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The role of catestatin in left ventricular myocardial remodelling in patients with combined cardiometabolic pathology

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Abstract. The study is necessitated by the need to investigate the effect of catestatin on the structural and functional myocardial state in patients with chronic heart failure under conditions of cardiometabolic polymorbidity (type 2 diabetes mellitus and obesity). The aim was to evaluate the role of catestatin in the formation of structural and functional changes in the myocardium in patients with chronic heart failure in coronary artery disease with concomitant type 2 diabetes mellitus and obesity. The study involved 225 patients who were divided into four groups depending on the presence of metabolic disorders. A transthoracic echocardiographic examination was performed to assess the morphofunctional state of the myocardium. The level of catestatin in blood serum was determined by immunoenzymatic method. Spearman's correlation coefficient was used to assess the degree of correlation. The results showed that the most unfavourable indicators of left ventricular remodelling, including the maximum increase in end-systolic volume (101.57 mL) and end-diastolic volume (192.16 mL), as well as the lowest ejection fraction (42.67%), were recorded in patients with a combination of chronic heart failure, coronary artery disease, type 2 diabetes mellitus and obesity. This group had the lowest level of catestatin (1.53 ng/mL), which was 78.0% lower than in patients without metabolic disorders. Correlation analysis confirmed a strong direct relationship between catestatin levels and left ventricular ejection fraction ($r = 0.68$), as well as strong inverse correlations with end-diastolic volume ($r = -0.69$) and end-systolic volume ($r = -0.67$). A decrease in catestatin concentration is closely associated with an increase in left ventricular volume, its pathological remodelling, and a decrease in pumping function. The presence of polymorbid pathology leads to the most pronounced dilated type of left ventricular remodelling, and low catestatin levels are not only a marker but also a probable participant in the pathogenesis of adverse structural and functional changes in the myocardium

Keywords: chronic heart failure; coronary artery disease; type 2 diabetes mellitus; obesity; morpho-functional state of the myocardium

INTRODUCTION

Chronic heart failure (CHF) remains a global challenge for modern medicine, due to high mortality and disability rates among populations around the world. The problem becomes particularly acute in cases of ischaemic origin, when the pathological process is aggravated by comorbid conditions. The combination of myocardial ischaemia with metabolic disorders, in particular type 2 diabetes mellitus (T2DM) and obesity, creates a complex pathogenetic knot that accelerates the degradation of cardiac function. The search for new biological markers capable of reflecting the depth of structural changes in the myocardium under such conditions is critically important for improving the diagnosis and prognosis of the disease.

An analysis of scientific literature indicated that researchers were paying close attention to the problem of polymorbidity in cardiovascular pathology. In a large-scale review, B. Shahim *et al*. [1] emphasised that despite advances in therapy, the global burden of heart failure continues to grow, requiring an update of strategies for monitoring high-risk patients. Supplementing these data, A.D. Soto-mayor-Julio *et al*. [2], based on the AMERICCAASS registry, analysed the clinical characteristics of more than 2,500

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patients, proving that the presence of concomitant metabolic disorders significantly complicates the achievement of target indicators with standard drug therapy. The state of renal and metabolic functions plays a special role in the progression of ischaemic heart damage. Ukrainian scientists H.B. Mankovsky *et al.* [3] studied in detail the mechanisms of development of coronary artery disease (CAD) disease in patients with T2DM through the prism of renal filtration, demonstrating that insulin resistance is a trigger for microvascular complications that directly affect myocardial viability. In parallel with this, M. Mazurkiewicz *et al*. [4] investigated the role of adipokines and adipose tissue in patients with heart failure (HF), emphasising that obesity creates a specific pro-inflammatory environment that stimulates pathological remodelling of the left ventricle (LV).

The issue of structural remodelling of the heart in the context of hypertension, diabetes and obesity remains the focus of attention of both Ukrainian and foreign specialists. B.O. Shelest *et al*. [5] demonstrated in their study that the combined effect of T2DM and obesity in patients with hypertension leads to the most pronounced types of LV remodelling, in particular eccentric hypertrophy. These findings correlate with the results of the Framingham Heart Study presented by B. von Jeinsen *et al*. [6], where a large population sample confirmed the independent contribution of each metabolic factor to changes in heart geometry and volume parameters. Modern molecular cardiology is actively seeking explanations for these processes at the cellular level. S. Appunni *et al*. [7] presented the concept of molecular remodelling in comorbid conditions in their report, pointing to the activation of specific signalling pathways leading to myocardial fibrosis and a decrease in its contractile capacity under the influence of systemic inflammation. In this context, catestatin, a peptide derived from chromogranin A, is of particular interest. The role of catestatin as a multifunctional regulator was described in detail by E. Zalewska *et al*. [8], who characterised it as an endogenous negative regulator of the sympathoadrenal system (SAS) with cardioprotective and metabolic effects. This topic was further developed in the work of J. Kulpa *et al*. [9], where it was shown that this peptide not only inhibits the secretion of catecholamines, but also actively influences the oxidation of fatty acids and insulin sensitivity, which is critical for patients with T2DM. A study by Z. Qiu *et al*. [10] found that catestatin can protect the heart from diastolic dysfunction by reducing the generation of mitochondrial reactive oxygen species. This opens up new prospects for the use of the peptide as a marker of early stages of HF. On the other hand, the clinical significance of plasma catestatin levels was confirmed by S. Izci *et al*. [11], who demonstrated its prognostic value for mortality and severity of cardiovascular events, although their study focused on the acute phase of pulmonary embolism, highlighting the versatility of this biomarker.

Despite such a wide range of studies, it remains unclear how exactly catestatin levels correlate with specific morphofunctional parameters of the heart in patients who have concomitant CAD, T2DM and obesity. Most of the available studies focused on individual nosologies, while polymorbidity creates a unique metabolic profile that requires separate study. Thus, the aim of this study was to determine the role of catestatin in the mechanisms of structural and functional changes in the myocardium in patients with CHF of ischaemic origin with concomitant T2DM and obesity.

MATERIALS AND METHODS

The present clinical study was carried out during the period from 2022 to 2025 and involved a cohort of 225 individuals diagnosed with CHF of ischemic etiology who received specialised care at the cardiology unit of the Municipal Clinical Hospital No. 27 of the Kharkiv City Council. To allow for a comparative analysis of the disease course, participants were categorised into four distinct groups based on their metabolic status, where Group 1 comprised 75 patients with CHF arising from CAD with coexisting T2DM and obesity, Group 2 included 50 individuals with CHF and CAD accompanied by T2DM, Group 3 consisted of 50 patients with ischemic CHF and concomitant obesity and Group 4 served as a comparison group consisting of 50 patients presenting with signs of ischemic-origin CHF without any associated metabolic pathologies.

The criteria for inclusion of patients in the analysis were: age over 18 years; verified diagnosis of CAD with clinical and instrumental signs of CHF; presence or absence of concomitant metabolic disorders, namely: overweight, obesity of I-III degree (according to the World Health Organization [12] classification by body mass index) and T2DM in the stage of compensation or subcompensation; the presence of the patient's voluntary written consent to participate in the study and to the processing of personal data. The study protocols excluded pregnant women along with individuals suffering from acute infections, autoimmune disorders, or diffuse connective tissue pathologies. Potential participants were also ineligible if they presented with oncological conditions, disorders of the pituitary and hypothalamic axis, or chronic kidney disease characterised by a Glomerular Filtration Rate below 35 mL/min/1.73 m^2. Additional exclusion factors comprised symptomatic hypertension, a history of acute coronary syndrome, or cerebrovascular accidents occurring within the previous six months. Furthermore, the study did not enroll patients experiencing exacerbations of chronic inflammation, those with documented alcohol misuse or psychiatric illnesses, and individuals deemed unlikely to adhere to the research procedures. Finally, non-citizens of Ukraine were not considered for inclusion in this clinical investigation.

The studies were approved by the Ethics and Bioethics Committee of the Kharkiv National Medical University (Protocol No. 2 dated 12 October 2022) and conducted with the written consent of the participants and in accordance with the principles of bioethics set out in The Helsinki Declaration [13] and The UNESCO Universal Declaration on Bioethics and Human Rights [14]. All patients underwent transthoracic echocardiography using standard methodology on a RADMIR (Ultima PRO 30) ultrasound machine (Kharkiv, Ukraine). To assess cardiovascular coupling (CVC), the ratio of effective elasticity (Ea) to end-systolic elasticity of the LV (Es) was calculated using the LV volume-pressure curve: CVC = Ea/Es. Ea and Es were calculated non-invasively using echocardiographic parameters:

$$Ea = \frac{ESP}{SV}, \quad (1)$$

where ESP – the end-systolic pressure, SV – the stroke volume.

ESP was calculated using the formula:

$$ESP = 0.9 \times SBP, \quad (2)$$

where SBP – systolic blood pressure.

$$Es = \frac{ESP}{ESV}, \quad (3)$$

where ESV – the end-systolic volume.

The Ea/Es ratio within the range of 0.6 to 1.2 under physiological conditions was taken as an indicator reflecting the optimal interaction between the arterial system and the LV. The serum concentration of catestatin (ng/mL) was quantified via enzyme-linked immunosorbent assay (ELISA) utilising the CUSABIO Human Catestatin-1 ELISA Kit. The procedure strictly followed the manufacturer's protocol and was executed on a Labline-90 automated microplate analyser (Austria). All laboratory measurements were conducted at the Biochemical Department of the Central Research Laboratory within Kharkiv National Medical University (Ministry of Health of Ukraine). The primary data management, including the systematisation and visualisation of findings, was performed using Microsoft Office Excel. Comprehensive statistical processing was carried out using the Statistica 14.0 (TIBCO Software Inc., USA) software package. The normality of data distribution was verified through the Kolmogorov-Smirnov test. Quantitative variables following a normal distribution are expressed as the arithmetic mean (M) and standard deviation (SD). Inter-group differences for continuous variables were evaluated using Fisher's F-test (ANOVA). The strength and direction of associations between the studied myocardial parameters and catestatin levels were determined using Spearman's rank correlation coefficient (r). For all statistical tests, a p-value of less than 0.05 was considered to indicate statistical significance.

RESULTS AND DISCUSSION

The initial stage of the study involved a meticulous analysis of the age and gender distribution among the surveyed groups to ensure the validity of subsequent comparisons. Analysis of demographic indicators confirmed the homogeneity of the formed groups. No statistically significant differences were found between patients in terms of gender composition ($\chi^2 = 1.844$; $p = 0.606$) and average age ($F = 0.57$; $p = 0.636$), which allowed to conclude that the samples are comparable. A comparison of the study groups was presented in Table 1.

Table 1. Clinical characteristics of the examined groups

Indicator, units	Observation groups			
	Patients with CHF against a background of CAD, T2DM and obesity (n = 75)	Patients with CHF, CAD and concomitant T2DM (n = 50)	Patients with CHF, CAD and concomitant obesity (n = 50)	Patients with ischaemic CHF without metabolic disorders (n = 50)
Male, abs (%)	42 (56%)	27 (54%)	22 (44%)	26 (52%)
Female, abs (%)	33 (44%)	23 (46%)	28 (56%)	24 (48%)
Age, years	63.44 ± 2.06	64.47 ± 1.88	60.59 ± 2.43	63.27 ± 1.72

Source: compiled by the author

The study revealed deep structural and functional transformations of the LV myocardium in patients with ischemic CHF, particularly when complicated by metabolic disorders. The cumulative effect of T2DM and obesity significantly exacerbated the processes of pathological remodelling. As indicated in Table 2, patients in Group 1 exhibited the most severe deviations in all echocardiographic parameters. The LV end-systolic dimension (ESD) reached 4.86 ± 0.18 cm and the end-diastolic dimension (EDD) reached 6.56 ± 0.28 cm. When compared to Group 4, where ESD and EDD were 3.06 ± 0.17 cm and 4.08 ± 0.11 cm respectively, it becomes evident that the presence of T2DM and obesity promotes significant chamber dilatation ($p < 0.05$). The volumetric indicators showed even more alarming trends. The LVESV in Group 1 was 101.57 ± 4.16 mL, which is 117.6% higher than in Group 4. LV end-diastolic volume (EDV) was 192.16 ± 3.57 mL, a 76.9% increase compared to the group without metabolic disorders. Such dramatic expansion of the LV cavity in polymorbid patients suggests a severe loss of myocardial elasticity and a shift towards eccentric remodelling. The Left Ventricular Myocardium Mass Index (LVMMI) and Left Ventricular Myocardium Mass (LVMM) were highest in patients of Group 1 (171.64 ± 12.34 g/m^2 and 313.87 ± 17.34 g respectively). This indicated that the combination of ischemic damage and hyperinsulinemia, as a characteristic of T2DM, triggers robust hypertrophic signals. Interestingly, while Left Ventricular Posterior Wall (LVPW) and Interventricular Septum (IVS) thickness were slightly thinner in Group 1 compared to Group 4, this does not signify a lack of hypertrophy, but rather the transition to eccentric hypertrophy, where the wall thickness is insufficient for the vastly increased chamber volume. This is confirmed by the Relative Wall Thickness (RWT) value of 0.48 ± 0.02 in Group 1, which is significantly lower than the 0.67 ± 0.03 found in Group 4. Systolic function, measured by the Ejection Fraction (EF), was most compromised in the polymorbid group (42.67 ± 2.32%), representing a significant drop from the 54.43 ± 1.45% seen in Group 4. This drop below the 45-50% threshold in Group 1 highlighted the transition from CHF with preserved or mildly reduced EF to a more severe clinical phenotype. The serum concentration of catestatin varied dramatically between groups. The lowest level of catestatin (1.53 ± 0.21 ng/mL) was found in Group 1, which was statistically significantly lower than in Group 4 (6.96 ± 0.17 ng/mL). This 78% reduction in polymorbid patients indicated a massive exhaustion of the body's cardioprotective resources. Catestatin inhibit the release of catecholamines from chromaffin cells. Therefore, its critical deficiency in patients with

CAD, T2DM, and obesity likely results in "unchecked" sympathetic activity. This, in turn, accelerates heart rate, promotes arrhythmias, and worsens the ischemic state of the myocardium, creating a vicious cycle of damage.

Table 2. Myocardial morphofunctional parameters and catestatin levels

Indicator, units	Observation groups				p
	Patients with CHF against a background of CAD, T2DM and obesity (n = 75)	Patients with CHF, CAD and concomitant T2DM (n = 50)	Patients with CHF, CAD and concomitant obesity (n = 50)	Patients with ischaemic CHF without metabolic disorders (n = 50)	
	1	2	3	4	
ESD, cm	4.86 ± 0.18	4.09 ± 0.13	4.44 ± 0.12	3.06 ± 0.17	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
EDD, cm	6.56 ± 0.28	5.48 ± 0.14	6.23 ± 0.16	4.08 ± 0.11	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} < 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
LVPW, cm	1.29 ± 0.02	1.31 ± 0.01	1.30 ± 0.03	1.44 ± 0.04	$p_{1-2} > 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
IVS, cm	1.25 ± 0.02	1.29 ± 0.03	1.27 ± 0.04	1.36 ± 0.03	$p_{1-2} > 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
RWT	0.48 ± 0.02	0.51 ± 0.02	0.54 ± 0.01	0.67 ± 0.03	$p_{1-2} > 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
LVMMI, g/cm^2	171.64 ± 12.34	156.78 ± 8.67	169.31 ± 11.26	123.72 ± 9.78	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
LVMM, g	313.87 ± 17.34	258.76 ± 9.78	265.38 ± 11.76	203.51 ± 11.48	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
ESV, mL	101.57 ± 4.16	78.89 ± 3.56	94.12 ± 5.23	46.67 ± 3.12	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} < 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
EDV, mL	192.16 ± 3.57	139.25 ± 3.66	176.93 ± 4.28	108.64 ± 2.39	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} < 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
EF, %	42.67 ± 2.32	51.48 ± 2.71	49.34 ± 1.86	54.43 ± 1.45	$p_{1-2} < 0.05$ $p_{1-3} < 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} > 0.05$ $p_{3-4} < 0.05$

Table 2. Continued

Indicator, units	Observation groups				p
	Patients with CHF against a background of CAD, T2DM and obesity (n = 75)	Patients with CHF, CAD and concomitant T2DM (n = 50)	Patients with CHF, CAD and concomitant obesity (n = 50)	Patients with ischaemic CHF without metabolic disorders (n = 50)	
	1	2	3	4	
LAD, cm	4.93 ± 0.09	4.38 ± 0.06	4.78 ± 0.11	4.04 ± 0.05	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} < 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
RAD, cm	4.00 ± 0.08	3.52 ± 0.05	3.89 ± 0.07	3.44 ± 0.04	$p_{1-2} < 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} < 0.05$ $p_{2-4} > 0.05$ $p_{3-4} < 0.05$
Ea/Es	2.01 ± 0.06	1.89 ± 0.03	1.99 ± 0.02	1.78 ± 0.04	$p_{1-2} > 0.05$ $p_{1-3} > 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$
Catestatin, ng/mL	1.53 ± 0.21	4.86 ± 0.19	4.99 ± 0.20	6.96 ± 0.17	$p_{1-2} < 0.05$ $p_{1-3} < 0.05$ $p_{1-4} < 0.05$ $p_{2-3} > 0.05$ $p_{2-4} < 0.05$ $p_{3-4} < 0.05$

Source: compiled by the author

The correlation analysis of catestatin with indicators of the morpho-functional state of the myocardium is shown in Table 3. A strong inverse correlation was found between the level of catestatin and EDV (r = -0.69, p < 0.001), ESV (r = -0.67, p < 0.001); inverse correlations of moderate strength were found with ESD (r = -0.61, p < 0.001), EDD (r = -0.56, p < 0.001), LVMM (r = -0.56, p < 0.001), left atrium dimension (LAD) (r = -0.55, p < 0.001), right atrium dimension (RAD) (r = -0.49, p < 0.001), Ea/Es (r = -0.49, p < 0.001), left ventricular posterior wall (LVPW) (r = -0.44, p < 0.001) and LVMMI (r = -0.43, p < 0.001). Most importantly, the strong direct correlation with EF (r = 0.68, p < 0.001) provides evidence that maintaining catestatin levels may be essential for preserving the systolic pump function of the heart.

Table 3. Correlations between catestatin levels and parameters of the morphofunctional state of the myocardium ($r_{crit} = 0.41$)

Indicator, units	r	p
ESD, cm	−0.61	<0.001
EDD, cm	−0.56	<0.001
LVPW, cm	−0.44	<0.001
IVS, cm	−0.36	0.074
RWT	−0.33	0.065
LVMI, g/cm^2	−0.43	<0.001
LVMM, g	−0.56	<0.001
ESV, mL	−0.67	<0.001
EDV, mL	−0.69	<0.001
EF, %	0.68	<0.001
LAD, cm	−0.55	<0.001
RAD, cm	−0.49	<0.001
Ea/Es	−0.49	<0.001

Source: compiled by the author

The correlations found showed that a decrease in catestatin concentration is closely associated with an increase in LV volume, its pathological remodelling, and a decrease in pumping function. This confirms the hypothesis that low catestatin levels are not only a marker but also, probably, a participant in the pathogenesis of adverse structural and functional changes in the myocardium in patients with CHF complicated by metabolic disorders. The results obtained in this study provided compelling evidence that serum catestatin levels serve as a critically important biomarker

for assessing the severity of ischemic CHF, particularly in the complex setting of comorbid metabolic disorders. The synthesis of authors' findings with existing international data allows for a deeper understanding of the pathogenetic role of this peptide.

According to the comprehensive clinical and experimental studies conducted by S.K. Mahata *et al*. [15] and E. Zalewska *et al*. [16], catestatin functions as a pleiotropic cardioprotective peptide. Its primary mechanism involves counteracting the deleterious effects of catecholamine excess by inhibiting their secretion from chromaffin cells and adrenergic nerve endings. In this study, the lowest levels of catestatin (1.53 ng/mL) were recorded in Group 1 (CHF + T2DM + Obesity). This significant decline, when viewed alongside the most unfavorable LV parameters, reflects a state of "exhaustion" or decompensation of this endogenous protective mechanism. This aligns with the findings of J.S. Rathee *et al*. [17], who recently emphasised that catestatin and its variants play a pivotal role in physiological cardiovascular regulation, and its deficiency leads to an inability to suppress the SAS effectively. Consequently, low catestatin levels fail to mitigate the proarrhythmic, vasoconstrictive, and remodelling effects of chronic SAS hyperactivation.

The relationship between catestatin and myocardial structure is a central theme in modern cardiology. Research by Z. Qiu *et al*. [10] indicated that catestatin is not merely a marker but an active protector against diastolic dysfunction. In their experimental models, catestatin was shown to attenuate mitochondrial reactive oxygen species generation, thereby reducing myocardial hypertrophy and fibrosis. Authors' clinical data strongly correlate with these experimental findings: the high inverse correlations found between catestatin and LV volumes (EDV r = -0.69; ESV r = -0.67) suggest that in patients with low catestatin, the heart lacks a critical defense against oxidative stress. This is further supported by Q. Yan *et al*. [18], who highlighted targeting oxidative stress as a vital preventive approach for cardiovascular disease, identifying peptides like catestatin as key components of this strategy.

A significant contribution to the understanding of post-infarction remodelling was made by D. Zhu *et al*. [19], who identified catestatin as a novel predictor of LV remodelling after acute myocardial infarction. While their study focused on the acute phase, authors' results extend this observation to CHF, showing that persistent catestatin deficiency in polymorbid patients is associated with the most pronounced dilated remodelling (ESV increase of 117.6%). The prognostic value of this biomarker deserves special attention. Ł. Wołowiec *et al.* [20] established that a decrease in catestatin is associated with a worsening two-year prognosis for patients with heart failure and reduced ejection fraction. Conversely, S.Y. Chu *et al*. [21] found that elevated catestatin might be a more sensitive predictor of cardiac death in patients with mildly reduced or preserved ejection fraction compared to those with severely reduced EF. Authors' findings bridge these perspectives: the lowest catestatin levels in this study were associated with the lowest ejection fraction (42.67 ± 2.32%), reinforcing the hypothesis that catestatin deficiency is a marker of severe systolic dysfunction and heightened cardiovascular risk in polymorbid states.

Metabolic integration is another facet of catestatin's action. M.P. Gallo *et al*. [22] demonstrated that catestatin induces glucose uptake and $GLUT_4$ translocation in cardiomyocytes, playing a role in metabolic homeostasis. This is particularly relevant to authors' results in Group 1. The presence of T2DM and obesity likely creates a state of "metabolic exhaustion". As I. Dunaieva & O. Bilovol [23] observed in their research on comorbid hypertension, catestatin levels are significantly altered in patients with combined cardiovascular and metabolic disorders, serving as a sensitive indicator of metabolic syndrome-related sympathetic overactivation. Authors' study confirmed this, showing that the combination of T2DM and obesity leads to a much steeper decline in catestatin (1.53 ng/mL) than either condition alone (Groups 2 and 3). Furthermore, the work of J.A. Borovac *et al*. [24] noted that catestatin levels are dynamic in acutely decompensated HF. Authors' data suggested that in chronic stable patients with polymorbidity, catestatin levels do not "recover" but remain low, contributing to the persistent progression of LV dilatation.

In conclusion, this data demonstrated that catestatin is a critically important biomarker. The results of the study, supported by the findings of international scientific community, suggest that low catestatin levels in this cohort not only reflect but may also exacerbate the degree of pathological LV remodelling. This emphasised the urgent need for clinical strategies aimed at correcting SAS hyperactivation. Moreover, the strong correlations with contractile function observed in research highlighted the potential prospect of catestatin-based replacement therapy or pharmacological stabilisation as a future therapeutic avenue for patients with ischemic HF and metabolic syndrome.

CONCLUSIONS

The combination of metabolic disorders in the form of T2DM and obesity critically worsens the structural and functional state of the myocardium and leads to a maximum deficiency of catestatin. Patients with CHF of ischaemic origin against a background of concomitant T2DM and obesity had the worst indicators, which included the maximum increase in end-systolic volume (101.57 ± 4.16 mL) and end-diastolic volume (192.16 ± 3.57 mL), the highest left ventricular myocardial mass (313.87 ± 17.34 g) and the lowest left ventricular ejection fraction (42.67 ± 2.32%) compared to all other groups. At the same time, this group had the lowest level of catestatin (1.53 ± 0.21 ng/mL), which was significantly lower than in all other groups. This indicates that the presence of polymorbid pathology leads to the most pronounced dilated type of left ventricular remodelling.

Correlation analysis confirmed a strong direct correlation between the level of catestatin and left ventricular ejection fraction ($r = 0.68$, $p < 0.001$), and also revealed strong inverse correlations between catestatin and left ventricular volume parameters: end-diastolic ($r = -0.69$, $p < 0.001$) and end-systolic volumes ($r = -0.67$, $p < 0.001$). This demonstrates that a decrease in catestatin concentration is closely associated with an increase in left ventricular volumes, its pathological remodelling, and a decrease in pumping function. The data obtained confirm the hypothesis that low catestatin levels are not only a marker but also a probable participant in the pathogenesis of adverse

structural and functional changes in the myocardium. Further study of the relationship between low catestatin levels and systemic markers will help confirm the hypothesis that catestatin deficiency leads to a lack of myocardial protection against oxidative stress and fibrosis, as well as to establish optimal catestatin threshold values that can be used for risk stratification and identification of patients with polymorbid pathology at high risk of decompensation and rapid progression of left ventricular remodelling.

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CONFLICT OF INTEREST

The author confirms that there is no conflict of interest regarding the published material.

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Роль катестатину в ремоделюванні міокарда лівого шлуночка у хворих із поєднаною кардіометаболічною патологією

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Анотація. Актуальність роботи зумовлена необхідністю вивчення впливу катестатину на структурно-функціональний стан міокарда у пацієнтів із хронічною серцевою недостатністю за умови кардіометаболічної поліморбідності (цукрового діабету 2 типу та ожиріння). Мета полягала в оцінці ролі катестатину у формуванні структурно-функціональних змін міокарда у хворих з хронічною серцевою недостатністю, що виникла на тлі ішемічної хвороби серця з супутнім цукровим діабетом 2 типу та ожирінням. Дослідження залучило 225 пацієнтів, які були розподілені на чотири групи залежно від наявності метаболічних порушень. Для оцінки морфо-функціонального стану міокарда проводилось трансторакальне ехокардіографічне дослідження. Рівень катестатину в сироватці крові визначали імуноферментним методом. Для оцінки ступеня взаємозв'язку використовували коефіцієнт кореляції Спірмена. Результати продемонстрували, що найбільш несприятливі показники ремоделювання лівого шлуночка, включаючи максимальне зростання кінцево-систолічного об'єму (101,57 мл) та кінцево-діастолічного об'єму (192,16 мл), а також найнижчу фракцію викиду (42,67 %), були зафіксовані у пацієнтів із поєднанням хронічної серцевої недостатності, ішемічної хвороби серця, цукрового діабету 2 типу та ожиріння. У цій групі виявлено найнижчий рівень катестатину (1,53 нг/мл), знижений на 78,0 % порівняно з пацієнтами без метаболічних порушень. Кореляційний аналіз підтвердив сильний прямий зв'язок між рівнем катестатину та фракцією викиду лівого шлуночка (r = 0,68), а також сильні зворотні зв'язки з кінцево-діастолічним об'ємом (r = -0,69) та кінцево-систолічним об'ємом (r = -0,67). Зниження концентрації катестатину тісно асоційоване зі збільшенням об'ємів лівого шлуночка, його патологічним ремоделюванням та зниженням насосної функції. Наявність поліморбідної патології призводить до найбільш вираженого дилатаційного типу ремоделювання лівого шлуночка, а низький рівень катестатину є не лише маркером, а й вірогідним учасником патогенезу несприятливих структурно-функціональних змін міокарда

Ключові слова: хронічна серцева недостатність; ішемічна хвороба серця; цукровий діабет 2 типу; ожиріння; морфо-функціональний стан міокарда