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Research article

Serum myeloperoxidase, paraoxonase, and plasma asprosin concentrations in patients with acute myocardial infarction

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ABSTRACT

Introduction: The objective of this study was to evaluate the usefulness of the serum biomarkers myeloperoxidase (MPO), paraoxonase (PON), and plasma asprosin in acute myocardial infarction (AMI) diagnosis and assess their compatibility with routinely screened cardiac biomarkers.

Methods: This study was conducted using a prospective cross-sectional design and included 90 patients, consisting of 60 patients diagnosed with AMI (30 with ST-segment elevation and 30 with non-ST-segment elevation on ECG) and 30 controls (without a diagnosis of AMI). Changes in the levels of cardiac biomarkers (Hs-cTnI, CK, CK-MB), lipid profile (TC, TG, LDL, HDL), MPO, PON, asprosin, and routine biochemical parameters of patients were evaluated. Furthermore, receiver operating characteristic curve analysis revealed the diagnostic value of Hs-cTnI, MPO, PON, and asprosin in predicting AMI. Binary logistic regression analysis of cardiac marker concentrations was used to predict the presence of AMI. In contrast, multinomial logistic regression analysis was conducted to predict the type of AMI and the control group.

Results: The median levels of MPO and plasma asprosin were found to be higher in the patient group (3.22 [interquartile range {IQR}: 2.4–4.4] ng/ml and 10.84 [IQR: 8.8–17.8] ng/ml, respectively) than in the control group (2.49 [IQR: 1.9–2.9] ng/ml and 4.82 [IQR: 4.6–8.0] ng/ml, respectively) ($p = 0.001$ and $p < 0.001$, respectively). The median levels of PON were 8.94 (IQR: 7.6–10.4) ng/ml in the patient group and 10.44 (IQR: 9.1–20.0) ng/ml in the control group ($p < 0.001$). In the binary logistic regression model, compared with the control group, a 1 ng/ml increase in MPO level increased the odds of having AMI by 3.61 ($p = 0.041$, 95% CI: 1.055–12.397), whereas a 1 ng/ml increase in asprosin level increased the odds of having AMI by 2.33 ($p < 0.001$, 95% CI: 1.479–3.683). In the multinominal logistic regression model, compared with the control group, a 1 ng/ml increase in the MPO level increased the odds of having NSTEMI by 4.14 ($p = 0.025$, 95% CI: 1.195–14.350), whereas a 1 ng/ml increase in asprosin concentrations increased the odds of having NSTEMI by 2.35 ($p < 0.001$, 95% CI: 1.494–3.721).

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Conclusion: Herein, MPO and asprosin concentrations increased with Hs-cTnI, and a decrease in PON concentration indicated that oxidant–antioxidant parameters and adipokines were related to AMI pathogenesis.

1. Introduction

Acute myocardial infarction (AMI) is a common cardiac emergency with significant morbidity and mortality potential. Based on electrocardiogram (ECG) findings, it is classified as AMI with ST-segment elevation (STEMI) and AMI without non-ST-segment elevation (NSTEMI). Acute coronary syndrome (ACS) involves STEMI, NSTEMI, and unstable angina (UA) [1]. When a patient's ST-segment elevation is not persistent on ECG and cardiac biomarkers are above normal values, the patient is often diagnosed with NSTEMI. If cardiac biomarkers are within normal limits, the patient is considered to have UA [2].

In patients with symptoms consistent with an ACS, an increase in serum troponin I or T of at least one value above the 99th percentile is diagnostic for AMI. Troponin is sensitive and specific for cardiac myocardial necrosis. Still, troponin as a marker of myocardial necrosis may be elevated for many reasons other than ACS (e.g., aortic dissection, valvular heart disease, pulmonary hypertension). New high-sensitivity cardiac troponins (Hs-cTnI) more readily detect ischemia. Nevertheless, increasing false-positive results are worrisome since they may lead to unnecessary procedures and hospitalizations [3]. Knowing that oxidant/antioxidant parameters are also involved in the development of atherosclerosis, which is prominent in the pathophysiology of ACS, has led to the search for alternative markers for long-term troponin follow-ups in NSTME and UA [4].

Cells produce reactive oxygen species (ROS), including superoxide, hydrogen peroxide, and hydroxyl radicals, while performing their normal cellular functions. ROS have high chemical reactivity and are oxidant parameters causing the oxidation of lipids, proteins, and DNA. Antioxidant parameters control oxidant parameters with this destructive effect [5]. Enzyme systems, such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and paraoxonase, ensure protection against ROS. Additionally, paraoxonase plays a significant role in preventing LDL oxidation since it is an enzyme associated with Apo AI transported on HDL. Therefore, antioxidants can inhibit atherogenesis and improve vascular function [6].

Lipid-laden macrophages that are involved in all stages of atherosclerosis have ROS-producing pathways. Macrophages produce superoxide using a membrane-associated nicotinamide adenine dinucleotide phosphate oxidase, which can mutate to form hydrogen peroxide. Myeloperoxidase (MPO), a secreted heme protein, is an important component of the oxidative pathways in these cells. Myeloperoxidase utilizes hydrogen peroxide to produce considerably more potent cytotoxic oxidants. Myeloperoxidase secreted by macrophages in the intermedia layer of the vessel wall in the atherosclerotic area can cause acute obstruction and rupture in the arterial lumen. This situation shows that myeloperoxidase may participate in atherosclerotic vascular diseases [7].

Asprosin is a peptide adipokine secreted by white adipose tissue. Asprosin activates the G-protein-cAMP-PKA pathway, thus increasing glucose secretion from the liver. It is stressed that elevated asprosin concentration are related to insulin resistance in humans and mice. Furthermore, an injection of recombinant asprosin causes an elevation in blood glucose and insulin concentrations [8]. Studies have demonstrated that asprosin concentrations increase in diabetes, and preclinical investigations have shown that asprosin concentration increases and may be effective in preventing apoptosis in myocytes and reducing ROS with malondialdehyde [9].

The purpose of this investigation was to evaluate the relationship between asprosin, a new adipokine, in addition to oxidative stress-related parameters (myeloperoxidase, paraoxonase) with routine biochemical parameters, such as troponin (Hs-cTnI), in patients followed up with acute myocardial infarction. Our goal is to identify new parameters that can support or create alternatives for Hs-cTnI in patients presenting to the emergency department with chest pain and suspected of having ACS, due to long hours of emergency service follow-up.

2. Materıals and methods

The current study was conducted in a cross-sectional design with the ethics committee approval dated July 01, 2021 and numbered 80576354-050-99/184 from the Local Ethics Committee of the Dean of the Faculty of Medicine of Kafkas University.

2.1. Study design

Patients who presented to the emergency department of Kafkas University Health Research and Application Center Hospital between July 2021 and March 2022 with cardiac symptoms (acute chest, epigastric, neck, jaw, or arm pain; discomfort or pressure sensation without apparent non-cardiac source) starting within the first 6 h were included in the study [10]. The patient group comprised patients who were diagnosed with acute myocardial infarction with cardiac symptoms (receiving $\geq$3 points according to the TIMI scoring; STEMI and NSTEMI) and were referred to the coronary intensive care unit; these patients were considered to have (i) STEMI with at least 1 mm ST-segment elevation in at least two adjacent ECG leads, regardless of serum creatine kinase and cardiac Hs-cTnI elevation (n = 30), and (ii) NSTEMI with serum creatine kinase and cardiac Hs-cTnI elevation and without ST-segment elevation on ECG (n = 30). The control group was selected from the hospital staff and relatives of patients who did not have coronary artery disease, infection or inflammatory disorder, autoimmune diseases, and other diseases that cause increased levels of cardiac biomarkers (Hs-cTnI), diabetes mellitus, and BMI of $\geq$30 kg/m^2 (n = 30) [11]. Written informed consent was acquired from the

participants before starting the research. The participants' age, sex, systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse values were recorded in the data form. Participants with any infection or inflammatory disorder, autoimmune diseases, unstable angina, and other diseases that cause increased levels of cardiac biomarkers (Hs-cTnI), diabetes mellitus, and BMI of $\geq$30 kg/m^2 were excluded from the research.

2.2. Blood samples

A total of 10 ml blood samples, 5 ml whole blood, and 5 ml gel biochemistry tubes were collected from individuals with brachial vascular access and informed consent form for biochemical examinations. Serum and plasma samples were taken before angiography and heparin administration. Hemogram markers were studied without delay (detailed below). The collected blood samples were centrifuged at 4 °C and 1600×*g* for 15 min without losing time in the Biochemistry Laboratory of Kafkas University Health Research and Application Center Hospital. This procedure was continued until the plasma and serum samples became clear. Routine biochemical and cardiac markers were studied (detailed below) from the serum samples obtained. After the routine parameters were analyzed, the remaining plasma and serum samples were aliquoted into Eppendorf tubes and stored at −80 °C until ELISA analysis.

2.3. Analysis of laboratory parameters

2.3.1. Routine analyses

The routine biochemistry parameters, including serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), and urea, were tested using the kinetic UV test method. Creatinine was tested with the kinetic color method, glucose enzyme with the UV method, triglyceride (TG) and total cholesterol (TC) with the enzymatic-color test method, low-density lipoprotein (LDL) and high-density lipoprotein (HDL) with the enzymatic-color test and immunoinhibition method. The C-reactive protein (CRP) was tested with the immunoturbidimetric method using the AU480 clinical chemistry system (Beckman Coulter, USA) analyzer. For the cardiac routines, creatine kinase (CK) was tested using the kinetic UV method and creatine kinase-MB (CK-MB) concentrations using the chemiluminescence method. Hemoglobin-A1c (HbA1c) concentration was tested with the chemiluminescence method using the AU5800 clinical chemistry system (Beckman Coulter, USA). Serum Hs-cTnI analysis was tested with the hormone analyzer UniCel DxI 600 Access Immunoassay System (Beckman Coulter, USA) using the chemiluminescence method. The reference test ranges for these analytical methods are as follows: ALT: 0–50 U/L, AST: 0–50 U/L, Urea: 17–43 mg/dL, Creatinine: 0.67–1.17 mg/dL, LDH: 0–248 U/L, Glucose: 70–100 mg/dL, Hb-A1c: 3.5–5.6%, TG: 0–150 mg/dL, TC: 0–200 mg/dL, HDL: 40–60 mg/dL, LDL: 0–130 mg/dL, CK: 0–171 IU/L, CK-MB: 0–24 U/L, Hs-cTnI: <17.5 ng/L (gender specific 99th percentiles of 11.6 ng/L for women and 19.8 ng/L for men, with an overall value of 17.5 ng/L), CRP: 0–0.5 mg/L. The hemogram parameters were analyzed with the flow cytometric method on the ABX-Pentra DX 120 (Horiba LTD, Japan) device. The reference test ranges for these analytical methods are as follows: White blood count (WBC): 3.7–10.4 × 109 L^{-1}, Neutrophil count (Neu): 1.8–7.8 × 109 L^{-1}, Lymphocyte count (Lym): 0.9–3.7 × 109 L^{-1}, Hemoglobin (Hb): 10.8–15.1 g/dL, Platelet (Plt): 149–371 × 109 L^{-1}.

2.3.2. ELISA method

Myeloperoxidase and paraoxonase concentrations in the serum samples and asprosin concentration in plasma samples were studied using human ELISA kits (catalog no: E0880Hu and E0931Hu, Lot no: 202011017 and 202011017; catalog no: E4095Hu, Lot no: 202011017, respectively, BT Lab/Bioassay Technology Laboratory, Zhejiang, China), as indicated in the kit procedures. Absorbances were read spectrophotometrically at 450 nm with an ELx800 ELISA reader (BioTek Instruments, Winooski, VT, USA). Bio-Tek ELX50 (BioTek Instruments, USA) was utilized as an automatic washer in plate washing. The results were reported as ng/ml for serum myeloperoxidase and paraoxonase concentrations and ng/ml for plasma asprosin concentration. The measurement ranges of the kits were 0.1–30 ng/ml and 0.3–90 ng/ml for serum myeloperoxidase and paraoxonase concentrations, respectively, and 0.5–100 ng/ml for plasma asprosin concentration. The minimum measurable concentrations of the kits were 0.05 ng/ml and 0.15 ng/ml for serum myeloperoxidase and paraoxonase, respectively, and 0.23 ng/ml for plasma asprosin concentration. The intra-assay and inter-assay coefficient variables (%CV) of all kits were <10%. All ELISA analyses in the present research were conducted in the Medical Biochemistry R&D laboratory of the Faculty of Medicine of Kafkas University.

2.4. Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences 18.0 program. In descriptive analyses, frequency data were presented as number (n) and percentage (%), while numerical data were reported as arithmetic mean ± standard deviation (sd) and median (min-max). The suitability of numerical data to normal distribution was examined by the Kolmogorov–Smirnov and Shapiro–Wilk tests. The independent samples T-test evaluated the distribution of normally distributed numerical data in two independent groups, and the one-way ANOVA test assessed the distribution in more than two groups. The distribution of non-normally distributed numerical variables in two independent groups was assessed by the Mann–Whitney *U* test, and the Kruskal–Wallis test assessed the distribution in more than two groups. In the groups with significant Kruskal–Wallis test results, the Mann–Whitney *U* test was used for the post hoc test, and the Dunn–Bonferroni correction was performed. Spearman's correlation analysis examined the relationship between two non-normally distributed numerical variables. The cut-off features of the cardiac markers measured by ELISA for the presence of disease were assessed by receiver operating characteristics (ROC) curve. Binary logistic regression analysis was used for cardiac marker concentrations to predict the presence of STEMI and NSTEM. Multinominal logistic regression analysis was conducted

for cardiac markers to predict the type of STEMI, NSTEM and control group. As a result of the power analysis conducted to ensure that the sample to be selected in the study represents the universe; It has been calculated that if the number of individuals to be sampled is at least 80 (at least 40 individuals for patient and control groups), with a medium effect size ($f = 0.25$), 80% power can be achieved with 95% confidence (Type I error, $\alpha = 0.05$) [12].

3. Results

The current study was conducted on 60 patients diagnosed with AMI and 30 healthy individuals. NSTEMI was present in 50% ($n = 30$) and STEMI was in 50% ($n = 30$) of patients diagnosed with acute myocardial infarction. Males constituted 75% ($n = 45$) of the patients and 53.30% of the control group. There was a history of at least one chronic disease in 78.34% ($n = 47$) of the patient group. Table 1 contains the patient and control groups' demographic characteristics and laboratory values. The patients' age, SBP, DBP, Hs-cTnI, CK, CK-MB, WBC, Neu count, CRP, HbA1c, glucose, AST, LDH, TG, TC, and LDL measurements were revealed to be higher in comparison with the control group ($p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.001$, $p < 0.001$, $p = 0.020$, $p < 0.001$, $p < 0.001$, $p = 0.005$, $p = 0.012$, $p = 0.020$, $p = 0.005$, $p < 0.001$).

Table 2 shows the distribution of the cardiac markers measured by ELISA in the patient and control groups. MPO and asprosin parameters were in the patient group than in the control group, and the PON parameter was determined to be lower ($p = 0.001$, $p < 0.001$, $p < 0.001$, respectively).

The type of AMI in the patients and the distribution of the demographic and laboratory parameters in the control group were vared in Table 3. Although age, SBP, DBP, Hs-cTnI, CK, CK-MB, WBC, glucose, and LDL concentrations were lower in the control group than in the NSTEMI and STEMI groups, HDL concentration was higher in the control group ($p = 0.006$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.002$, $p = 0.001$, $p = 0.044$, $p = 0.003$, respectively). Neutrophil count and LDH measurements were lower in the control group in comparison with the STEMI group ($p = 0.001$, $p = 0.044$). CRP, HbA1c, AST, and cholesterol measurements were lower in the control group in comparison with the NSTEMI group ($p = 0.015$, $p = 0.003$, $p = 0.015$, $p = 0.006$, respectively). The triglyceride concentration was revealed to be higher in the patient group with NSTEMI than in the STEMI and control groups ($p = 0.003$).

Table 4 shows the distribution of the cardiac parameters measured by ELISA according to the type of AMI and control group. Asprosin concentration was lower in the control group than in the NSTEMI and STEMI groups ($p < 0.001$), and the PON concentration was higher in the control group than in the NSTEMI and STEMI groups ($p < 0.001$). MPO concentration was lower in the control group than in the NSTEMI group ($p = 0.001$).

The relationship of the cardiac markers measured by ELISA with the lipid profile, glucose, and HbA1c is presented in Table 5. A significant positive correlation at a good level was found between Hs-cTnI and CK and CK-MB measurements (r and p values, respectively; $r = 0.640$, $p < 0.001$; $r = 0.602$, $p < 0.001$). A positive correlation was detected between Hs-cTnI and MPO, LDL, glucose, and HbA1c, and a negative low-moderate significant correlation was determined with PON (r and p values, respectively; $r = 0.363$, $p < 0.001$; $r = 0.335$, $p = 0.001$; $r = 0.368$, $p < 0.001$; $r = 0.336$, $p = 0.001$; $r = -0.378$, $p < 0.001$). A moderately significant positive

Table 1
Distribution of the demographic characteristics and laboratory values between patient and control groups.

	Patient (n = 60)	Control (n = 30)	p-value
Age (years)	66.47 ± 12.28 (58.5–77.0)	54.70 ± 21.50 (33.7–73.7)	0.008[a]
Pulse (beats/min)	83.00 (76.25–95.7)	85.00 (75.00–90.0)	0.647[b]
SBP (mmHg)	140.00 (121.2–150.0)	120.00 (110.0–130.0)	<0.001[b]
DBP (mmHg)	85.00 (70.0–98.7)	70.00 (65.0–80.0)	<0.001[b]
Hs-cTnI(ng/mL)	224.00 (87.5–519.0)	6.90 (3.0–13.9)	<0.001[b]
CK (IU/L)	223.00 (150.7–466.2)	73.91 (65.0–87.7)	<0.001[b]
CK-MB (U/L)	41.00 (28.2–76.7)	22.00 (16.5–28.2)	<0.001[b]
WBC ($\times 10^9$ L^{-1})	9.85 (8.1–13.1)	7.80 (6.1–9.3)	0.001[b]
Hgb (gr/dL)	14.57 ± 1.97 (15.9–13.4)	14.13 ± 1.98 (12.8–15.6)	0.324[a]
Neu($\times 10^9$ L^{-1})	7.25 (5.3–10.1)	4.85 (3.8–6.6)	<0.001[b]
Lym ($\times 10^9$ L^{-1})	1.81 (1.3–2.5)	2.00 (1.4–2.5)	0.713[b]
Plt ($\times 10^9$ L^{-1})	241.00 (206.5–279.2)	227.50 (198.0–266.2)	0.467[b]
CRP (mg/L)	0.49 (0.2–1.2)	0.28 (0.1–0.7)	0.020[b]
HbA1c (%)	6.30 (5.8–7.2)	5.72 (5.5–6.2)	<0.001[b]
Glucose (mg/dL)	137.00 (116.0–188.2)	107.50 (99.5–127.2)	<0.001[b]
Urea (mg/dL)	37.50 (30.0–48.0)	35.00 (26.7–48.7)	0.213[b]
Creatinine (mg/dL)	0.95 (0.8–1.1)	0.94 (0.7–1.0)	0.592[b]
AST (U/L)	29.50 (21.0–55.7)	24.00 (17.0–31.0)	0.005[b]
ALT (U/L)	20.50 (14.0–31.0)	23.00 (14.5–23.0)	0.489[b]
LDH (U/L)	243.50 (203.5–304.2)	182.00 (158.5–271.5)	0.012[b]
TG (mg/dL)	102.00 (75.0–183.0)	96.50 (54.0–106.7)	0.020[b]
TC (mg/dL)	171.00 (153.2–199.0)	149.50 (119.0–179.0)	0.005[b]
HDL (mg/dL)	42.95 ± 24.71 (32.2–44.7)	50.20 ± 12.63 (40.5–56.0)	0.135[a]
LDL (mg/dL)	113.20 ± 36.16 (84.6–134.8)	85.32 ± 25.31 (52.2–103.0)	<0.001[a]

[a] Independent samples *t*-test, values are expressed as means ± standard deviations (IQR).
[b] Mann–Whitney *U* Test, values are expressed as medians (IQR).

Table 2
Distribution of circulating MPO, PON, and asprosin values by the patient and control groups.

	Patient (n = 60)	Control (n = 30)	p-value[a]
MPO (ng/mL)	3.22 (2.4–4.4)	2.49 (1.9–2.9)	0.001
PON (ng/mL)	8.94 (7.6–10.4)	10.44 (9.1–20.0)	<0.001
Asprosin (ng/mL)	10.84 (8.8–17.8)	4.82 (4.6–8.0)	<0.001

[a] Mann–Whitney *U* test, values are expressed as medians (IQR).

Table 3
Distribution of the laboratory parameters by the NSTEMI, STEMI, and control groups.

	NSTEMI $(n = 30)_a$	STEMI $(n = 30)_b$	Control $(n = 30)_c$	p	posthoc
Age (years)	66.73 ± 11.62 (55.5–77.2)	66.20 ± 13.10 (60.0–77.0)	54.70 ± 21.50 (33.7–73.7)	0.006[a]	a–c, b–c
Pulse (beats/min)	85.00 (74.5–100.5)	82.00 (76.7–94.2)	85.00 (75.00–90.0)	0.775[b]	
SBP (mmHg)	132.50 (120.0–150.0)	142.00 (130.0–160.0)	120.00 (110.0–130.0)	<0.001[b]	a–c, b–c
DBP (mmHg)	80.00 (70.0–91.2)	90.00 (80.0–100.0)	70.00 (65.0–80.0)	<0.001[b]	a–c, b–c
Hs-cTnI(ng/L)	428.00 (124.2–1212.7)	120.00 (57.0–289.1)	6.90 (3.0–13.9)	<0.001[b]	a–b, b–c
CK (IU/L)	243.00 (139.7–460.7)	244.00 (167.2–560.5)	73.91 (65.0–87.7)	<0.001[b]	a–c, b–c
CK-MB (U/L)	42.00 (25.0–81.2)	38.50 (30.0–74.7)	22.00 (616.5–28.2)	<0.001[b]	a–c, b–c
WBC (10^3/μL)	9.60 (7.6–12.8)	10.40 (8.4–14.7)	7.80 (6.1–9.3)	0.002[b]	a–c, b–c
Hgb (gr/dL)	14.86 ± 1.69 (14.1−15.8)	14.27 ± 1.98 (12.7−16.2)	14.13 ± 1.98 (12.8−15.6)	0.319[a]	
Neu($\times 10^9$ L^{-1})	6.95 (4.7–9.8)	7.64 (5.7–10.5)	4.85 (3.8–6.6)	0.001[b]	b–c
Lym($\times 10^9$ L^{-1})	1.81 (1.3–2.5)	1.81 (1.2–2.6)	2.00 (1.4–2.5)	0.911[b]	
Plt ($\times 10^9$ L^{-1})	236.00 (212.5–264.0)	248.00 (200.0–303.2)	227.50 (198.0–266.2)	0.620[b]	
CRP (mg/L)	0.72 (0.3–1.3)	0.41 (0.2–0.7)	0.28 (0.1–0.7)	0.015[b]	a–c,
HbA1c	6.60 (5.8–8.2)	6.18 (5.7–6.9)	5.72 (5.5–6.2)	0.003[b]	a–c,
Glucose (mg/dL)	137.50 (112.5–212.7)	137.00 (117.5–184.7)	107.50 (99.5–127.2)	0.001[b]	a–c, b–c
Urea (mg/dL)	35.50 (29.7–49.5)	42.50 (30.7–48.0)	35.00 (26.7–48.7)	0.238[b]	
Creatinine (mg/dL)	0.92 ± 0.20 (0.8−1.0)	1.16 ± 0.46 (0.8–1.3)	0.94 (0.7–1.0)	0.033[a]	a–b
AST (U/L)	33.50 (20.7–57.7)	27.00 (20.7–48.00)	24.00 (17.0–31.0)	0.015[b]	a–c,
ALT (U/L)	19.50 (14.0–28.7)	22.00 (13.7–36.2)	23.00 (14.5–23.0)	0.596[b]	
LDH (U/L)	243.00 (190.0–317.0)	244.00 (209.0–279.0)	182.00 (158.5–271.5)	0.044[b]	b–c
TG (mg/dL)	135.00 (94.0–208.5)	81.00 (59.0–141.5)	96.50 (54.0–106.7)	0.001[b]	a–b, a–c
Cholesterol (mg/dL)	185.50 (155.5–219.0)	163.00 (146.5–182.5)	149.50 (119.0–179.0)	0.006[b]	a–c
HDL (mg/dL)	41.50 (33.50– 44.25))	40.50 (32.00– 46.00))	55.5 (40.50– 56.00)	0.003[b]	a–c, b–c
LDL (mg/dL)	115.04 ± 41.49 (78.9–142.2)	111.37 ± 30.53 (94.1–124.3)	85.32 ± 25.31 (52.2–103.0)	0.001[a]	a–c, b–c

[a] One-way ANOVA test, values are expressed as means ± standard deviations (IQR).
[b] Kruskal–Wallis test, values are expressed as medians (IQR).

Table 4
Distribution of circulating MPO, PON, and asprosin values by NSTEMI, STEMI, and control groups.

	NSTEMI $(n = 30)_a$	STEMI $(n = 30)_b$	Control $(n = 30)_c$	p[a]	posthoc
MPO (ng/ml)	3.56 (2.5–7.7)	3.05 (2.3–4.1)	2.49 (1.9–2.9)	0.001	a–c,
PON (ng/ml)	8.69 (7.5–9.8)	9.19 (7.8–11.5)	10.44 (9.1–20.0)	<0.001	a–c, b–c
Asprosin (ng/ml)	10.05 (6.0–18.6)	11.25 (9.8–18.4)	4.82 (4.6–8.0)	<0.001	a–c, b–c

[a] Kruskal–Wallis test, values are expressed as medians (IQR).

correlation was identified between Hs-cTnI and asprosin, and a moderately significant negative correlation was revealed with HDL (r and p values, respectively; $r = 0.484$, $p < 0.001$; $r = -0.405$, $p < 0.001$).

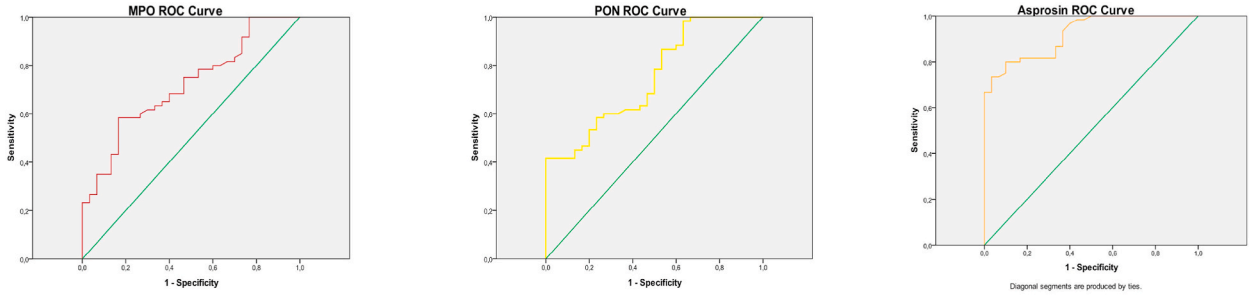
To identify the diagnostic value of the laboratory parameters (MPO, asprosin, and PON), ROC curves were constructed and area under the curves were calculated. Thus, cut-off values for these parameters were presented in order to reveal the distinction between patient and control groups. It was shown that values of 2.75 and higher for MPO could predict ACS patients with 65.0% sensitivity and 63.3% specificity compared to the control group. The area under the curve was determined as 0.717 ($p = 0.001$, 95% CI: 0.609–0.825). It was indicated that values of 8.11 and higher for asprosin could predict ACS patients with 81.7% sensitivity and 83.3% specificity compared to the control group. The area under the curve was 0.920 ($p < 0.001$, 95% CI: 0.867–0.973). It was demonstrated that values of 9.32 and lower for PON could predict ACS patients with 61.7% sensitivity and 63.3% specificity compared to the control group. The area under the curve was found as 0.748 ($p < 0.000$, 95% CI: 0.645–0.852, Fig. 1).

A binary logistic regression model was established to predict serum MPO, PON and plasma asprosin concentrations could be independent risk factors in the etiopathogenesis of AMI. The model fit was good (Nagelkarke R Square: 0.782; $p = 0{,}002$). A 1 ng/ml increase in the MPO measurement increases the odds of having AMI by 3.61 ($p = 0.041$, 95% CI: 1.055–12.397). According to the established model, a 1 ng/ml increase in the asprosin measurement increases the odds of having AMI by 2.33 ($p < 0.001$, 95% CI: 1.479–3.683) (Table 6).

Table 5
Relationship between biochemical parameters, MPO, PON, and asprosin.

	Hs-cTnI		CK		CK-MB		MPO		PON		Asprosin	
	r	p	r	p	r	p	r	p	r	p	r	p
Hs-cTnI	–	–	0.640	<0.001	0.602	<0.001	0.363	<0.001	−0.378	<0.001	0.484	0.001
CK	0.640	<0.001	–	–	0.686	<0.001	0.324	<0.001	−0.281	0.007	0.439	<0.001
CK-MB	0.602	<0.001	0.686	<0.001	–	–	0.207	0.050	−0.226	0.033	0.266	0.011
MPO	0.363	<0.001	0.324	<0.001	0.207	0.050	–	–	−0.127	0.234	0.143	0.179
PON	−0.378	<0.001	−0.281	0.007	−0.226	0.033	−0.127	0.234	–	–	−0.223	0.034
Asprosin	0.484	0.001	0.439	<0.001	0.266	0.011	0.143	0.179	−0.223	0.034	–	–
TG	0.296	0.005	0.167	0.119	0.066	0.541	0.073	0.495	−0.182	0.087	0.205	0.054
Cholesterol	0.225	0.033	0.199	0.060	0.157	0.139	0.088	0.409	−0.135	0.204	0.120	0.259
HDL	−0.405	<0.001	−0.271	0.010	−0.182	0.086	−0.237	0.024	0.119	0.264	−0.385	<0.001
LDL	0.335	0.001	0.258	0.014	0.180	0.089	0.098	0.358	−0.197	0.063	0.262	0.013
Glucose	0.368	<0.001	0.293	0.005	0.368	<0.001	0.128	0.229	−0.094	0.377	0.226	0.032
HbA1c	0.336	0.001	0.280	0.008	0.416	<0.001	0.133	0.216	−0.174	0.104	0.224	0.036

*: Spearman's correlation test, r: correlation coefficient, *p*-value of <0.05 was considered to indicate statistical significance.



(A) (B) (C)

Fig. 1. Receiver operating characteristic curves for myeloperoxidase (MPO; A), paraoxonase (PON; B), and asprosin (C).

A multinomial logistic regression model was established to predict AMI groups (NSTEMI, STEMI, control) with MPO, PON, and asprosin measurements. The model fit was good (Nagelkerke R Square: 0.666; $p < 0.001$). Although a 1 ng/ml increase in the MPO measurement increased the odds of having NSTEMI by 4.14 ($p = 0.025$, 95% CI: 1.195–14.350) compared to control patients, a 1 ng/ml increase in asprosin concentration increased the odds of having NSTEMI by 2.35 ($p < 0.001$, 95% CI: 1.494–3.721) compared to control patients. Furthermore, a 1 ng/ml increase in asprosin concentration increased the odds of having STEMI by 2.31 ($p < 0.001$, 95% CI: 1.469–3.655) compared to control patients (Table 7).

4. Discussion

In the present study, although routine parameters were within normal test ranges in patients diagnosed with AMI, significant differences were observed compared to the control group. Specifically, high LDL and TC concentrations and low HDL concentration were detected in the patients. Triglyceride concentrations were low in patients with STEMI and high in patients with NSTEMI. MPO, asprosin, and PON studied as representatives of oxidant and antioxidant parameters, show AMI changes. Thus, these parameters make attractive candidates to help evaluate ACS.

Myocardial infarction occurs when the atherosclerotic process blocks blood flow from the coronary artery. Angiographic studies demonstrate that plaque activation rather than stenosis in the existing atherosclerotic plaque accelerates ischemia and infarction. Most infarction cases result from forming an occlusive thrombus on the plaque surface. Plaque rupture and endothelial erosion are the two leading causes of coronary thrombosis. Cells involved in inflammation (such as macrophages and mast cells) that can weaken the atherosclerotic fibrous cap and activate cells in the nucleus produce many inflammatory molecules and proteolytic enzymes. Thus, rupture may occur in the atherosclerotic plaque, and the formation of a thrombus may be induced and transformed into a sensitive, unstable structure that can lead to ACS [13].

Myeloperoxidase is a member of the peroxidase superfamily [14]. It is mostly present in neutrophils, monocytes, and tissue macrophages and is released in response to various stimuli. Myeloperoxidase and its oxidation products are found in atheroma and have possible functions such as participating in atherosclerotic plaque formation and destabilization. Hence, MPO is a marker of the inflammatory state, and inflammation is involved in all stages of the atherosclerotic process, from initial endothelial dysfunction to plaque rupture [15]. Circulating neutrophils and monocytes together provide the source of MPO production. In a study conducted, it was stated that MPO was localized with iron-containing macrophages on the surface and its density in thrombotic lesions correlates well with the size of the thrombus [16]. In their research in which they measured MPO concentration in patients with ACS before angiography and heparin therapy, Ndrepepa et al. found the plasma MPO concentration to be higher than the control group. They even found that the MPO concentration increased progressively with the increasing clinical severity of CAD (progression from stable CAD, NSTEMI, to STEMI). The researchers attributed this situation to the persistence of inflammation at all stages, from inflammation and endothelial dysfunction to atherosclerotic plaque rupture, and indicated that elevated MPO concentration might reflect the inflammatory state [17]. In their research, Sawicki et al. revealed that MPO and cTnI values were higher in patients diagnosed with ACS. According to this study, a single plasma MPO measurement acquired within 6 h of the onset of chest pain gives important diagnostic information, especially in patients with negative troponin at baseline [18]. In our study, whereas the MPO concentration was higher in AMI patients compared to the control group, it was similar between AMI subgroups (STEMI, NSTEMI). These results may be related to

Table 6
Binary logistic regression analysis of MPO, PON, and asprosin.

Model (According to the control patient)		Exp (B)	Sig.	95.0% confidence interval for exp (B)	
				Lower Bound	Upper Bound
ACS	**MPO**	3.617	0.041	1.055	12.397
	PON	0.579	0.084	0.312	1.076
	Asprosin	2.334	<0.001	1.479	3.683

Table 7
Multinominal logistic regression analysis of MPO, PON, and asprosin.

Model (According to the control patient)		Exp (B)	Sig.	95.0% confidence interval for exp (B)	
				Lower Bound	Upper Bound
NSTEMI	**MPO**	4.141	0.025	1.195	14.350
	PON	0.534	0.053	0.283	1.007
	Asprosin	2.358	<0.001	1.494	3.721
STEMI	**MPO**	3.301	0.059	0.957	11.388
	PON	0.611	0.121	0.328	1.138
	Asprosin	2.317	<0.001	1.469	3.655

the small sample size. The measurement of MPO and Hs-cTnI may be supportive for early diagnosis of AMI in patients who present to the emergency department with chest pain complaints and have a preliminary ACS diagnosis.

LDL oxidation products, which are effective in developing atherosclerotic plaque and formed during lipid peroxidation, are responsible for oxidative damage to the heart. Detecting this oxidative damage in the heart early, the presence of serum-specific antioxidants and serum paraoxonase enzyme activity may provide important information in cardiovascular diseases. Paraoxonase enzyme hydrolyzes the toxic metabolite of parathion and paraoxon and shows vascular oxidative stress. The paraoxonase enzyme has three isoforms, PON1, PON2, and PON3, reducing oxidative stress [19]. PON1 exhibits the strongest antioxidant activity. PON1, which can protect both LDL and cell membranes from oxidation, displays atheroprotective properties. Atherosclerosis is the inflammatory condition causing PON1 downregulation and HDL lipoprotein dysfunction. PON1 protects LDL from oxidation and inhibits its oxidation by binding to HDL in a calcium-dependent manner. Atheroprotective HDL is controlled by reverse cholesterol transport and antioxidative HDL proteins [lecithin: cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein, lipoprotein-associated phospholipase A2 and PON1] [20]. A study found that PON1 activity and HDL concentrations were significantly lower in patients with coronary heart disease compared to the control group [21].

In their study, Thakkar et al. associated higher cholesterol efflux capacity, PON1 activity, and apolipoprotein A-I concentration with a lower probability of developing ACS in ACS patients [22]. Another study revealed a relationship between a decrease in PON activity and a decrease in HDL functions in patients with type 2 DM [23]. Our study found PON activity and HDL to be lower in patients diagnosed with AMI compared to the control group. Moreover, high glucose and HbA1c levels in patients indicate poor glycemic control and contribute to atherosclerosis by increasing oxidative stress. It is thought that decreased PON activity and poor glycemic control are insufficient to inhibit HDL and LDL oxidation and cause deterioration of HDL functions. Hence, it indicates that a decrease in PON concentration as an antioxidant parameter in the development of AMI can be evaluated in the diagnosis of ACS.

Asprosin has recently been defined as a fasting-induced glucogenic hormone [24]. Asprosin represents a hormone that directs hepatic glucose release through the signaling pathway of G-protein cyclic adenosine monophosphate (cAMP)/protein kinase A (PKA) released from white adipose tissue, can cross the blood-brain barrier to induce hypothalamic feeding circuits, and thus stimulates appetite and affects obesity. Asprosin is important in many CAD risks, including insulin resistance and inflammation. Moradi et al. revealed that circulating asprosin concentration was significantly elevated in patients diagnosed with ACS compared to controls [25]. Adipose tissue is a dynamic organ and the adipokine profile changes depending on the amount and condition of the adipose tissue. Adipokines have both central (regulates appetite and energy expenditure) and peripheral (insulin sensitivity, lipid uptake and oxidative capacity) regulatory effects. In the presence of obesity, adipokine release causes an increase risk of cardiovascular disease, and the development of type 2 diabetes and insulin resistance. In the presence of obesity, adipokine release causes an increase in the risk of insulin resistance and cardiovascular disease, and the development of insulin resistance and type 2 diabetes [26]. Therefore, in our study, individuals with a BMI $\geq$30 kg/m^2 were excluded from the study to prevent that asprosin levels were not affected by obesity. In our research, the higher asprosin concentration in patients diagnosed with AMI compared to controls indicates insulin resistance and increased inflammation. It was even determined that a 1 ng/ml increase in asprosin concentration increased the probability of having AMI by 2.33 times in comparison with control patients ($p < 0.001$, 95% CI: 1.479–3.683). Furthermore, a positive correlation with Hs-cTnI, glucose, Hb-A1c, and LDL and a negative correlation with PON suggest a possible relationship of asprosin in the pathophysiology of CAD. Hence, it can be considered a possible biomarker to assess in patients followed up with ACS.

5. Limitations

This investigation has several limitations that should be considered. Firstly, the results may not represent a larger population due to the small sample size. Secondly, the study was conducted at a single center, which could limit the generalizability of our findings. Finally, it was impossible to obtain repeated biomarkers measurements after the diagnosis of AMI, so the changes in these markers following angiography are unknown. This is a significant limitation to our ability to understand the dynamics of biomarker changes in the context of AMI. Therefore, in new studies, a timeline can be created with measurements to be taken in consecutive time periods before and after angiography. Therefore, in new studies, a timeline can be created by measuring blood samples taken from patients at consecutive time periods before and after angiography, after the onset of AMI symptoms.

Although there are limitations mentioned in our study, to the best of our knowledge, this is one of the first studies in its area in the literature review. In our study, the diagnostic value of oxidative stress parameters (MPO and PON) and adipokine peptide hormone (asprosin), which can create alternative to troponin in AMI were studied together.

6. Conclusion

In our study, the AMI diagnostic values of MPO, PON, and asprosin were lower than troponin. However, the blood concentrations of these biomarkers varied in patients with AMI, they were correlated with HcTnI, and when looking at the ROC curve, their AUC values were above 0.70, so they were thought to be associated with AMI. The oxidant–antioxidant imbalance leads to lipid peroxidation and atherosclerosis development. This process is primarily driven by factors, such as adipose tissue, insulin resistance, and dyslipidemia. The use of newly developed biomarkers can aid in the early detection and diagnosis of AMI, but further research is needed to confirm their effectiveness.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Handan Ciftci: Writing – original draft, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Huseyin Fatih Gul:** Project administration, Investigation, Conceptualization. **Levent Sahin:** Methodology, Investigation, Data curation. **Turgut Dolanbay:** Methodology, Investigation, Data curation. **Omer Canacik:** Resources, Data curation. **Emre Karsli:** Resources, Formal analysis, Data curation. **Dogan Ercin:** Validation, Data curation. **Mahmut Karapehlivan:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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