнів дуже низької щільності та коефіцієнт атерогенності, а також визначення сироваткового рівня галектину-3 імуноферментним методом. Отримані результати продемонстрували, що концентрація галектину-3 у сироватці крові достовірно зростає пропорційно до ступеня метаболічного обтяження, досягаючи найвищих значень у хворих з поєднанням хронічної серцевої недостатності, цукрового діабету 2 типу та ожиріння, що було більш ніж удвічі вищим порівняно з пацієнтами без супутньої метаболічної патології (p<0,05). У цій же групі виявлено найбільш виражене погіршення ліпідного профілю: холестерин ліпопротеїнів низької щільності збільшився на 99,2 % порівняно з групою без метаболічної патології, а коефіцієнт*

ISSN 2786-6661
eISSN 2786-667X

*атерогенності збільшився на 300,9 % (p<0,001). Одночасно зафіксовано значне зниження антиатерогенного холестерину ліпопротеїнів високої щільності. Кореляційний аналіз підтвердив, що сироватковий галектин-3 має тісні зв'язки з дисліпідемічними процесами, причому сила кореляції залежить від коморбідного статусу. Найбільш потужні прямі кореляції з проатерогенними фракціями, такими як тригліцериди і холестерин ліпопротеїнів низької щільності, були встановлені у хворих із супутнім ожирінням. Ці зв'язки вказують, що галектин-3 активно залучений до механізмів дисліпідемії і відображає тригліцерид-залежний аспект порушень, тісно пов'язаний з інсулінорезистентністю та хронічним запаленням. Дослідження також показало, що навіть у пацієнтів без супутньої метаболічної патології зберігається статистично значущий зв'язок галектину-3 із загальним холестерином і тригліцеридами, що підкреслює його роль як маркера фундаментального запалення та фіброзу, незалежного від зовнішніх метаболічних факторів. Таким чином, отримані результати розширюють розуміння ролі галектину-3 як ключового медіатора, що інтегрує запальні, фібротичні та дисліпідемічні процеси, надаючи вагоме обґрунтування для включення галектину-3 у стратегії стратифікації кардіометаболічного ризику та пошуку нових терапевтичних мішеней у пацієнтів із хронічною серцевою недостатністю.*

**Ключові слова:** галектин-3, дисліпідемія, ішемічна хвороба серця, ожиріння, хронічна серцева недостатність, цукровий діабет 2 типу.