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Features of adipokine-mediated myocardial injury in patients with ST-segment elevation myocardial infarction

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Abstract. The aim of the study was to determine the features of adipokine-mediated myocardial injury in patients with ST-elevation myocardial infarction and excess body weight/obesity by assessing the relationship between leptin levels and metabolic disturbances with the severity of atherothrombosis and the severity of the course of acute coronary syndrome according to laboratory and instrumental data. A single-centre prospective cohort study was conducted, which included 120 patients with ST-segment elevation myocardial infarction, who were divided into three groups according to the body mass index: group 1 – excess body weight (25.0-29.9 kg/m², n = 42); group 2 – obesity (⩾ 30 kg/m², n = 34); group 3 – normal body mass index (18.5-24.9 kg/m², n = 44). In the obesity group, the highest concentrations of leptin (57.27 ± 4.1 ng/mL) and troponin I (4.09 ± 4.33 ng/mL) were found, which significantly exceeded the indicators of the other groups (ANOVA $p < 0.001$). A strong positive relationship was established between the body mass index and leptin ($r = 0.87$; $p < 0.001$) and between leptin and troponin I ($r = 0.46$; $p = 0.008$), which indicated the functioning of a single adipokine-apoptotic axis in the context of myocardial injury. Instrumental methods confirmed a more severe nature of myocardial damage in obesity: lower left ventricular ejection fraction (46.3 ± 6.2%), higher left ventricular mass index (131 ± 22 g/m²), increased wall thickness, the greatest elevation of the ST segment (4.88 ± 2.10 mm; ANOVA $p = 0.013$), higher frequency of three-vessel lesion (28.6%), and maximal values according to the SYNTAX scale (24.5 ± 8.9 points; $p < 0.001$). Multiple regression analysis confirmed that the body mass index ($\beta = 0.42$; $p < 0.001$), SYNTAX ($\beta = 0.36$; $p = 0.004$), and reduced ejection fraction ($\beta = -0.33$; $p = 0.008$) are independent predictors of increased levels of troponin I

Keywords: obesity; excess body weight; leptin; acute coronary syndrome; coronarography; ejection fraction; body mass index

INTRODUCTION

ST-elevation myocardial infarction (STEMI) remains a leading cause of mortality, and concomitant obesity and other comorbid conditions form a proatherogenic and proinflammatory phenotype that deepens ischemic and reperfusion injury. Adipose tissue under metabolic dysfunction produces adipokines (leptin, resistin) and cytokines that contribute to endothelial dysfunction, thrombus formation, activation of caspases, and death of cardiomyocytes. Despite the available data from modern scientific research, the study of the relationship between adipokine levels and the nature of atherothrombosis and the degree of myocardial injury in STEMI according to instrumental diagnostic data remains relevant.

Recent studies on adipokine-dependent myocardial injury emphasised the persistent increase in obesity among adults worldwide up to 2022, which highlighted the importance of obesity-related myocardial injury for public health. As indicated in the work of O.Ye. Labinska [1] a clear association was established between obesity and the occurrence of cardiovascular diseases due to the fact that adipose tissue produces more than 100 adipokines, which include interleukins, prostaglandins, tumour necrosis factor alpha, leptin, adiponectin, angiotensinogen, resistin. Certain chemokines expressed by adipose tissue, including caspase-9, play an important role in attracting inflammatory leukocytes to adipose tissue, which is a key link in the development of obesity-associated inflammatory processes. According to the results of the study by V.M. Zhebel & O.L. Starzhynska [2], oxidative stress plays a special role in acute coronary syndrome (ACS), in particular, it is the lead-

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ing link in the pathogenesis of reperfusion injury of the myocardium. The products of free radical oxidation can initiate processes of cardiomyocyte death and be responsible for 50% of the final size of the necrotic area in ACS, as well as the occurrence of reperfusion arrhythmias and systolic microvascular dysfunction.

The involvement of leptin in inflammatory processes underlying atherosclerosis has raised interest in its potential as a biomarker of cardiovascular diseases, particularly among the authors A. Ismaiel *et al.* [3], who noted that previous studies demonstrated a positive correlation between increased leptin levels and the development of ischemic heart disease (IHD) and, as a consequence, ACS. It is known that elevated leptin levels in patients with ACS and concomitant metabolic syndrome may indicate that leptin may serve both as a biomarker and a potential therapeutic target for risk stratification and treatment of patients with STEMI. At the same time, in the work of B. Du *et al.* [4], it is emphasised that during the period of myocardial ischemia the process of apoptosis occurs slowly; however, after the transition to the reperfusion phase, oxidative stress, inflammatory reactions, and mitochondrial damage intensify, leading to activation of death receptors such as TNF-R and Fas. This activation triggers both external (through caspase-9, caspase-8, caspase-3) and internal (through cytochrome c) pathways of apoptosis.

Translational reviews by S.H. Liu *et al*. [5] confirmed that chronic hyperleptinemia in obesity promotes inflammation, fibrosis, autonomic dysregulation, and metabolic remodelling, thereby creating susceptibility to unfavorable postischemic remodelling of the myocardium. However, due to the phenomenon of the "obesity paradox", in acute vascular catastrophes obesity plays a positive role in greater adaptive mechanisms during ischemia and hypoxia of the myocardium. G. Ndrepepa *et al*. [6] demonstrated that leptin derived from epicardial or pericardial adipose tissue induces apoptosis of cardiomyocytes and disrupts myocardial homeostasis, which provides a plausible paracrine link between regional obesity and the biology of infarction. In particular, the study by T. Vilariño-García *et al*. [7] described that in most cases hyperleptinemia is associated with adverse cardiovascular outcomes. In fact, leptin may be produced by the heart itself to function as an autocrine/paracrine factor. Nevertheless, documented cases in rodent studies indicated that animals with leptin deficiency may exhibit a cardioprotective effect. This protection is attributed to coronary artery vasodilation, activation of endothelial nitric oxide synthase, and activation of endothelial progenitor cells. The findings of R.A. Byrne *et al*. [8] within the structure of the European recommendations of 2023 indicated that the morphological characteristics of the coronary arteries after STEMI are significantly altered by cardiometabolic comorbid conditions and systemic inflammation, despite advances in primary percutaneous coronary intervention (PCI) and supportive pharmacotherapy.

The longitudinal cohort study by L. Liu *et al.* [9] demonstrated that lower levels of adiponectin and higher levels of leptin are independently associated with higher levels of residual cholesterol and its progression, and that atherogenic features are closely related to plaque burden and vulnerability. According to the results of the study by D. Skrypnik *et al.* [10], an elevated serum leptin level is significantly associated with IHD. Due to the growing amount of scientific evidence, leptin has begun to be considered not as a marker but as a trigger of IHD, mediating atherosclerotic processes independently of traditional cardiovascular risk factors and of body weight status. Higher serum leptin concentrations were associated with arterial stiffness and an increased number of stenotic coronary arteries in patients with IHD. Acute myocardial infarction also significantly increases leptin concentration in the blood. Dysregulation of leptin metabolism has a negative impact on the heart, affecting cardiac remodelling, contractile function, and cardiac metabolism. In addition, leptin enhances platelet activation in patients with IHD and alters the morphology of the left ventricle [11].

In the work of J. Wang *et al*. [12], it is reported that a significant correlation was found between leptin and several indicators related to heart rate, arterial pressure, peripheral vascular resistance, the pumping and contractile function of the heart, as well as pulmonary ventilation function. The angiographic complexity and spread of disease in ACS are more consistently associated with high-risk clinical profiles. K. Skalsky *et al.* [13] identified numerous predictors of multivessel disease, including dyslipidemia, renal dysfunction, and a history of heart failure, factors that often coexist with obesity.

Aim of the study – to evaluate the effect of obesity and overweight on adipokine-dependent mechanisms of myocardial damage in patients with ST-segment elevation myocardial infarction.

MATERIALS AND METHODS

A single-centre prospective cohort study was conducted from 2022 to 2025, covering 120 hospitalised patients with ST-segment elevation myocardial infarction at the Zaporizhzhia Regional Clinical Hospital. Diagnosis, reperfusion strategy, and inpatient treatment were carried out in accordance with the recommendations of R.A. Byrne *et al.* [8] and the national unified clinical protocol of the Ministry of Health of Ukraine [14]. The study protocol No. 10 dated 18.09.2022 received approval from the institutional ethics committee, and written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the Declaration of Helsinki [15].

Inclusion criteria were patient age from 18 to 90 years, the presence of confirmed ST-elevation myocardial infarction according to symptoms, typical ischemic chest pain, ST-segment elevation on 12-lead electrocardiography (ECG), and elevated levels of high-sensitivity cardiac troponin I, availability of general clinical laboratory data, and performance of echocardiography. All patients underwent primary percutaneous coronary intervention as the reperfusion method. A mandatory condition for inclusion was the signing of informed consent to participate in the study. Exclusion criteria included myocardial infarction without ST-segment elevation, decompensated chronic renal or hepatic insufficiency, acute surgical pathology of non-cardiac origin, active inflammatory diseases, confirmed sepsis, malignant neoplasms, or refusal to participate in the study.

All patients were stratified according to body mass index (BMI) in accordance with the generally accepted classification according to the Centers for Disease Control and

Prevention [16]: group 1 included patients with overweight (25.0-29.9 kg/m², n = 42), group 2 included patients with obesity (≥ 30.0 kg/m², n = 34), and group 3 represented the control group with normal BMI (18.5-24.9 kg/m², n = 44). Standard 12-lead electrocardiograms were recorded at admission to determine the infarct-related artery, to quantify cumulative ST-segment elevation, and to detect reciprocal changes or rhythm disturbances. The degree of ischemic injury was assessed using an ECG-based injury index representing the total sum of ST elevation in all affected leads.

Transthoracic echocardiography was performed within 24-48 hours after hospitalisation using standard two-dimensional and Doppler imaging techniques. Left ventricular end-diastolic and end-systolic volumes were measured, and ejection fraction was calculated using the modified biplane Simpson method. In addition, the thickness of the interventricular septum (IVS) and the posterior wall of the left ventricle, as well as the left ventricular myocardial mass index, were assessed. All patients underwent coronary angiography to identify the infarct-related artery, to assess the type and morphology of coronary lesions, and to evaluate blood flow before and after the intervention according to the Thrombolysis in Myocardial Infarction (TIMI) scale [17]. The number of affected vessels and the complexity of coronary artery disease were quantified using the SYNTAX score [18] calculated by a specialised scoring calculator. Optimal reperfusion was defined as achieving TIMI 3 flow after PCI.

Statistical analysis included tests for normality of data distribution using the Shapiro-Wilk test and for homogeneity of variances using Levene's test. For comparisons among the three BMI groups, one-way analysis of variance (ANOVA) with Tukey's post-hoc test was applied for normally distributed variables, while the Kruskal-Wallis test with Dunn's correction was applied for non-parametric data. For comparisons between two groups, an unpaired t-test or the Mann-Whitney U test was used, as appropriate. Correlations between variables were assessed using Pearson or Spearman coefficients, with a two-tailed p-value < 0.05 considered statistically significant. Statistical analysis was based on measurement of mean values and standard deviation across the three groups. Anthropometric data (age, height, weight, sex), laboratory indicators (quantitative troponin I level, immunoassay data via ELISA assessing levels of caspase-9 and leptin), and instrumental findings (electrocardiographic data – ST elevation amplitude in leads; echocardiographic data – ejection fraction by Simpson, left ventricular wall thickness, IVS; coronary angiographic data – degree of stenosis of the left coronary artery, circumflex artery, left anterior descending artery, and right coronary artery) were evaluated. To determine independent predictors of high-sensitivity cardiac troponin I levels, a multiple linear regression model was constructed, including BMI, leptin, caspase-9, age and sex as covariates. All statistical analyses were performed using Statistica 13 and Microsoft Excel 2016.

RESULTS AND DISCUSSION

Demographic and clinical-anamnestic characteristics. The mean age of the patients included in the study was 64.9 ± 12.86 years. There are no significant differences in this indicator were found stratified by BMI: in the excess body weight (EBW) group, the mean age was 65.36 ± 12.64 years; in the obesity group, 63.85 ± 11.83 years; and in the control group, 65.27 ± 14.03 years. Preliminary analysis using the Shapiro–Wilk test demonstrated no significant deviations from the normal age distribution in all three groups ($p > 0.05$), and Levene's test showed homogeneity of variances ($p > 0.05$), allowing the use of ANOVA. The difference between the mean age values across the BMI groups did not reach statistical significance ($p > 0.05$), indicating the comparability of the samples by age.

Gender analysis revealed marked age differences between men and women. In all three groups, male patients were statistically significantly younger than female patients. The parametric t-test was used to compare age between genders. In particular, in the first group, the mean age of men was 58.96 ± 10.45 years, whereas that of women was 75.75 ± 8.23 years (a difference of 16.79 years, $p < 0.01$ according to the unpaired t-test). In the second group, the mean age of men was 60.08 ± 11.62 years versus 72.90 ± 6.28 years in women (a difference of 12.82 years, $p < 0.02$), and in the third group, 59.69 ± 13.35 years in men and 73.33 ± 10.93 years in women (a difference of 13.64 years, $p < 0.02$). In terms of sex distribution, the sample was generally characterised by a predominance of men – 76 individuals vs 44 women. The proportion of men increased in parallel with rising BMI: in the excess body weight group – 61.9%, in the obesity group – 70.6%, and in the control group – 59.1%. Gender-age data of the participants were presented in Figure 1.

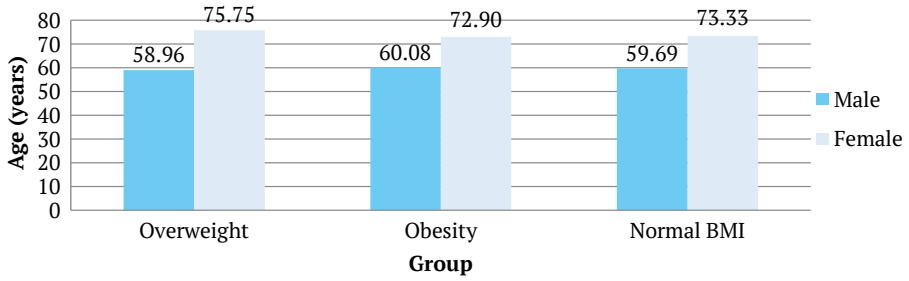

Figure 1. Gender-age characteristics of the sample by groups

Source: author's research

Analysis of sex distribution among the three groups using Pearson's χ^2 test showed no statistically significant differences ($\chi^2 = 3.98$; df = 2; $p = 0.13$). An additional trend test demonstrated only a tendency toward an increasing proportion of men with rising BMI ($p \approx 0.08$), which did not reach the threshold for statistical significance. Pairwise

comparisons of proportions (using χ^2 or Fisher's exact test, depending on expected frequencies) likewise revealed no significant differences between individual groups ($p > 0.29$). At the same time, for the obesity group, elevated relative odds for male sex were calculated (OR = 1.67; RR = 1.19) compared with the control group, reflecting a clinically noticeable, although statistically nonsignificant, tendency toward a higher proportion of men in this cohort.

Biochemical parameters and adipokine profile. Biochemical profiling demonstrated a pronounced metabolic gradient between the groups. The mean leptin concentration was 36.60 ± 2.9 ng/mL in group 1, 57.27 ± 4.1 ng/mL in group 2, and 28.92 ± 2.5 ng/mL in the control group. With acceptable values ($p > 0.05$), one-way ANOVA was used for between-group comparison, which revealed statistically significant differences in mean leptin levels among the three groups ($p < 0.001$). Subsequent Tukey post-hoc analysis showed that leptin levels in the obesity group were significantly higher compared with both the control group and the EBW group ($p < 0.05$ for both comparisons), and patients with EBW also had higher values compared with controls ($p < 0.05$). The mean troponin I levels across the groups were as follows: group 1 – 3.46 ± 2.17 ng/mL, group 2 – 4.09 ± 4.33 ng/mL, group 3 – 2.54 ± 2.19 ng/mL. Correlation analysis demonstrated a strong positive relationship between leptin and BMI ($r = 0.87$; $p < 0.001$), and a moderate positive relationship between leptin and troponin I ($r = 0.46$; $p = 0.008$).

Caspase-9 concentrations mirrored the leptin gradient: maximal values in the obesity group, intermediate values in the EBW group, and minimal values in the normal BMI group. Correlation analysis showed an exceptionally strong positive relationship between leptin and caspase-9 ($r \approx 0.99$; $p < 0.001$), indicating their parallel increase within a single adipokine-apoptotic axis. Comorbid conditions were represented predominantly by arterial hypertension (AH) and type 2 diabetes mellitus (T2DM). The prevalence of AH was 73.3%, and that of T2DM was 19.8%, consistent with the typical profile of patients with STEMI. Comparison of AH and T2DM frequencies between BMI groups using the χ^2 test did not show statistically significant differences ($p > 0.05$), although the proportion of such conditions was slightly higher in the obesity group.

ECG and echocardiographic parameters. ECG analysis revealed differences reflecting the degree of ischemic and reperfusion injury of the myocardium. The QRS ECG complex duration in patients with obesity was 101 ± 13 ms, whereas in the control group it was 92 ± 10 ms. According to results of the unpaired t-test, QRS ECG complex prolongation in the obesity group was statistically significant ($p = 0.016$). The magnitude of ST-segment elevation – a key marker of acute ischemia – also differed substantially between BMI groups. The mean values were as follows: 3.46 ± 1.23 mm in the EBW group, 4.88 ± 2.10 mm in the obesity group, and 3.22 ± 1.89 mm in the normal BMI group. The maximal recorded ST-elevation values were 6.8 mm in a patient with obesity, 5.3 in a patient with EBW, and 5.1 mm in the control group.

The Shapiro-Wilk test showed no significant deviations from normal distribution of ST elevation in any group ($p > 0.05$), and Levene's test confirmed comparable variance ($p > 0.05$). This allowed the use of one-way ANOVA, which demonstrated statistically significant between-group differences ($F = 4.62$; $p = 0.013$). Subsequent Tukey post-hoc testing showed that patients with obesity had significantly higher ST-elevation compared with the control group ($p = 0.009$) and with the EBW group ($p = 0.018$). No statistically significant difference was found between the EBW group and the control ($p = 0.74$). Correlation analysis demonstrated a positive association between the degree of ST elevation and biochemical markers of myocardial injury and metabolic stress: troponin I ($r = 0.57$; $p = 0.003$) and leptin ($r = 0.42$; $p = 0.015$). For these variables, Pearson's correlation coefficient was applied, given the approximate normality of distributions and linearity of relationships. The presented statistical findings were shown in Figure 2 in the form of box plots. Box plots showed median values (horizontal line), interquartile ranges (boxes), and range (whiskers).

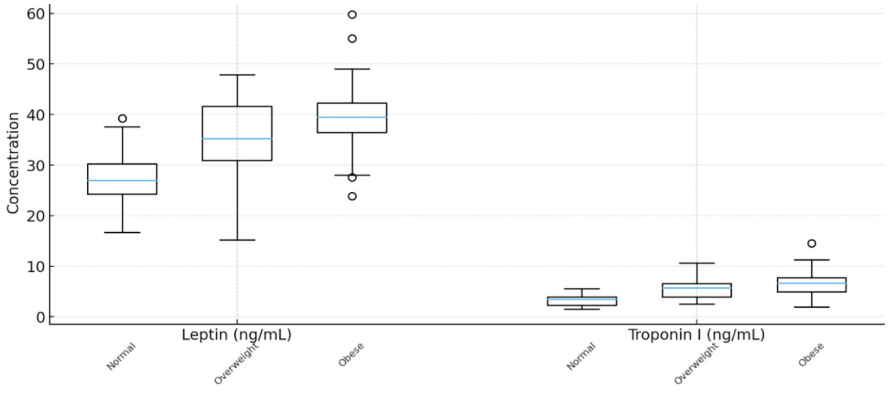

Figure 2. Distribution of serum leptin and cardiac troponin I levels across BMI categories in patients with STEMI
Source: author's research

Echocardiographic data confirmed progressive deterioration of systolic function and structural myocardial remodelling with increasing BMI. The left ventricular ejection fraction (LVEF) was 46.3 ± 6.2% in patients with obesity, 51.8 ± 5.9% in individuals with EBW, and 55.9 ± 5.6% in the control group. The Shapiro-Wilk test confirmed normal distribution of LVEF, and Levene's test indicated homogeneity of variances ($p > 0.05$), allowing the use of ANOVA. Between-group differences in LVEF were statistically significant ($p < 0.001$), and Tukey post-hoc analysis

demonstrated a consistent decrease in LVEF from the control group to EBW and further to obesity (all $p < 0.05$ in pairwise comparisons). Parallel to the decline in LVEF, an increase in the left ventricular mass index (LVMI) was observed: 131 ± 22 g/m² in the obesity group, 112 ± 17 g/m² in the EBW group, and 97 ± 14 g/m² in the control group ($p < 0.001$ by ANOVA). A similar pattern was observed for left ventricular wall thickness: IVS – 11.3 ± 1.2 mm in the obesity group, posterior wall – 11.4 ± 1.3 mm, with statistically significant differences compared with the other two groups ($p < 0.001$). All calculated echocardiographic parameters are presented in the summary diagram shown in Figure 3.

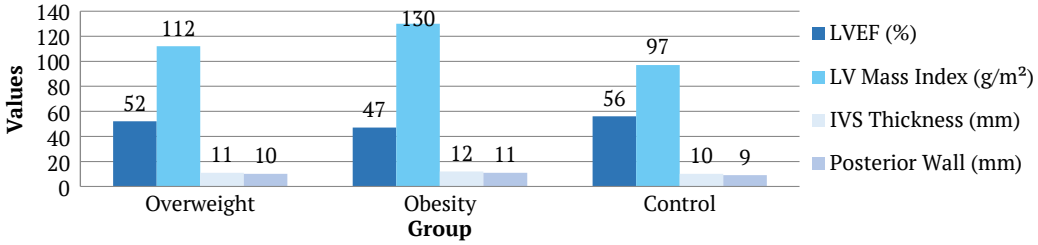

Figure 3. Echocardiographic parameters: LVEF, LVMI, posterior wall thickness, IVS across study groups
Source: author's research

Correlation analysis demonstrated inverse associations between LVEF and leptin ($r = -0.47$; $p = 0.009$), indicating that each incremental rise in leptin concentration was accompanied by a measurable reduction in systolic performance. A similarly strong negative relationship was identified between LVEF and BMI ($r = -0.58$; $p < 0.001$), with regression analysis showing that a 1 kg/m² increase in BMI was associated with an average 0.6-0.8% decrease in LVEF. Moreover, multivariate modelling confirmed that both BMI ($\beta = -0.52$; $p < 0.001$) and leptin ($\beta = -0.39$; $p = 0.014$) independently contributed to the decline in ejection fraction, explaining nearly 42% of the total variance in LVEF. These findings clearly demonstrated that rising body weight and adipokine dysregulation exert a quantifiable negative impact on left ventricular systolic function in patients with acute coronary syndrome.

Angiographic and reperfusion parameters. According to coronary angiography findings, multivessel disease was more frequently recorded in patients with obesity. The incidence of triple-vessel disease was 28.6% in the obesity group, 19.1% in the EBW group, and 15.9% in the control group ($p = 0.042$ according to Pearson's χ^2 test), indicating a greater prevalence of diffuse atherosclerotic involvement in obesity. The mean SYNTAX score, reflecting the anatomical complexity and extent of coronary atherosclerosis, was significantly highest in the obesity group. Based on the angiographic data obtained after coronary angiography, the SYNTAX score values were 24.5 ± 8.9 in patients with obesity, 18.7 ± 7.2 in individuals with EBW, and 14.2 ± 5.6 in the control group ($p < 0.001$ by ANOVA). Tukey post-hoc analysis demonstrated significant differences among all three groups ($p < 0.05$), confirming a progressive increase in anatomical complexity of coronary artery disease with rising BMI.

Correlation analysis revealed a strong positive association between the SYNTAX score and leptin level ($r = 0.64$; $p < 0.001$). The correlation coefficient between SYNTAX and BMI was $r = 0.71$ ($p < 0.001$). These correlations indicate a close interplay between the metabolic and anatomical components of atherosclerosis. Reperfusion parameters according to the TIMI scale showed that preprocedural blood flow TIMI 0-1 was more frequently observed in patients with obesity (78.6%) compared with the control group (63.6%), although these differences did not reach statistical significance according to the χ^2 test ($p > 0.05$). Restoration of full coronary blood flow TIMI 3 after primary PCI was 85.7% in the obesity group, 91.0% in the EBW group, and 93.2% in the control cohort.

Multivariable determinants of myocardial injury. To integrate the obtained data, a multiple linear regression analysis was performed with troponin I concentration as the dependent variable. According to the analysis, BMI showed $\beta = 0.42$ ($p < 0.001$), the SYNTAX score $\beta = 0.36$ ($p = 0.004$), and reduced LVEF $\beta = -0.33$ ($p = 0.008$). These factors represented independent predictors of troponin I level, and the constructed model explains 63% of the total variance of this indicator ($R^2 = 0.63$). This indicated that metabolic (BMI), anatomical (SYNTAX score), and functional (LVEF) parameters jointly contribute to the extent of myocardial necrosis in STEMI. A summary of the multivariable statistical analysis and linear regression results for predictors of troponin I levels was presented in Table 1.

Table 1. Multiple linear regression for determinants of adipokine-mediated myocardial injury and troponin I

Predictor	β coefficient	Standard error	p-value
BMI (kg/m²)	0.42	0.08	<0.001
SYNTAX score	0.36	0.10	0.004
LVEF (%)	–0.33	0.11	0.008
Leptin (ng/mL)	0.29	0.09	0.013
Caspase-9 (pg/mL)	0.25	0.08	0.021
Age (years)	0.10	0.06	0.18
Low-Density Lipoprotein Cholesterol (mmol/L)	0.12	0.07	0.14

Source: author's research

The obtained results indicated that even with a similar mean age across BMI groups, men with STEMI manifest the disease at a substantially younger age than women. Age-related trends point to an earlier manifestation of STEMI in patients with obesity in this study, which is consistent with the findings of D. Demirci *et al.* [19], who reported that patients with ACS and severe obesity were younger than those with ACS in the classes of class I obesity, EBW, and normal weight (52.8 ± 9.9 versus 55.3 ± 10.9, 56.8 ± 11.4, and 61.4 ± 14.2, respectively; $p < 0.001$). BMI showed a strong inverse linear association with earlier age of first ACS. Patients with EBW, class I obesity, and severe obesity experienced their first ACS episode earlier than normal-weight patients by 3.9, 6.1, and 7.7 years, respectively ($p < 0.001$).

In the study by A.J. Fischer *et al.* [20], similar gender and age trends in STEMI were confirmed. Women accounted for 32.8% of STEMI cases (n = 5714). They were older than men (women: median 74 years, interquartile range [IQR] 22; men: 60 years, IQR 19). Among 11,629 patients with STEMI in the study by J. Schmucker *et al.* [21], 2.3% had severe obesity. These patients were more frequently women and were on average 8.6 years younger than normal-weight patients (57.8 ± 12 versus 66.4 ± 14 years, $p < 0.01$). In author's study, the identified metabolic gradient (increasing leptin, troponin I, and caspase-9 with rising BMI) confirms that obesity forms an unfavourable prognostic STEMI phenotype. The strong correlation of leptin with BMI and troponin, as well as the nearly linear association between leptin and caspase-9 ($r \approx 0.99$), supports the concept of adipokine-mediated myocardial injury through activation of mitochondrial apoptosis.

In the study by O.Ye. Labinska [1], the serum leptin level upon hospital admission in patients with STEMI and normal body weight was 6.65 ± 0.55 ng/mL, in individuals with STEMI and EBW – 16.01 ± 1.73 ng/mL, and in patients with STEMI and class I-III obesity – 38.64 ± 3.1 ng/mL. In patients with EBW and obesity, these values were significantly higher than in normal-weight individuals. Similar findings were reported in the by A. Ismaiel *et al*. [3], where leptin levels were measured in serum or plasma and compared between patients diagnosed with ACS and healthy controls. The pooled analysis of leptin levels resulted in a mean difference of 10.508 ng/mL (95% CI 3.670-17.346). Significant heterogeneity was also observed, with $I^2 = 98.63\%$ and a p-value < 0.001.

ECG findings (greater ST elevation and QRS prolongation in patients with obesity), combined with higher troponin I levels, reflect a larger volume of ischemic and necrotic myocardial injury. The positive correlations between ST elevation, troponin I, and leptin indicate a link between metabolic inflammation and the electrical manifestations of acute myocardial necrosis. Echocardiographic data (reduced LVEF, increased LVMI, thickening of left ventricular walls) are consistent with the pattern of concentric hypertrophy and maladaptive remodelling in obesity. In this context, earlier studies by I.O. Yastremska [22] have shown that endothelial dysfunction and oxidative stress substantially aggravate myocardial injury in acute myocardial infarction, especially when combined with metabolic syndrome, highlighting the pathogenic relevance of metabolic-vascular interactions. The inverse correlations between LVEF and leptin, as well as LVEF and BMI, support the hypothesis of dose-dependent systolic dysfunction worsening against the background of hyperleptinemia and metabolic stress, and align with the findings of O.Ye. Labinska [1], where it was shown that as body weight increased, there was a tendency toward reduced LVEF in patients with obesity (group III) compared with those of normal weight and EBW ($p1\text{-}2 = 0.69$, $p1\text{-}\text{–}3 = 0.32$, $p2\text{-}3 = 0.57$). Among patients with obesity, left ventricular dimensions were significantly larger compared with the control group ($p1\text{-}2 < 0.05$).

In the study by K. Puchałowicz *et al.* [23], the mean levels of adiponectin, leptin, and resistin were 5.25 ± 3.22 μg/mL, 15.3 ± 17.9 ng/mL, and 7.81 ± 3.28 ng/mL, respectively. Significantly higher adiponectin levels were observed in patients with heart failure. The authors also reported an association between adiponectin and echocardiographic parameters. Author's data demonstrated a different pattern: although adiponectin was not directly assessed, patients with obesity exhibited substantially higher levels of leptin and caspase-9, accompanied by reduced LVEF and increased LVMI. Whereas adiponectin played a central role in the work of K. Puchałowicz *et al*., in this study the dominant factor was hyperleptinemia, which is more characteristic of obesity and exerts a stronger proinflammatory effect.

According to coronary angiography results in the study by O. Labinska *et al.* [24], multivessel coronary artery lesions were significantly more common in individuals with EBW and obesity. In patients with obesity, hemodynamically significant lesions were most frequently localised in the mid-segment of the left anterior descending artery ($p < 0.05$), and there was also a tendency toward more frequent chronic occlusions ($p = 0.08$). Author's results align with these findings, indicating that the higher frequency of triple-vessel involvement, higher SYNTAX scores in the obesity group, and strong correlations between SYNTAX, BMI, and leptin demonstrated that obesity is associated not only with a more severe course of ACS but also with anatomically more complex and diffuse coronary artery disease.

According to the data reported by K. Samak *et al*. [25], serum leptin levels were significantly higher in patients with high SYNTAX scores compared with those with low and intermediate scores ($p < 0.05$). A positive association was identified between serum leptin concentrations and the SYNTAX score. Individuals classified into the high SYNTAX score category were significantly older (61.8 ± 10.63 years) and exhibited a higher body mass index (38.5 ± 7.04 kg/m²) compared with patients in the intermediate (54.8 ± 9.62 years; 34.9 ± 5.19 kg/m²) and low (48.8 ± 9.36 years; 32.9 ± 5.4 kg/m²) SYNTAX score groups. In parallel, leptin concentrations increased progressively with rising anatomical complexity of coronary artery disease. Specifically, mean serum leptin levels were highest in the high SYNTAX group (12.6 ± 5.34 ng/mL), exceeding those observed in the intermediate (9.6 ± 3.3 ng/mL) and low (7.5 ± 2.66 ng/mL) SYNTAX score groups.

In the study by K. Samak *et al*. [25], it was shown that patients with a high SYNTAX score had markedly elevated leptin levels (12.6 ± 5.34 ng/mL) compared with the intermediate- and low-risk groups (9.6 ± 3.3 ng/mL and 7.5 ± 2.66 ng/mL, respectively). Furthermore, the SYNTAX score correlated with leptin, as well as with age, BMI, and traditional cardiovascular risk factors. In this study, a similar relationship between metabolic and anatomical

alterations was observed. The SYNTAX score was higher in patients with obesity (24.5 ± 8.9) compared with those with EBW (18.7 ± 7.2) and normal weight (14.2 ± 5.6), $p < 0.001$. The correlation between the SYNTAX score and leptin was $r = 0.64$ ($p < 0.001$), and the correlation between the SYNTAX score and BMI was $r = 0.71$ ($p < 0.001$). When comparing author's findings with those of K. Samak *et al.*, author's results demonstrated even stronger statistical associations, which may be attributed to the more acute course of STEMI and more pronounced adipokine activation.

Despite this, the achievement of TIMI 3 flow after PCI in most patients across all groups indicates preserved effectiveness of contemporary reperfusion strategies, although microvascular disturbances in obesity may contribute to the "no-reflow" phenomenon and suboptimal restoration of tissue perfusion. Comparable results were demonstrated in the study by A. Mohamed [26], where the frequency of the no-reflow phenomenon in the visceral obesity group included 62 cases in which angiographic flow was less than TIMI III (89.9%), while no cases of angiographic no-reflow were observed in the non-visceral group. Regarding coronary vessel involvement in both groups, single-vessel disease was identified in 24.6% of patients in the obesity group versus 86.4% in the control group. Multivessel disease was found in 75.4% of patients in the obesity group versus 13.6% in the control group. Thus, there was a statistically significant difference between the two groups, with $p = 0.0005$. Leptin, acting through the Ob-Rb receptor, activates proapoptotic signaling pathways (Bax, caspase-9), promotes endothelial dysfunction, reduces the bioavailability of nitric oxide, and enhances the expression of adhesion molecules, thereby exacerbating ischemic and reperfusion injury [3].

The integration of biochemical, echocardiographic, and angiographic data in this study provides a comprehensive pathophysiological understanding of adipokine-mediated myocardial injury. Obesity creates a chronic proinflammatory and proapoptotic environment that predisposes the myocardium to enhanced damage during acute ischemic stress. Upregulation of caspase-9 in patients with obesity and STEMI is likely the result of sustained mitochondrial injury induced by hyperleptinemia and oxidative imbalance. The entirety of the obtained findings allows obesity to be viewed not as a "background" comorbidity but as an active pathogenic factor within the context of adipokine-mediated myocardial injury, determining the depth of myocardial damage in STEMI. The concept of the "obesity paradox", in which some individuals with EBW demonstrate better early survival after myocardial infarction, requires reconsideration: author's data indicate that during longer follow-up, apoptosis, fibrosis, and remodelling predominate, ultimately worsening long-term outcomes.

CONCLUSIONS

The results of this study clearly demonstrated that EBW and obesity are key modifiers of the extent of myocardial injury in ST-elevation myocardial infarction, exerting their influence through adipokine- and apoptosis-mediated mechanisms. Patients with obesity had significantly higher leptin levels (F ANOVA, $p < 0.001$), and Tukey post-hoc testing confirmed significant differences among all groups (all $p < 0.05$). A strong positive correlation was demonstrated between leptin concentration and BMI ($r = 0.87$; $p < 0.001$), as well as between leptin and caspase-9 ($r \approx 0.99$; $p < 0.001$), indicating the formation of a potent adipokine-apoptotic axis. Parallel increases in troponin I ($r = 0.46$; $p = 0.008$) further confirmed that leptin-mediated metabolic activation is closely linked to the degree of cardiomyocyte necrosis.

Instrumental methods were consistent with the biochemical findings and demonstrated progressive myocardial remodelling with increasing BMI. LVEF declined along the gradient "control → EBW → obesity" (ANOVA $p < 0.001$; all Tukey comparisons $p < 0.05$), whereas LVMI and wall thickness were significantly higher in the obesity group ($p < 0.001$). Higher ST-segment elevation ($F = 4.62$; $p = 0.013$) and its correlations with troponin I ($r = 0.57$; $p = 0.003$) and leptin ($r = 0.42$; $p = 0.015$) further emphasised the more pronounced ischemic burden in patients with obesity. Angiographic findings also confirm greater severity of atherothrombotic disease in obesity: the frequency of triple-vessel disease reached 28.6% ($p = 0.042$), and the mean SYNTAX score was significantly highest in this group (24.5 ± 8.9; ANOVA $p < 0.001$; Tukey $p < 0.05$). Substantial correlations between SYNTAX and leptin ($r = 0.64$; $p < 0.001$), as well as SYNTAX and BMI ($r = 0.71$; $p < 0.001$), confirmed a close link between metabolic inflammation and the anatomical complexity of atherosclerotic disease.

Thus, the results confirmed that obesity is not a passive background condition but an active pathophysiological factor that amplifies ischemic myocardial injury through leptin-induced inflammation, increased oxidative stress, and caspase-9 activation. Adipokine dysregulation forms the basis for a more severe course of STEMI, deeper myocardial necrosis, more pronounced systolic dysfunction, and more complex coronary involvement. Promising therapeutic directions for modifying adipokine-mediated myocardial injury may include leptin-receptor inhibitors, mitochondrial-stabilising agents (mitochondria-targeted cardioprotectors), antiapoptotic agents (caspase-9 blockers), and therapies aimed at reducing systemic inflammation (IL-6 antagonists). Future research may focus on validating these mechanisms in larger cohorts and evaluating pharmacological interventions capable of reducing adipoinflammatory and apoptotic burden on the myocardium.

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CONFLICT OF INTEREST

None.

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Особливості адипокін-опосередкованих процесів ушкодження міокарда у пацієнтів з інфарктом міокарда з елевацією сегмента ST

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Анотація. Метою дослідження було визначити особливості адипокін-опосередкованого ушкодження міокарда у пацієнтів з інфарктом міокарда з елевацією сегмента ST та надмірною масою тіла/ожирінням шляхом оцінки зв'язку рівнів лептину й метаболічних порушень із вираженістю атеротромбозу та тяжкістю перебігу гострого коронарного синдрому за лабораторними та інструментальними даними. Проведено одноцентрове проспективне когортне дослідження, яке включало 120 пацієнтів з інфарктом міокарда з підйомом сегмента ST, які були поділені на три групи за індексом маси тіла: група 1 – надмірна вага (25,0-29,9 кг/м², n = 42); група 2 – ожиріння (⩾ 30 кг/м², n = 34); група 3 – нормальний індекс маси тіла (18,5-24,9 кг/м², n = 44). У групі ожиріння виявлено найвищі концентрації лептину (57,27 ± 4,1 нг/мл) та тропоніну I (4,09 ± 4,33 нг/мл), що достовірно перевищували показники інших груп (ANOVA p < 0,001). Встановлено сильний позитивний зв'язок між індексом маси тіла та лептином (r = 0,87; p < 0,001) та між лептином і тропоніном I (r = 0,46; p = 0,008), що свідчило про функціонування єдиної адипокін-апоптотичної осі у контексті ушкодження міокарду. Інструментальні методи підтвердили більш тяжкий характер ураження міокарда при ожирінні: нижча фракція викиду лівого шлуночка (46,3 ± 6,2 %), вищий індекс маси лівого шлуночка (131 ± 22 г/м²), збільшена товщина стінок, найбільша елевація сегмента ST (4,88 ± 2,10 мм; ANOVA p = 0,013), вища частота трисудинного ураження (28,6 %) та максимальні значення за шкалою SYNTAX (24,5 ± 8,9 балів; p < 0,001). Множинний регресійний аналіз підтвердив, що індекс маси тіла (β = 0,42; p < 0,001), SYNTAX (β = 0,36; p = 0,004) та знижена фракція викиду (β = –0,33; p = 0,008) є незалежними предикторами підвищення рівня тропоніну I

Ключові слова: ожиріння; надлишкова маса тіла; лептин; гострий коронарний синдром; коронарографія; фракція викиду; індекс маси тіла