International Journal of Medicine and Medical Research

ISSN 2413-6077, e-ISSN 2414-9985
Journal homepage: https://ijmr.com.ua/
Volume 11, No. 2. 2025

UDC 616.12-009.72-002-06:616-056.257
DOI: 10.63341/ijmmr/2.2025.81

Article's History:
Received: 12.08.2025; Revised: 21.11.2025;
Accepted: 30.12.2025; Published: 06.01.2026

Evaluation of the adipose-dependent proinflammatory markers level in patients with acute coronary syndrome

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Abstract. Obesity is a predictor of the development of acute coronary syndrome with ST segment elevation and is realised through increased apoptotic processes. The objective of the study was to evaluate the relationship between body mass index, troponin I as a specific marker of myocardial necrosis and adipose-dependent non-specific markers in patients with acute coronary syndrome with ST segment elevation affected by obesity. An open-label longitudinal comparative cohort study was conducted involving 120 patients with acute coronary syndrome with ST segment elevation, stratified by body mass index into three groups. The levels of troponin I, leptin and caspase-9 (ELISA method) were determined, followed by the use of statistical research methods. In obese patients, a significant increase in the levels of caspase-9 (62.40 ± 3.8 ng/mL) and leptin (57.27 ± 4.1 ng/mL) was found compared to the overweight groups (45.27 ± 2.26 ng/mL and 36.60 ± 2.9 ng/mL) and controls (38.08 ± 2.1 ng/mL and 28.92 ± 2.5 ng/mL; $p < 0.001$). In group 2, there was a nearly linear relationship between leptin and caspase-9 ($r = 0.999$; $p < 0.001$) and a moderate correlation of troponin I with body mass index ($r = 0.632$; $p < 0.001$) and with leptin ($r = 0.316$; $p < 0.05$). With increasing body mass index in patients with ST-elevation myocardial infarction, there is an increased correlation between leptin, caspase-9, and troponin I, which promotes the activation of the adipokine-apoptosis-necrosis sequential cascade. Leptin-dependent activation of apoptosis may be one of the key mechanisms of metabolically mediated myocardial damage. The obtained results support the use of leptin and caspase-9 as additional risk stratification markers in acute coronary syndrome

Keywords: obesity; troponin I; leptin; caspase-9; apoptosis; adipokines; myocardial necrosis; myocardial infarction

Introduction

Acute coronary syndrome (ACS) remains a leading cause of mortality worldwide, with obesity significantly increasing its incidence and severity. Dysfunctional adipose tissue acts as an endocrine organ, producing pro-inflammatory adipokines such as leptin, resistin, caspase-9, interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-α), which accelerate atherosclerosis, promote plaque instability and enhance myocardial ischemic injury. However, the clinical significance of these biomarkers in ACS is not fully defined. Assessing adipose-related inflammatory markers is essential for improving risk stratification and identifying new therapeutic targets in ACS what makes the research relevant.

Obesity is a key factor in the formation of chronic low-level inflammation and remodeling of the endocrine function of adipose tissue, which, due to the imbalance of adipokines (in particular leptin), worsens the course of

Suggest Citation:
Kovalenko V, Lashkul D. Evaluation of the adipose-dependent proinflammatory markers level in patients with acute coronary syndrome. Int J Med Med Res. 2025;11(2):81–91. DOI: 10.63341/ijmmr/2.2025.81

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cardiovascular diseases, including acute coronary syndrome with ST segment elevation (STEMI) [1]. According to the study by N.K. Pokrovska [2], adipose tissue is one of the principal regulators of energy balance and a cornerstone of inflammation, energy homeostasis, and atherosclerosis. Endothelial activation is the initial step of endothelial injury and is accompanied by abnormal secretion of pro-inflammatory and pro-thrombotic factors. In the study of O.S. Shchukina [3], particular attention was given to endothelial dysfunction as one of the major pathogenetic mechanisms in coronary artery disease and acute coronary syndromes. Early phases of vascular disease are characterised by endothelial dysfunction; endothelial tissues play an essential role in inflammation, coagulation, and angiogenesis by orchestrating ligand-receptor interactions and secretion of various mediators, including adipose-dependent pro-inflammatory markers. According to A.E. Berezin & A.A. Berezin [4], increased circulating concentrations of high-sensitivity cardiac troponins T (hs-TnT) and I (hs-TnI) serve as diagnostic and prognostic biomarkers of acute coronary syndromes and acute myocardial infarction, as well as independent predictors of cardiovascular risk in the general population. R.A. Byrne's *et al.* [5] guidelines emphasised the leading role of high-sensitivity troponins in the diagnosis and risk stratification of STEMI; however, metabolic and inflammatory alterations associated with obesity may modify the disease phenotype and influence treatment outcomes.

Patients with hypertension and obesity in the study by N.K. Pokrovska [2] demonstrated a more severe clinical course, characterised by higher systolic and pulse blood pressure values ($p < 0.05$), increased left ventricular posterior wall thickness ($p < 0.05$), increased left ventricular myocardial mass and relative wall thickness ($p < 0.05$), and more frequent left atrial enlargement ($p < 0.05$). The study showed that leptin is involved in inflammatory signaling and increases the expression of proinflammatory cytokines in macrophages and T lymphocytes. Regarding cytokines, P.M. Ridker & M. Rane [6] emphasised that, beyond primary prevention, both high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) have long demonstrated predictive value for adverse outcomes in acute coronary ischemia. Notably, IL-6 levels rised locally at the site of plaque rupture. M.A. Matter *et al.* [7] described that, at the molecular level, acute ischemia activates pro-inflammatory pathways (including the IL-6→CRP axis), apoptosis, and cardiomyocyte necrosis, all of which determine the degree of myocardial injury and subsequent remodeling. In A. Demarchi *et al.* [8], among adipokines, leptin attracted particular attention as a marker of fat-dependent changes; its level increased with obesity and was associated with insulin resistance, endothelial dysfunction, activation of immune cells and platelets. Systematic analyses by T. Vilariño-García *et al.* [9] confirmed elevated leptin levels in patients with acute coronary syndrome, especially in those with type 2 diabetes and excess body weight. In non-ST-elevation myocardial infarction, leptin concentrations correlated with inflammatory biomarkers and may have prognostic significance.

Experimental data by M. Wu *et al.* [10] showed that obesity promotes hyperactivation of caspase-9 through mitochondrial dysfunction, oxidative stress, and impaired mitophagy. Therefore, in patients with obesity and STEMI, more pronounced caspase-9-mediated apoptosis is expected, particularly in the context of hyperleptinemia. Simultaneously, the study by H.S. Abd-Alwahab *et al.* [11] confirmed that high-sensitivity cardiac troponins remain the principal markers of myocardial necrosis; however, the relationship between caspase-9 and troponin levels has not been sufficiently explored. Since obesity exacerbates endothelial injury, a stronger association between caspase-9, leptin, and necrosis markers can be anticipated. This justifies evaluating caspase-9 in patients with STEMI, considering BMI and leptinemia as key metabolic modifiers of disease progression.

Objective was to evaluate the associations between body mass index, the specific necrosis marker Troponin I, and the adipose-dependent non-specific markers leptin and caspase-9 in patients with acute coronary syndrome affected by obesity.

Materials and Methods

This study was conducted as an open-label, non-randomised, prospective cohort observational study, involving 120 patients with confirmed acute coronary syndrome with ST-segment elevation. The Municipal Non-profit Enterprise Zaporizhzhia Regional Clinical Hospital of the Zaporizhzhia Regional Council served as the clinical base for the study. The study protocol No. 10 dated 18.02.2025 received approval from the institutional ethics committee. All patients were informed about the study and signed consent to participate in the study. The study was conducted in accordance with European Commission [12] and Declaration of Helsinki [13]. Patients were divided into three groups based on their body mass index (BMI): Group I – 42 overweight patients (BMI 25.0-29.9 kg/m^2); Group II – 34 obese patients (BMI ≥30.0 kg/m^2); Group III (control) – 44 patients with normal body weight (BMI 18.5-24.9 kg/m^2). Eligibility (inclusion) criteria: age 18-90 years; confirmed diagnosis of STEMI in accordance with the Order No. 1936 of the Ministry of Health [14], lack of incapacity or independent ability to sign consent, provision of written informed consent to participate in the study. Exclusion criteria: age <18 or >90 years (all patients were competent and had no guardians); absence of clinical and electrocardiographic signs of STEMI on admission; presence of decompensated chronic renal failure or liver failure; acute surgical pathology of non-cardiac origin; patient refusal to participate in the study, the presence of incapacity or the ability to sign consent independently.

Subjects were assessed for anthropometric data (weight, height), age, gender, laboratory troponin I levels, and underwent laboratory ELISA testing of leptin and caspase-9, which were collected within the first 24 hours

of hospitalisation. The ELISA immunoenzymatic assay using the blinded randomised study methodology included 96 wells for leptin level analysis and 96 wells for caspase-9 analysis. For 120 blood samples of the subjects, patterns were randomly selected separately for leptin and caspase-9 from the entire sample. From one pallet of leptin reagents for 96 wells, 7 were used for calibration of the apparatus, the number of tested materials was 89. The pallet of caspase-9 reagents for 96 wells had 8 for calibration of the apparatus, and the number of results obtained was 88. A statistical analysis was conducted to determine the correlation between BMI, a specific marker of myocardial necrosis, and adipose-dependent nonspecific markers. The first stage of the study was the formation of selection criteria for the subjects, and then, accordingly, their selection. The next stage of the study was the determination of gender, age, and anthropometric data. This was followed by the stage of blood serum collection with centrifugation to obtain plasma. The next stage was the study of patient histories with available laboratory and instrumental characteristics. The next stage of the study was the conduct of enzyme-linked immunosorbent assay with the determination of leptin and caspase-9 from the selected samples. The last stage was mathematical analysis and statistical calculation of the data.

The methods used on research; general clinical with questionnaires, biochemical (troponin I), laboratory ELISA test of leptin (ALPCO, United states of America), caspase-9 (BioVendor, Czech Republic), mathematical and statistical analysis using statistical programs Microsoft Excel 2020, Statistica 13. The statistical methods applied in the study included tests for normality and homogeneity of variances, specifically the Shapiro-Wilk test and Levene's test. Parametric methods comprised one-way analysis of variance (ANOVA), Tukey's post hoc test, and the unpaired t-test for independent samples. Non-parametric comparison methods included the Kruskal-Wallis test, Dunn's post hoc test with Bonferroni correction. Additionally, analyses of frequencies and proportions were performed using Pearson's χ^2 test and Fisher's exact test. Correlation analysis was conducted with determination of Pearson correlation coefficients (r) and/or Spearman's rank correlation coefficients (ρ). A p-value of less than 0.05 ($p < 0.05$) was considered statistically significant for all analyses.

Results

In the first stage, a sample structure analysis was conducted. The total number of patients examined was 120, including 76 men (63.3%) and 44 women (36.7%). Within each BMI category, the following gender distribution was found: group 1 (overweight, n = 42): 26 men (61.9%), 16 women (38.1%); group 2 (obese, n = 34): 24 men (70.6%), 10 women (29.4%); group 3 (control, n = 44): 26 men (59.1%), 18 women (40.9%). Thus, in all study groups, a predominance of men over women was observed, and it was most pronounced among obese patients (group II). The distribution of subjects by gender is presented in Figure 1, which clearly demonstrated the male predominance in each group, with a gradual increase in the proportion of men as BMI increases.

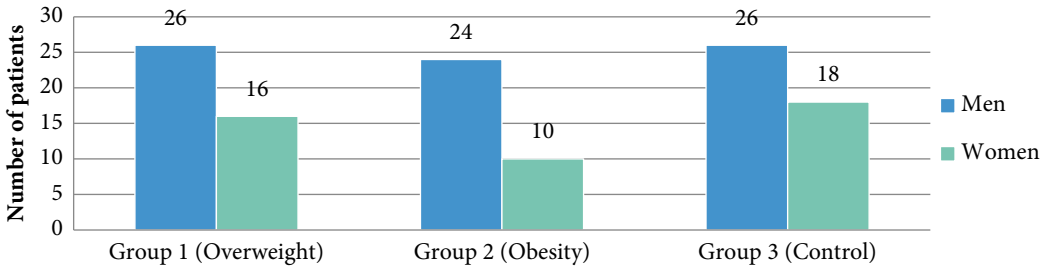

Figure 1. Distribution of patients by gender in the study sample

Source: authors' research

The average BMI in the study population was 27.8 kg/m^2. Men had a slightly higher BMI than women, with a statistically significant difference ($p = 0.038$), supporting the concept of gender-related variability in body weight. BMI differed markedly between the three study groups, reflecting the predefined stratification. Overweight patients had moderately elevated BMI, while the obesity group demonstrated the highest values; both groups significantly exceeded the control group ($p < 0.01$). Median values and nonparametric testing (Kruskal-Wallis, $p < 0.001$) confirmed these differences, with post-hoc comparisons showing consistently higher BMI in groups 1 and 2 relative to normal-weight individuals. BMI mean, median, and standard deviation data are presented in Table 1.

Table 1. Intergroup differences in BMI indicators

Group	Mean BMI ± SD, kg/m^2	Median (IQR), kg/m^2
Group 1 (overweight)	27.73 ± 1.46	28.10 (26.62-28.72)
Group 2 (obesity)	36.14 ± 7.27	33.88 (31.40-37.77)
Group 3 (normal/control)	22.50 ± 1.65	22.84 (21.06-23.94)

Source: authors' research

The average patient age was 64.9 years, with no significant age differences between BMI groups ($p > 0.05$). However, gender-specific analysis showed that men were consistently and significantly younger than women across all BMI categories. In the overweight group, men were approximately 17 years younger than women ($p < 0.01$); in the obesity group – about 13 years younger ($p < 0.02$); and in the control group – nearly 14 years younger ($p < 0.02$). These findings align with established epidemiological data indicating that men typically present with STEMI at a younger age than women. Age-specific differences in STEMI stratification by gender are shown in Figure 2.

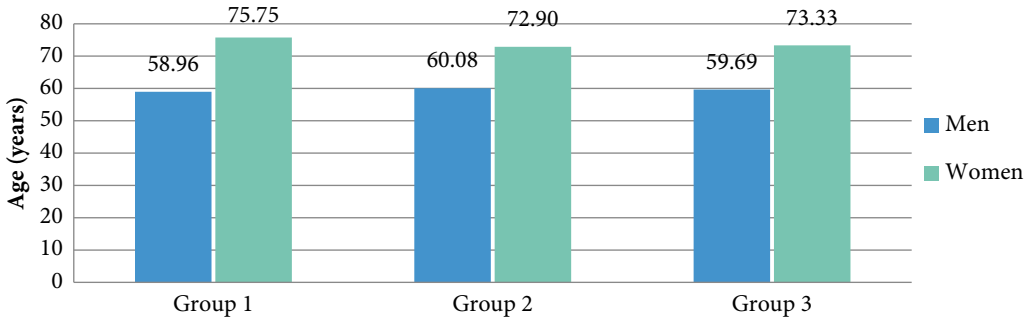

Figure 2. Data on average values by age and gender in the study groups
Source: authors' research

For the following analysis the reliability of data on adipose-dependent inflammatory markers (leptin, caspase 9), troponin I values were assessed as a specific and reference laboratory indicator of cardiomyocyte necrosis in STEMI. Analysis of troponin I concentrations at the time of hospitalisation showed a clear relationship between myocardial damage and the degree of excess body weight. Preliminary testing of the assumptions regarding the normality of distribution using the criterion for the Shapiro-Wilk test in all three BMI-stratified groups demonstrated statistically significant deviations from the normal distribution ($p < 0.01$), which led to the choice of nonparametric approaches for intergroup comparisons. The Kruskal-Wallis pooled test confirmed heterogeneity in troponin I levels between groups ($H = 7.67$; $p = 0.0216$), indicating that increasing BMI is associated with more intense myocardial necrotic damage in the acute phase of STEMI.

Expanded paired analysis using the Mann-Whitney test showed that patients with overweight (group 1) had significantly higher troponin I levels compared with the control group ($p = 0.0177$), whereas patients with obesity (group 2) demonstrated an additional significant increase ($p = 0.0196$). Mean values formed a clear ascending gradient: 2.54 ng/mL in the control group, 3.46 ng/mL in overweight patients, and 4.09 ng/mL in obese individuals. Compared with the control group, troponin I was higher by +0.92 ng/mL in group 1 ($p = 0.018$) and by +1.55 ng/mL in group 2 ($p = 0.006$). Median values showed the same trend (1.90 → 3.00 → 3.50 ng/mL). These findings confirm a progressive increase in myocardial necrotic burden with increasing BMI, consistent with the concept of an "adipo-inflammatory" STEMI phenotype. All quantative data for troponin I were presented in Table 2.

Table 2. Troponin I levels across BMI-stratified groups

Parameter	Group 1 (Overweight)	Group 2 (Obesity)	Group 3 (Control)
Mean ± SD (ng/mL)	3.46 ± 2.17	4.09 ± 4.33	2.54 ± 2.19
Median (ng/mL)	3.00	3.50	1.90
Δ vs Control (ng/mL)	+0.92	+1.55	–
Δ vs Control (%)	+26.59%	+37.00%	–
95% CI (Δ)	0.14-1.70	0.66-2.43	–
p-value vs Control	0.0177	0.0196	–
Overall trend	↑	↑↑	→

Note: CI – confidence interval
Source: authors' research

Determination of leptin levels according to the ELISA study was performed in 89 out of 120 patients (74.2% of the population), caspase-9 – in 88/120 (73.3%). The ranking was carried out in a random order, but the number of studied samples for which leptin and caspase-9 were determined according to their study group does not have a statistically significant discrepancy (the number of caspase-9 samples in group 1 is 85.7%, in group 2 – 67.6%, in group 3 – 68.2%, the number of leptin samples in group 1 is 83.33%, in group 2 – 58.82%, in group 3 – 77.27%). This is taken into account in the further analysis of the obtained results.

Troponin was moderately correlated with both leptin ($\rho = 0.325$; $p = 0.0019$) and caspase-9 ($\rho = 0.299$; $p = 0.0046$) in the overall population. This is consistent with the hypothesis of a more intense "adipo-inflammatory" load and apoptosis at higher BMI, which is associated with a larger area of myocardial damage. Caspase-9 levels demonstrated a clear BMI-dependent gradient. Median values increased from approximately 38 ng/mL in the normal-weight group to 45 ng/mL in the overweight group and exceeded 62 ng/mL in obese patients. ANOVA confirmed highly significant intergroup differences ($F \approx 82$; $p < 0.001$), and Tukey's post-hoc test showed that obese patients had markedly higher caspase-9 levels than both overweight and normal-weight individuals (all $p < 0.001$). Even overweight patients showed significantly elevated values compared with controls ($p < 0.01$), indicating progressive activation of the mitochondrial apoptotic pathway with rising BMI.

Leptin concentrations followed a similar trend, increasing from roughly 29 ng/mL in the normal-weight group to 37 ng/mL in the overweight group and surpassing 57 ng/mL in the obesity group. Intergroup differences were statistically robust ($F \approx 97$; $p < 0.001$). Post-hoc comparisons showed significantly higher leptin levels in obese patients relative to both other groups (all $p < 0.001$), with overweight individuals also differing significantly from controls ($p < 0.01$). Correlation analysis demonstrated strong positive associations between leptin and BMI ($r = 0.876$ in the overweight group; $r = 0.962$ in the obese group; $p < 0.001$), as well as between leptin and caspase-9, reaching almost perfect correlation in the obesity group ($r = 0.999$; $p < 0.001$).

The results demonstrated a consistent increase in leptin and caspase-9 levels as subjects transition from normal body weight to obesity. The highest values for both parameters were found in the obese group, confirming the parallelness of metabolic and apoptosis-mediated disturbances in the progression of metabolic syndrome. Furthermore, the very high correlation between leptin and caspase-9 in group 2 ($r = 0.999$; $p < 0.001$) suggests a direct mechanistic link between hyperleptinemia and caspase activation, potentially contributing to myocardial damage in obese patients. Statistical data for caspase-9 and leptin levels were analysed using ANOVA, pairwise comparison (t-test), and statistical significance testing. The results were shown in Table 3.

Table 3. Statistical measurements of the reliability and significance of caspase-9 and leptin indicators in the study groups

Indicator	Group 1 (overweight) M ± SD	Group 2 (obesity) M ± SD	Group 3 (normal) M ± SD	ANOVA (F)	p-value (ANOVA)	Pairwise comparison (Tukey post-hoc)	p-value
Caspase-9, pcs.	45.27 ± 2.26	62.40 ± 3.80	38.08 ± 2.10	82.47	<0.001	1-3	0.008
						2-3	<0.001
						1-2	<0.001
Leptin, ng/mL	36.60 ± 2.90	57.27 ± 4.10	28.92 ± 2.50	96.83	<0.001	1-3	0.009
						2-3	<0.001
						1-2	<0.001

Source: authors' research

For statistical analysis of intergroup differences, a two-sample t-test for independent populations was used for normal distribution, confirmed by the Shapiro-Wilk test, and homogeneity of variances was assessed using Levene's test. A correlation analysis was conducted between BMI and main laboratory parameters within three stratified groups of patients (overweight, obesity, control). In the obese group, a strong positive correlation relationship was found between troponin I levels and BMI ($r = 0.632$; $t = 5.29$; $p < 0.001$), indicating a significant association between the degree of myocardial damage and excess body weight. In the overweight group, a moderate positive relationship was observed between these indicators ($r = 0.402$; $t = 2.86$; $p < 0.01$), which also indicates a tendency for troponin levels to increase with increasing BMI, although less pronounced than in obese patients.

In the obese group, a significant positive correlation was found between caspase-9 and leptin levels ($r = 0.999$; $p < 0.001$), indicating a close relationship between the activation of mitochondrial apoptosis and the hormonal activity of adipose tissue. A similar, but less pronounced, relationship was also observed between caspase-9 and BMI ($r = 0.976$; $p < 0.001$), consistent with the hypothesis that apoptotic activity increases with increasing body weight. In the overweight group, a high correlation was observed between caspase-9 and leptin ($r = 0.856$; $p < 0.001$), and both parameters had statistically significant associations with BMI ($r = 0.728$ for caspase-9; $r = 0.876$ for leptin; $p < 0.001$). These results indicate that even a moderate increase in BMI is accompanied by activation of apoptosis and endocrine changes in adipose tissue. In the control group with normal BMI, correlations between the studied parameters were weak or absent, which confirms the physiological balance between metabolic and apoptotic processes under conditions of normal body weight.

An assessment of the relationship between markers of apoptosis and myocardial necrosis revealed significant differences between groups. In the obese group, a moderate positive correlation was found between caspase-9 and troponin I levels ($r = 0.217$; $p < 0.05$), which may indicate a synchronous increase in apoptotic activity and cardiomyocyte damage during metabolic overload. The

correlation between leptin and troponin I was also positive ($r = 0.316$; $p < 0.05$), reflecting the potential influence of adipokine dysfunction on the degree of ischemic myocardial damage. The intergroup correlation relationships of leptin, caspase-9, troponin I, and BMI are shown in Figure 3 as heat maps (cross-tabulation).

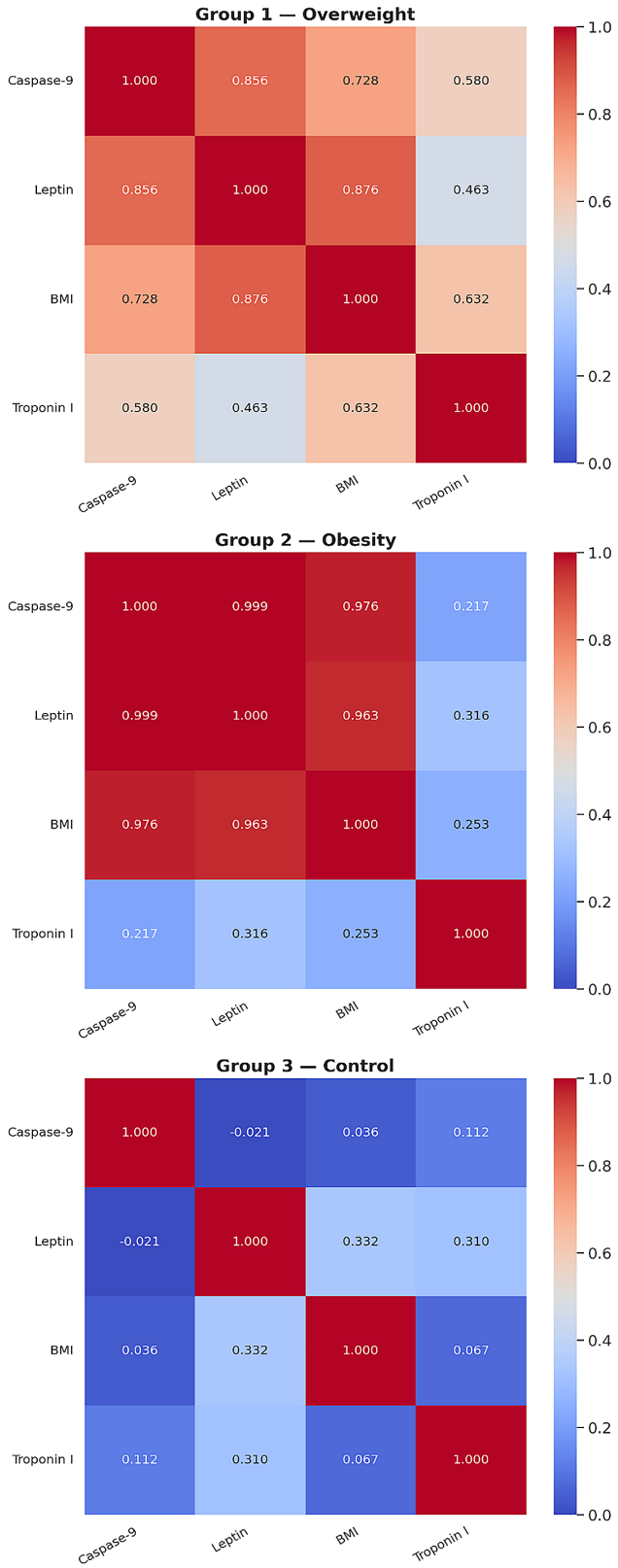

Figure 3. Heat maps of the correlation relationships between laboratory values and BMI
Source: authors' research

In the overweight group, the correlations were more pronounced: for caspase-9 and troponin ($r = 0.580$; $p < 0.01$), and for leptin and troponin ($r = 0.463$; $p < 0.01$). This dependence may reflect the early stages of metabolic imbalance, in which deep apoptotic activation has not yet formed, but a myocardial response to systemic inflammation and hyperleptinemia is already observed. In the control group, correlations between the parameters were weak and statistically insignificant. This indicates the absence of a significant relationship between markers of apoptosis and myocardial damage under conditions of normal body weight and metabolic homeostasis.

Discussion

The results of this study demonstrated that excess body weight and obesity substantially modify the inflammatory, metabolic, and apoptotic profiles of patients with myocardial infarction and ACS, which is consistent with accumulated international evidence. In patients with STEMI and obesity, metabolic inflammation of adipose tissue overlaps with the acute immune response to ischemic myocardial injury. This manifests as hyperleptinemia, activation of monocytes/macrophages, and a potential pro-aggregatory effect on platelets, thereby amplifying thrombosis and microvascular dysfunction [2,3].

In author's cohort, male patients predominated (63.3% overall; up to 70.6% in the obesity group), and men were significantly younger than women across all BMI categories (difference ≈ 13-17 years; $p < 0.02$). This corresponds with epidemiological observations that men more frequently develop STEMI at a younger age, whereas women tend to present at an older age and with a more severe clinical course, as reported by A.A. Dera *et al.* [15]. In their study, regarding sex, no significant differences ($p > 0.05$) were found between leptin concentrations in men and women in Group 1 ($r = 0.74$, $p = 0.139$) or Group 3 ($r = 0.044$, $p = 0.511$). Compared with the control group, women in Group 3 demonstrated a significantly higher BMI ($t = 2.656$; $df = 14$; $p = 0.0188$), Participants with acute myocardial infarction in Groups 2 and 3 also showed a significant difference ($t = 5.370$; $df = 46$; $p < 0.0001$).

The findings of that study are closely aligned with author's study, in which the mean BMI in the cohort was elevated (27.8 kg/m^2), and intergroup differences in BMI were, as expected, significant: the control group corresponded to normal body weight, whereas Groups 1 and 2 demonstrated excess body weight and obesity, respectively ($p < 0.01$ by ANOVA and by the Kruskal-Wallis test). In author's study, leptin levels increased progressively from approximately 28-29 ng/mL in the control group to approximately 36-37 ng/mL in the excess body weight group, and exceeded 57 ng/mL in patients with obesity, with very high statistical significance of intergroup differences ($F \approx 97$; $p < 0.001$) and consistent post hoc results ($p < 0.01$ for all key comparisons). These findings aligned well with the systematic review and meta-analysis by A. Ismaiel *et al.* [1], where leptin levels in patients with acute coronary syndrome were significantly higher than in controls (MD ≈ 10.5 ng/mL; 95% CI 3.67-17.35), particularly in patients with obesity. Similar conclusions were reported in the study by E. Ricottini *et al.* [16], in which patients with hyperleptinemia after percutaneous coronary intervention (PCI) exhibited nearly a twofold higher rate of major adverse cardiovascular events (MACE) compared with the normoleptinemic group (40% vs 21%; hazard ratio or HR 2.3; 95% CI 1.14-4.6). Leptin levels differed significantly across groups stratified by platelet reactivity (PR) ($P = 0.047$). Patients were divided into three PR-based groups defined as low (LPR), normal (NPR), and high (HPR) platelet reactivity. Leptin concentrations were higher in the HPR group (12.61 ± 16.58 ng/mL) compared with the LPR group (7.83 ± 8.87 ng/mL, $P = 0.044$) and the NPR group (7.04 ± 7.03 ng/mL, $P = 0.01$). These findings are consistent with author's data showing the coexistence of leptin-mediated inflammation and ischemic myocardial injury. Summarising the observations of T. Vilariño-García *et al.* [9], leptin is considered not only a marker of energy imbalance but also a pro-inflammatory adipokine that affects endothelial function, cardiac remodeling, and apoptosis. Author's demonstration of a strong relationship between leptin and BMI ($r = 0.876$-0.962; $p < 0.001$), along with its correlation with troponin I, confirmed this concept.

Caspase-9 levels in author's cohort also exhibited a clear BMI-dependent gradient: approximately 38 ng/mL in the control group, ≈45 ng/mL in patients with excess body weight, and >62 ng/mL in those with obesity. ANOVA analysis ($F \approx 82$; $p < 0.001$) and Tukey's post-hoc test confirmed a significant stepwise increase in caspase-9 when transitioning from normal weight to excess weight and obesity (all $p < 0.01$). The caspase-9 elevation observed in author's study fully aligns with current understanding of the intrinsic mitochondrial apoptotic pathway in myocardial ischemia-reperfusion injury, as demonstrated by M. Wu *et al.* [10]. K. Cai *et al.* [17] described caspase-9 activation as a central event in programmed cardiomyocyte death triggered by mitochondrial pore opening, cytochrome c release, and apoptosome formation. Clinically, Y. Liu *et al.* [18] reported that activation of caspase-associated proteins (CARD9) in macrophages enhances post-infarction remodeling, further supporting a multifactorial involvement of apoptosis in myocardial damage. These mechanisms are consistent with author's findings of increased caspase-9 in parallel with elevated troponin I and leptin, as well as their positive correlations. Additional confirmation was provided by A. Demarchi *et al.* [8], who demonstrated that serum leptin levels are directly associated with the inflammatory response during acute myocardial infarction and may play a role in risk stratification.

Author's data demonstrated a clear gradient of myocardial necrosis proportional to BMI: mean troponin I levels increased from 2.54 ng/mL in the control group to 3.46 ng/mL in the excess-weight group and 4.09 ng/mL in the obesity group. Compared with controls, the increase amounted to +0.92 ng/mL in Group 1 (≈ +26.6%) and +1.55 ng/mL in Group 2 (≈ +37%), with statistically significant p-values

($p = 0.018$ and $p = 0.006$, respectively). The strong positive association between BMI and troponin I in obese patients ($r = 0.632$; $p < 0.001$) highlighted that excess adiposity is associated with a greater area of necrosis in STEMI [19]. Similar trends were reported by A.A. Dera *et al.* [15], where patients with acute myocardial infarction and elevated BMI had higher troponin I, leptin, and additional markers of metabolic stress. Also a positive correlation was shown between troponin I (cTnI), creatine kinase MB (CK-MB), leptin, and resistin in patients with acute myocardial infarction. BMI and leptin showed a positive association in Group 3. For instance, among participants in Group 3, leptin showed a stronger correlation with BMI ($r = 125$, $p = 0.01$).

The findings of I. Chernyavska *et al.* [20] demonstrated that in all patient groups, cardiac troponin levels increased significantly both before and after PCI. The data also indicated that troponins begin to appear in the bloodstream 4-10 hours after the onset of acute myocardial infarction, while peak concentrations occur between 12 and 48 hours. The authors additionally reported a significant reduction ($p < 0.05$) in leptin levels during ACS treatment accompanied by parallel weight loss in both men and women. Correlation analysis between waist circumference and leptin levels in both sexes demonstrated a significant association. These results are consistent with author's findings showing elevated leptin levels in patients with ACS – particularly in those with obesity and excess body weight – as well as a positive correlation between BMI and troponin, and between leptin and BMI.

D. Skrypnik *et al.* [21] reported that elevated serum leptin levels are strongly associated with coronary artery disease (CAD). Serum leptin concentration positively correlated with coronary artery disease severity, being higher in patients with stable angina compared with controls, and highest in those with unstable angina. Their results also showed that serum leptin concentrations were higher in the control group (without cardiac rehabilitation) compared with group S, in which patients underwent a 2-week rehabilitation program. In author's study, leptin concentrations showed a similar pattern, increasing from approximately 29 ng/mL in the normal-weight group to 37 ng/mL in the excess body weight group, and exceeding 57 ng/mL in the obesity group. Troponin displayed a moderate positive correlation with leptin ($\rho = 0.325$; $p = 0.0019$).

Consistent with author's detection of higher troponin I levels in patients with overweight and obesity (up to 3.46 and 4.09 ng/mL, respectively), the findings of R.H. Al-Shibli *et al.* [22] also demonstrated markedly elevated troponin I levels in atherosclerotic groups both with and without obesity ($p \leq 0.001$). The authors additionally reported a unidirectional increase in other proinflammatory and pro-oxidant markers – CRP and malondialdehyde – which fully agrees with author's data showing activation of apoptosis and accentuated necrosis with rising BMI. Meanwhile, in the cohort of this study, the authors found a much stronger correlation between leptin and caspase-9 (up to $r = 0.999$ in the obese group) than was described in R.H. Al-Shibli *et al.* study, indicating a more pronounced "adipokine-apoptosis-necrosis" cascade reaction, particularly in conditions of acute myocardial infarction. The findings of R.H. Al-Shibli *et al.* regarding reduced total antioxidant capacity and increased MDA further confirmed the important role of oxidative stress in patients with obesity. Although these parameters were not measured in author's study, the elevated levels of caspase-9 in the overweight and obesity groups (45.27 and 62.40 units/mL, respectively) indirectly indicate activation of mitochondrial apoptosis, which is typically triggered by oxidative stress.

Additionally, results from O. Mayer *et al.* [23] confirmed the adverse prognosis associated with hyperleptinemia. Specifically, leptin concentrations ≥18.9 ng/mL were associated with more than a twofold increase in all-cause mortality (HR 2.10; 95% CI 1.29-3.42), cardiovascular mortality (HR 2.65; $p < 0.001$), and the risk of hospitalisation for heart failure (HR 1.95; $p < 0.020$). In current study, the leptin level in the obesity group averaged 57.27 ± 4.1 ng/mL, markedly exceeding these risk thresholds, and its correlation with troponin I ($r = 0.316$; $p < 0.05$) confirms the likely contribution of a leptin-dependent proinflammatory pathway to worsening the course of STEMI.

Thus, the results obtained in author's study are consistent with international findings and indicate that patients with ACS and obesity exhibit an enhanced interaction between leptin and caspase-9, which may serve as a marker of metabolically driven apoptotic stress in the myocardium. The extremely strong correlation ($r \approx 0.999$) between these biomarkers underscored that leptin-dependent activation of apoptosis may represent one of the central mechanisms of cardiac injury in this patient population. These observations open opportunities for further development of prognostic models and suggest that combined assessment of leptin and caspase-9 may serve as an additional tool for risk stratification in ST-segment elevation myocardial infarction.

Conclusions

The present study demonstrated a clear and statistically significant metabolic-inflammatory pattern linked to excess body weight. It was found that overweight and obese patients exhibited distinctly higher levels of adipose-derived biomarkers compared with normal-weight individuals. BMI differed significantly between groups ($p < 0.01$), confirming the validity of stratification. Although mean age did not differ across BMI categories, men consistently presented with ACS at a significantly younger age, which corresponds to known epidemiological characteristics of the syndrome. Analysis showed a progressive increase in the myocardial necrosis marker troponin I with rising BMI: from 2.54 ng/mL in normal-weight patients to 3.46 ng/mL in overweight and 4.09 ng/mL in obese individuals, with statistically significant differences ($p = 0.0177$ and $p = 0.0196$). Correlation testing proved that troponin I had a strong positive association with BMI in obese patients ($r = 0.632$; $p < 0.001$), supporting the link between excess adipose tissue and increased myocardial injury in ACS.

A central outcome of this research was the demonstration of a highly consistent adipokine-apoptotic response. Leptin increased from approximately 29 ng/mL in normal-weight patients to 37 ng/mL in overweight and exceeded 57 ng/mL in obese subjects ($p < 0.001$). Caspase-9 displayed a similar trend (38 → 45 → 62 ng/mL; $p < 0.001$). Moreover, it was demonstrated that the association between leptin and caspase-9 intensified dramatically with increasing BMI, reaching almost perfect correlation in obese patients ($r = 0.999$; $p < 0.001$). Both markers also correlated positively with troponin I, indicating the existence of an interconnected "adipokine-apoptosis-necrosis" axis in ACS. Overall, the study proved that obesity amplifies myocardial injury in ACS through adipose-related inflammatory and apoptotic mechanisms, characterised by hyperleptinemia, activation of mitochondrial apoptosis (caspase-9), and elevated troponin I levels. These findings highlighted the pathogenic value of adipose-dependent biomarkers in ACS and underscore their potential use for metabolic-inflammatory phenotyping of high-risk patients. Future perspectives include longitudinal evaluation of leptin and caspase-9 as prognostic markers of adverse outcomes, integration of adipokine-apoptotic indicators into ACS risk-stratification models, and exploration of therapeutic approaches targeting adipose-driven inflammation and apoptosis to improve outcomes in overweight and obese ACS patients.

Acknowledgements
None.

Funding
None.

Conflict of Interest
None.

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Оцінка рівня адипозалежних прозапальних маркерів у пацієнтів із гострим коронарним синдромом

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Анотація. Ожиріння є предиктором розвитку гострого коронарного синдрому з елевацією сегмента ST і реалізується через посилення апоптотичних процесів. Метою дослідження було оцінити взаємозв'язок між індексом маси тіла, тропоніном I як специфічним маркером некрозу міокарда та адипозалежними неспецифічними маркерами у пацієнтів із гострим коронарним синдромом з елевацією сегмента ST, які мають ожиріння. Було проведено відкрите проспективне порівняльне когортне дослідження за участю 120 пацієнтів із гострим коронарним синдромом з елевацією сегмента ST, стратифікованих за індексом маси тіла на три групи. Визначали рівні тропоніну I, лептину та каспази-9 (метод ELISA), після чого проводили статистичний аналіз. У пацієнтів з ожирінням виявлено значуще підвищення рівнів каспази-9 (62,40 ± 3,8 нг/мл) та лептину (57,27 ± 4,1 нг/мл) порівняно з групами з надмірною масою тіла (45,27 ± 2,26 нг/мл і 36,60 ± 2,9 нг/мл відповідно) та контрольною групою (38,08 ± 2,1 нг/мл і 28,92 ± 2,5 нг/мл; $p < 0,001$). У групі 2 виявлено майже лінійний зв'язок між лептином і каспазою-9 ($r = 0,999$; $p < 0,001$), а також помірну кореляцію тропоніну I з індексом маси тіла ($r = 0,632$; $p < 0,001$) та з лептином ($r = 0,316$; $p < 0,05$). Зі зростанням індексу маси тіла у пацієнтів із STEMI посилюється кореляція між лептином, каспазою-9 та тропоніном I, що сприяє активації послідовного каскаду «адипокін – апоптоз – некроз». Лептинзалежна активація апоптозу може бути одним із ключових механізмів метаболічно опосередкованого пошкодження міокарда. Отримані результати обґрунтовують використання лептину та каспази-9 як додаткових маркерів стратифікації ризику при гострому коронарному синдромі

Ключові слова: ожиріння; тропонін I; лептин; каспаза-9; апоптоз; адипокіни; некроз міокарда; інфаркт міокарда