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Evaluation of novel biomarkers for early diagnosis of bisphenol A-induced coronary artery disease

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ABSTRACT

Introduction: Bisphenol A (BPA), a ubiquitous synthetic monomer primarily used in the manufacture of polycarbonate plastic and epoxy resins and as a non-polymer additive to other plastics, can leach into the food and water supply and has been linked to cardiovascular disease (CVD). This study aimed to analyze BPA levels in patients with varying numbers of coronary artery stenosis and evaluate the prognostic value of new biomarkers cluster of differentiation 36 (CD36) and heart-type fatty acid-binding protein (H-FABP), compared to troponin I and creatine kinase (CK) MB, for detecting myocardial injury.

Method: Eighty nine patients undergoing angiography at Urmia Hospital from March 2019 to 2020 were included. Serum levels of BPA, CD36, H-FABP, troponin I, and CK-M were measured.

Results: When comparing CD36 and H-FABP with troponin I and CK-MB across coronary occlusion classes, receiver operating characteristic curves indicated CD36 and H-FABP had higher accuracy than troponin I and CK-MB for detecting stenosis stages. In patients with occlusion, significant alterations were detected in age, sex, BMI, hypertension, diabetes, dyslipidemia, and smoking. BPA serum concentration significantly increased compared to normal subjects.

Conclusions: Our study revealed that serum biomarkers were valuable for prognosticating myocardial injury. Among these, CD36 and H-FABP were more accurate. BPA concentration correlated with myocardial necrosis, underlying disease, and occlusion stage, suggesting BPA's harmful effects.

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1. Introduction

Cardiovascular disease (CVD) is a leading cause of death worldwide, with high rates in many countries [1,2]. Exposure to certain environmental chemicals, like BPA, may increase CVD risk [3,4]. Public health agencies have therefore paid increasing attention to risks posed by such chemicals [5].

During the last few years, public health agencies have been concerned about xenobiotic agents with hormonal influence on wildlife, humans, and environments [5]. Of concern is BPA, a common ingredient in many plastics and food packaging materials, linked to an increased CVD risk [4,6].

Endocrine-disrupting chemicals (EDCs) are natural or human-made chemicals that may mimic, block, or interfere with the body's hormones, which are part of the endocrine system. These chemicals are associated with a wide array of health issues [3,7]. BPA is an EDC that was initially used to improve the BMI, food intake, and performance of livestock [8,9]. BPA was administered to women as an alternative to diethylstilbestrol (DES) for its estrogenic effects [10].

BPA is found in special plastics that contact food and can be absorbed through ingestion, inhalation, and skin [11,12]. Approximately 9 % of BPA is used in the inner layer of canned food, with sterilization causing 80–100 % migration of BPA to the food, and heating the containers leading to increased BPA concentration [13–15]. BPA is also present in other products such as eyewear, plastic bottles, dental products, water supply pipes, and bottle tops, exposing humans and animals to high levels [6,16].

BPA can cause health problems like precocious puberty and cardiovascular effects [4,17]. Research on the correlation between BPA and CVD is limited, but recent studies suggest BPA could directly induce CVD [3,4,18]. However, epidemiological data is controversial, requiring further studies [19–22].

Traditionally, monitoring, treatment, or prevention strategies of patients with CVD have assessed cardiac troponin I, myoglobin, and CK-MB [23–27]. These biomarkers are usually elevated in the end stage of cardiac muscle degeneration stage, representing the "point of no return" for the patient [28]. Moreover, much research has detected that not only does the final stage of myocardial damage increase these biomarkers, but a chronic subclinical increase of these biomarkers also arises in an early stage of Heart failure (HF) patients [29–31]. However, recent research suggested that these biomarkers' elevation could be affected in different circumstances, including having underlying diseases such as diabetes, congenital diseases, musculoskeletal problems, and performing heavy sports that cause trauma to the body's muscles [23,32]. Currently, with the advancement of science, new markers have been suggested for more accurate and specific detection of cardiac injury, including CD36 and H-FABP, that can be used for early detection of complications compared to the traditional assessment of HF [33,34]. CD36 is a multipurpose receptor with various ligands. Its physiological function in myocardial muscle is the uptake of long-chain fatty acids (FAs). Under uncontrolled FA accumulation in the myocardial system, CD36 participated in lipid accumulation, inflammation induction, and heart malfunction [35]. Unbound free fatty acids (FFAu) and their intracellular lipid-binding proteins, H-FABP, have been reported as clinical indicators of myocardial ischemia and necrosis, respectively. These biomarkers are suggested for detecting myocardial ischemia in the lacking of heart cell necrosis which could be used for initial recognition of myocardial injury [36].

The main source of energy for the heart and skeletal muscles is fatty acids (FAs). FAs are bound by FABPs intracellularly, which makes them more soluble and helps move them to various cell compartments for storage, oxidation, membrane formation, transcriptional control, and even outside the cell for autocrine or paracrine signaling. H-FABP is highly expressed in cardiac and interacts with a putative membrane FA transporter CD36 in mammary tissue. Therefore, when cardiac myocytes are damaged, H-FABP and CD36 enter the blood in large quantities and can be measured. The functional role of H-FABP and CD-36 is shown in Fig. A [37].

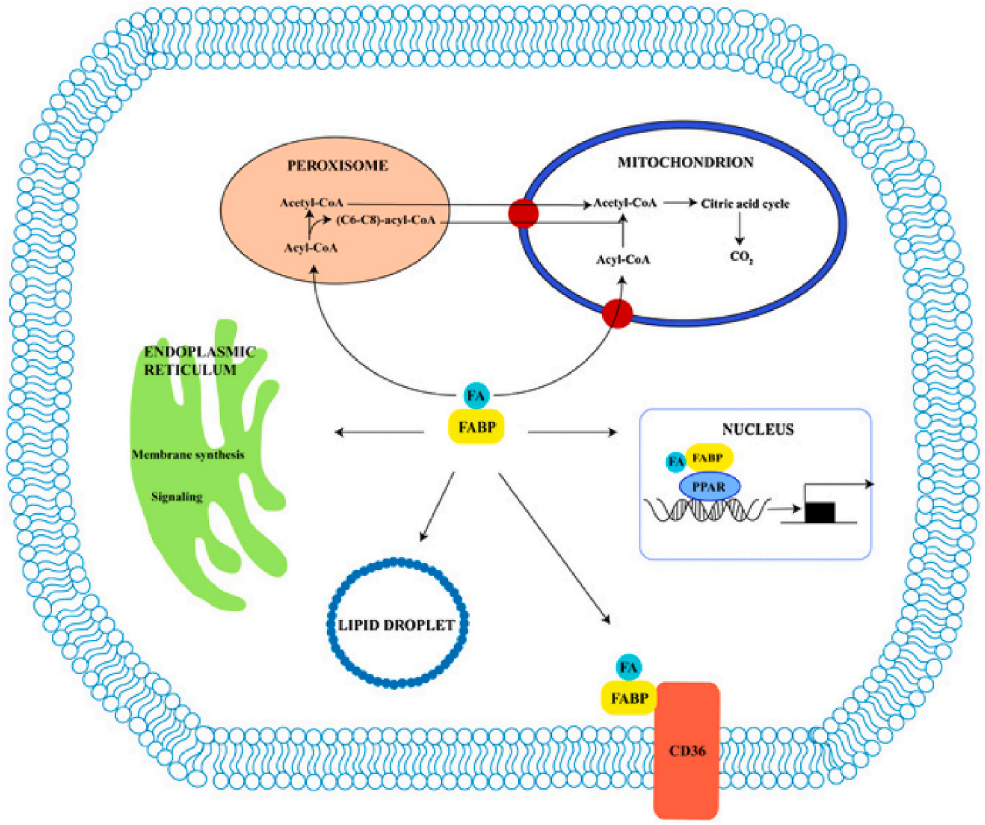

Fig. A. Potential roles for FABP in cells. The transport of fatty acids to specific cell compartments, such as lipid droplets for storage, the endoplasmic reticulum for membrane synthesis and signaling, the mitochondria and peroxisomes for oxidation, the nucleus for lipid-mediated transcriptional programs, or even to the outside of the cell to signal in an autocrine or paracrine manner, has been suggested to be a key function of FABPs [38].

This study aimed to assess the relationship between BPA and coronary artery disease (CAD). Blood samples were collected to determine BPA serum levels. Additionally, new biomarkers were examined for sensitivity and specificity in detecting early-stage CAD.

2. Material and method

2.1. Patients

This study enrolled patients with CVD who underwent coronary artery examination via angiography at Seyedoshohada Hospital between March 2019 and 2020. Hospitalized patients were included if they were detected with ASCAD following the national guidelines [38] and the New York Heart Association (NYHA) cardiac function classification standards. There were 55 males and 34 females with an average age of (61.65 ± 14.434) years ranging from 21 to 95 years old. Patients were excluded with a history of cancer, respiratory diseases, heart or brain surgery, trauma, or mental disease. Included patients were examined for coronary artery problems in Seyedoshohada Hospital before initiation of medical treatment. Patients who were removed from the angiography list for any reason (presence of severe peripheral vascular diseases, lack of satisfaction with angiography, death before angiography, etc.) and patients with renal and liver dysfunction were excluded. The overall system has been described in Fig. B.

Table 1
Significant multivariate effects (at $p < 0.05$ level).

Effect	Pillai's Trace[a]	F	df	*P*-Value	Eta2	Observed power†
Coronary Artery Occlusion	0.892	2.312	39.000	0.000	0.297	1.000
BPA	0.174	1.268b	12.000	0.257	0.174	0.655
Coronary Artery Occlusion[a] BPA	0.134	0.930b	12.000	0.522	0.134	0.491

[a] Pillai's trace is a test statistic produced by a MANOVA; df: degree of freedom; †Computed using alpha = 0.05.

Table 2
Baseline characteristics of the patients (n = 89).

	Normal	1VD	2VD	3VD	*P*-Value
Demographic characteristics					
Age, years (IQR)	57.35 (55.5)	63.55 (64.5)	60.56 (58)	68.03 (69)	0.015
Men, n (%)	16 (47 %)	12 (60 %)	13 (81 %)	14 (73 %)	0.037
Women, n (%)	18 (53 %)	8 (40 %)	3 (19 %)	5 (17 %)	
Measurements at baseline					
Body mass index, kg/m^2	24.21 ± 0/580	26.50 ± 0.647	27.75 ± 0.692	28.84 ± 0.514	0.000
HTN, n (%)	23 (67 %)	17 (85 %)	14 (87.5 %)	18 (94.7 %)	0.042
Diabetes mellitus, n (%)	8 (23 %)	10 (50 %)	7 (43.7 %)	17 (89.4 %)	0.001
Dyslipidemia	13 (38 %)	16 (80 %)	14 (87.5 %)	18 (94.7 %)	0.000
Smoking (%)	8 (23.5 %)	8 (40 %)	9 (56 %)	8 (44 %)	0.038

Values are mean standard deviation, median (IQR), or n (%).

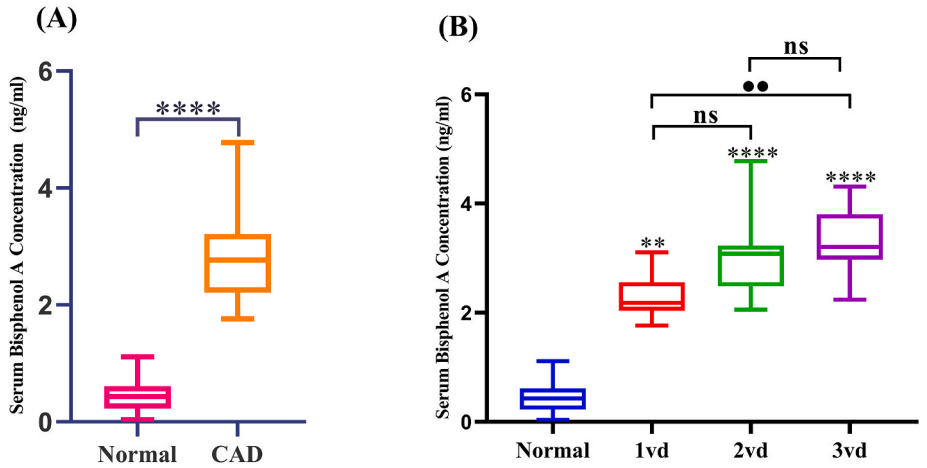

Fig. 1. Bisphenol A (BPA) concentrations in normal (Healthy subjects), and patients with coronary artery disease (CAD); including 1VD for one artery obstruction, 2VD for two artery obstructions, and 3VD for three artery obstructions groups. The asterisk indicates significant differences between Normal and CAD groups (including 1VD, 2VD, and 3VD). ** indicates P Value < 0.01; **** indicates P Value < 0.0001.

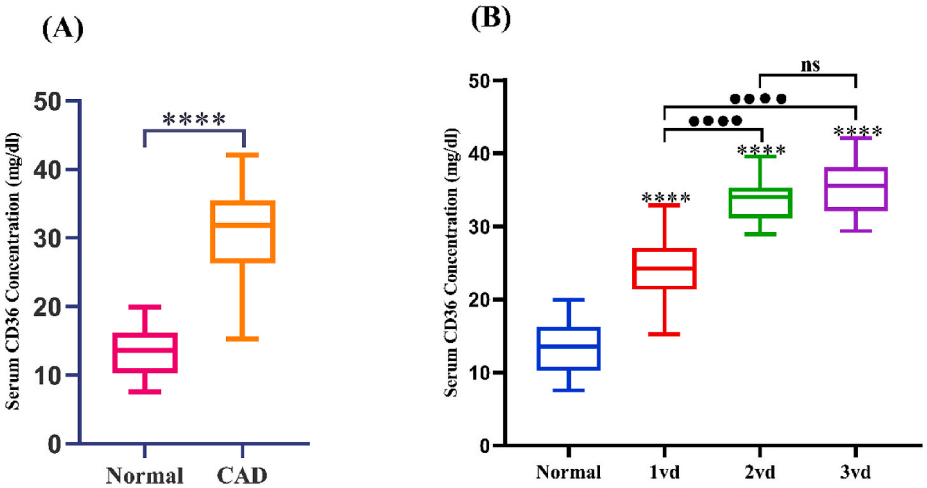

Fig. 2. Serum levels of CD36 in normal (Healthy subjects), and patients with coronary artery disease (CAD); including 1VD for one artery obstruction, 2VD for two artery obstructions, and 3VD for three artery obstructions groups. The asterisk indicates significant differences between Normal and CAD groups (including 1VD, 2VD, and 3VD). **** indicates P Value < 0.0001.

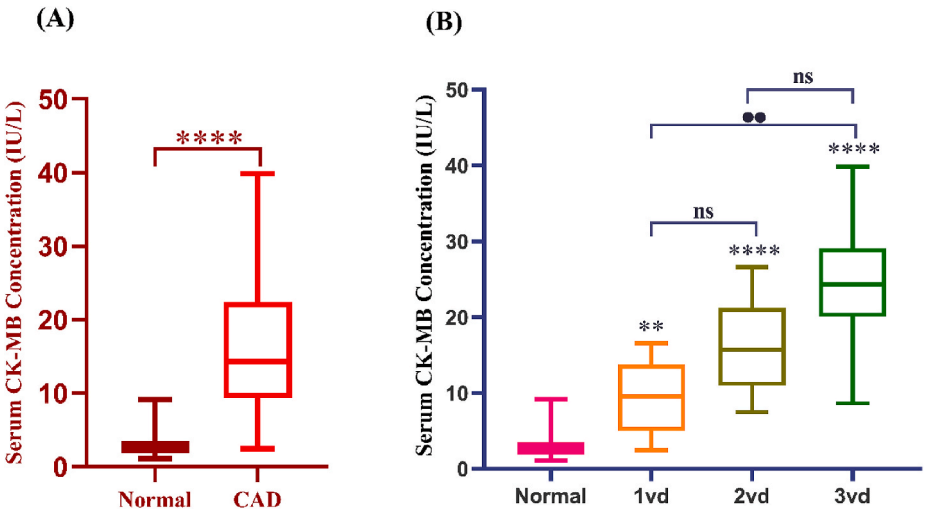

Fig. 3. Serum levels of CK-MB in normal (Healthy subjects), and patients with coronary artery disease (CAD); including 1VD for one artery obstruction, 2VD for two artery obstructions, and 3VD for three artery obstructions groups. The asterisk indicates significant differences between Normal and CAD groups (including 1VD, 2VD, and 3VD). ** indicates P Value < 0.01; **** indicates P Value < 0.0001.

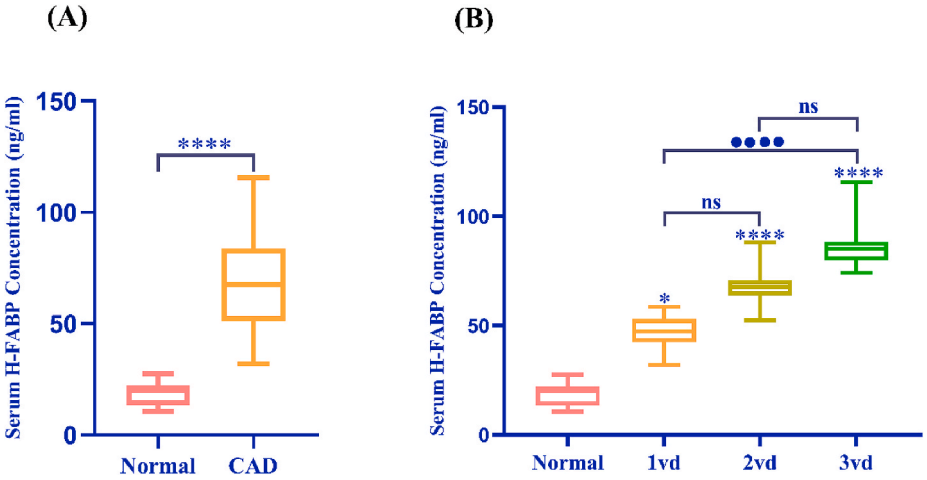

Fig. 4. Serum levels of H-FABP in normal (Healthy subjects), and patients with coronary artery disease (CAD); including 1VD for one artery obstruction, 2VD for two artery obstructions, and 3VD for three artery obstructions groups. The asterisk indicates significant differences between Normal and CAD groups (including 1VD, 2VD, and 3VD). * Indicates P Value < 0.05; **** indicates P Value < 0.0001.

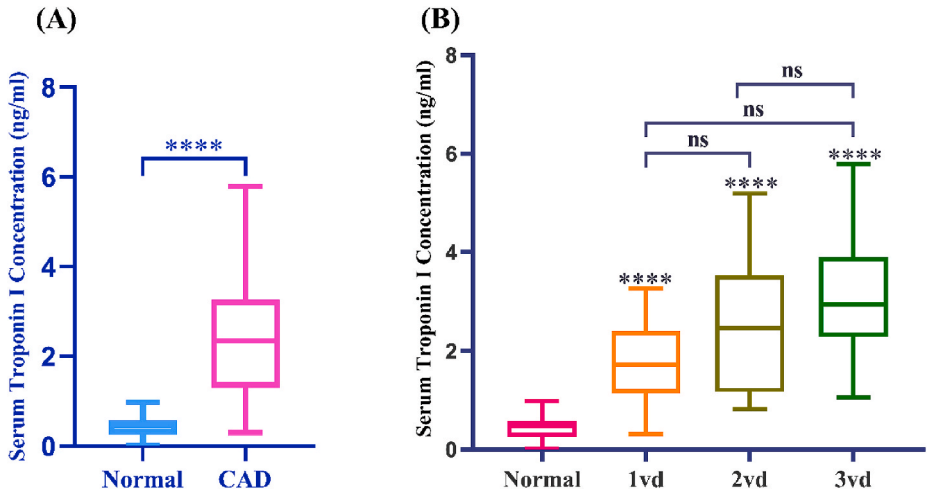

Fig. 5. Serum levels of Troponin I in normal (Healthy subjects), and patients with coronary artery disease (CAD); including 1VD for one artery obstruction, 2VD for two artery obstructions, and 3VD for three artery obstructions groups. The asterisk indicates significant differences between Normal and CAD groups (including 1VD, 2VD, and 3VD). **** indicates P Value < 0.0001.

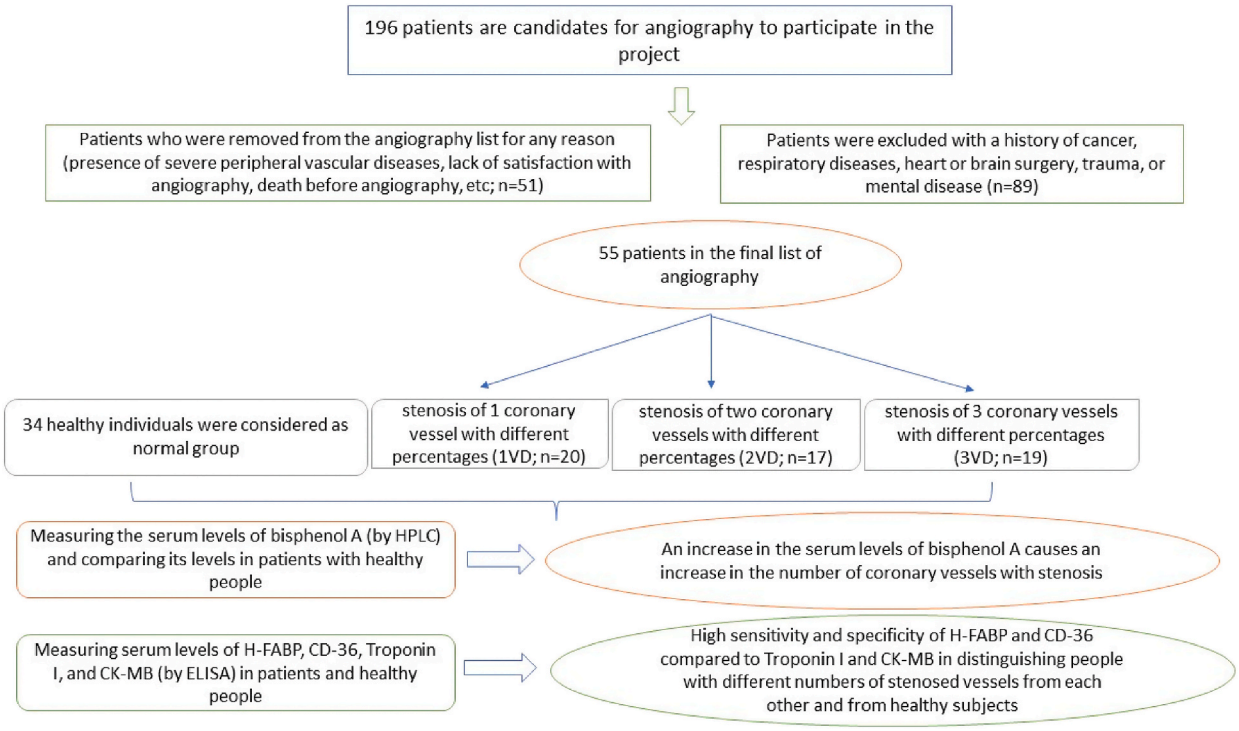

Fig. B. The overall system, approach, inclusion, exclusion criteria, and number of patients.

Clinical and demographic findings were assembled, including sex, age, other disease, and laboratory results (Table 2). The study was approved by the institutional ethics committee of the Aja University of Medical Sciences, Tehran province, Iran (IR.AJAUMS.REC.1400.049). The informed consent was signed by the patients or the guardians for all stages of the study.

2.2. Biochemical assessment

The peripheral venous blood sample was collected from fasted patients within 24 h after confirmation to determine regular blood examinations and biochemistry factors. H-FABP (Abcam, Cambridge, UK), CD36 (My BioSource, USA), and troponin I (Oxis Intl' Inc., USA) levels were analyzed using the ELISA kits, based on their instructions. CK-MB level was evaluated by spectrophotometer, according to kit instruction (Euro-BioGen). The assays were performed in triplicate according to the manufacturer's procedures. BPA

Table 3
Spearman's correlation coefficient between the results of all experimental blood samples.

	Age	Sex	BMI	HTN	DM	Dyslipidemia	Smoking	BPA	H-FABP	CD-36	Troponin I	CK-MB
Age	1	0.045	0.072	0.185	.247*	0.093	0.086	0.120	.303**	.240*	.246*	.243*
Sex		1	−0.001	−0.089	−0.002	−0.115	−.508**	−.280**	−.217*	−0.201	−0.157	−0.137
BMI			1	.307**	.309**	.413**	0.046	.605**	.516**	.492**	.458**	.405**
HTN				1	.230*	.225*	0.136	.298**	0.184	0.191	.265*	0.042
DM					1	.495**	−0.073	.418**	.444**	.380**	.418**	.325**
Dyslipidemia						1	−0.081	.508**	.479**	.453**	.501**	.331**
Smoking							1	.289**	0.110	0.148	.279**	0.158
BPA								1	.816**	.787**	.778**	.670**
H-FABP									1	.895**	.731**	.826**
CD-36										1	.707**	.804**
Troponin I											1	.769**
CK-MB												1

Table 4
Comparison of the prognostic value of serum H-FABP, CD36, Troponin I, and CK-MB levels with Coronary artery occlusion classification.

	AUC ± SE (P-Value)						Cutoff						Sensitivity (%)						Specificity (%)					
Parameters	Normal Vs. 1VD	Normal Vs. 2VD	Normal Vs. 3VD	1VD Vs. 2VD	1VD Vs. 3VD	2VD Vs. 3VD	Normal Vs. 1VD	Normal Vs. 2VD	Normal Vs. 3VD	1VD Vs. 2VD	1VD Vs. 3VD	2VD Vs. 3VD	Normal Vs. 1VD	Normal Vs. 2VD	Normal Vs. 3VD	1VD Vs. 2VD	1VD Vs. 3VD	2VD Vs. 3VD	Normal Vs. 1VD	Normal Vs. 2VD	Normal Vs. 3VD	1VD Vs. 2VD	1VD Vs. 3VD	2VD Vs. 3VD
Troponin I	0.946 ± 0.04 (P<0/0001)	0.99 ± 0.01 (P<0/0001)	1.000 ± 0.000 (P<0/0001)	0.65 ± 0.1 (p= 0.1346)	0.82 ± 0.07 (P= 0.0005)	0.64 ± 0.09 (P= 0.1643)	> 1.010	> 0.7943	> 1.012	> 2.724	> 2.669	> 2.208	90	100	100	44	68	84	100	88	100	95	95	44
CK-MB	0.906 ± 0.04 (P<0/0001)	0.99 ± 0.007 (P<0/0001)	0.99 ± 0.004 (P<0/0001)	0.78 ± 0.07 (P= 0.0046)	0.91 ± 0.05 (P<0/0001)	0.78 ± 0.07 (P= 0.0044)	> 4.737	> 6.291	> 8.593	> 15.46	> 15.82	> 22.33	80	100	100	56	84	68	91	94	97	95	95	87
H-FABP	1 ± 0.000 (P<0/0001)	1 ± 0.000 (P<0/0001)	1 ± 0.000 (P<0/0001)	0.98 ± 0.02 (P<0/0001)	1 ± 0.000 (P<0/0001)	0.91 ± 0.06 (P<0/0001)	> 29.69	> 39.88	> 50.81	> 59.19	> 66.36	> 72.78	100	100	100	94	100	100	100	100	100	100	100	88
CD36	0.982 ± 0.02 (P<0/0001)	1.000 ± 0.000 (P<0/0001)	1.000 ± 0.000 (P<0/0001)	0.97 ± 0.02 (P<0/0001)	0.98 ± 0.02 (P<0/0001)	0.66 ± 0.09 (P= 0.1047)	> 18.04	> 24.43	> 24.64	> 28.72	> 29.32	> 35.42	95	100	100	100	100	58	96	100	100	89	95	81

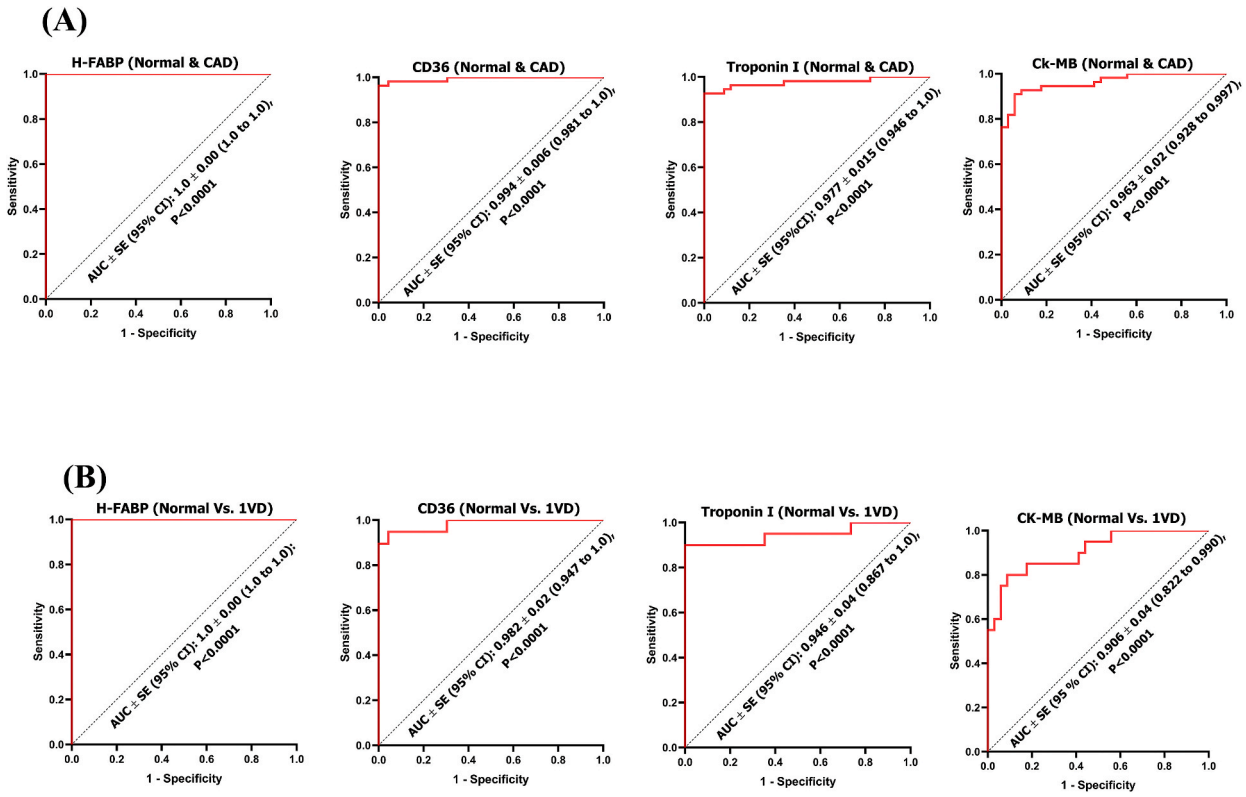

Fig. 6. ROC curve analysis of myocardial infarction biomarkers to compare the diagnostic potential of H-FABP, CD36, CK-MB, and Troponin I to differentiate between (A) normal (Healthy subjects) & CAD patients; (B) normal (Healthy subjects) & CAD patients with 1 vessel diseases (1VD).

concentration was measured in serum samples based on the modified method of Liao and Kannan (2012) using an HPLC device with a C18 column and UV detector [39].

2.3. Statistical analysis

The data were analyzed by SPSS software (SPSS, version 23, SPSS, Inc., IL, USA) and GraphPad Software (GraphPad Prism version 8.0.2, San Diego, California). The Shapiro-Wilk Test tested the normality of the distribution of continuous variables. All data were classified based on coronary artery occlusion stage (normal, 1VD for one artery obstruction, 2VD for two artery obstructions, 3VD for three artery obstructions). The nonparametric Kruskal–Wallis one-way and multivariate analysis of variance (MANOVA) tests were performed for multiple comparisons and the nonparametric Mann-Whitney *U* test was used for side-by-side comparisons. Spearman rank correlation was performed for the detection of correlations between variables.

The receiver operating characteristic (ROC) curves and calculation of area under the curve (AUC) were applied to compute the diagnostic myocardial infarction biomarkers value in healthy subjects and CAD patients. Consequently, the sensitivity and specificity at various cut-off points of biomarkers were calculated and the optimal cut-off value was determined based on the Youden index. The maximum vertical distance from the point (x,y) on the diagonal line of the ROC curve is used in the Youden index [40,41]. The selection of cut-off points for biomarkers at each site was undertaken using ROC-curve analysis. A cut-off value is a number that separates two groups (patients and healthy subjects) and has the highest sensitivity and specificity of the investigated marker. ROC analysis was performed twice to better evaluate the diagnostic value of biomarkers. The first time between the normal group and CAD group to assess the diagnostic accuracy of the parameter to differentiate the patients from the healthy individuals and the second time between the normal group and 1VD group to assess the ability to discriminate between different stages of diseases. *P*-values <0.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics

Altogether, 89 patients were included in the current study, and the comparisons were performed on the following parameters: age, smoking, body mass index (BMI), Hypertensive heart disease (HTN), DM, Dyslipidemia, Coronary Artery Bypass Grafting (CABG),

Coronary artery occlusion (classes normal, 1VD, 2VD, 3VD). Among them, 34 subjects were assessed as having normal coronary arteries.

Based on MANOVA analysis, significant differences were detected in the Coronary Artery Occlusion group. However, a non-significant alteration was detected in BPA and Coronary Artery Occlusion * BPA assessment (Table 1).

In an assessment of the patient according to coronary artery occlusion classification, a significant alteration was detected in all parameters, including age, sex, BMI, DM, Dyslipidemia, smoking, and HTN (Table 2).

Serum levels of BPA, CD36, CK-MB, H-FABP.

Serum levels of BPA were found to be significantly higher in patients with CAD compared to the control group (Fig. 1A). In addition, there was a positive correlation between the number of stenosed vessels and BPA levels, indicating that the number of stenosed vessels increases with increasing levels of BPA (Fig. 1B). Similarly, CD36 levels were found to be significantly increased in patients with CAD, and there was a positive correlation between CD36 levels and the number of stenosed vessels (Fig. 2 A and B). Additionally, our analysis revealed similar findings for CK-MB (Fig. 3 A and B), H-FABP (Fig. 4 A and B), and troponin I (Fig. 5 A and B). These markers exhibited higher levels in patients with CAD compared to the control group, and there was a positive correlation between their levels and the number of stenosed vessels.

Associations of H-FABP, CD36, Troponin I, and CK-MB status with Coronary artery occlusion and BPA concentration.

The correlation analysis results are presented in Table 3. Our analysis revealed a positive correlation between BPA and BMI, hypertension (HTN), diabetes mellitus (DM), dyslipidemia, and smoking. Furthermore, H-FABP showed a positive correlation with age, BMI, DM, dyslipidemia, and BPA. CD36 exhibited a positive correlation with age, BMI, DM, dyslipidemia, H-FABP, and BPA. Troponin I showed a positive correlation with age, BMI, HTN, DM, dyslipidemia, smoking, BPA, CD36, and H-FABP. Additionally, CK-MB displayed a positive correlation with age, BMI, DM, dyslipidemia, BPA, H-FABP, CD36, BPA, and troponin I. All heart biomarkers have a positive correlation with each other. However, a negative correlation was detected between Sex with Smoking, BPA, and H-FABP.

3.2. ROC curve assessment and risk categorization

ROC curve evaluation indicated the area under the curves of H-FABP, CD36, Troponin I, and CK-MB based on coronary artery occlusion classification (Table 4). The specificity and sensitivity of prediction were at the highest level with H-FABP, and CD36 groups.

The range of sensitivity and Specificity altered between 44 % and 100 %. All biomarkers [H-FABP, AUC ± SE (95 % CI): 1.0 ± 0.00 (1.0–1.0): $P < 0.0001$; CD36, AUC ± SE (95 % CI): 0.994 ± 0.006 (0.981–1.0), $P < 0.0001$; Troponin I, AUC ± SE (95%CI): 0.977 ± 0.015 (0.946–1.0), $P < 0.0001$; Ck-MB, AUC ± SE (95 % CI): 0.963 ± 0.02 (0.928–0.997), $P < 0.0001$] detected coronary artery occlusion compared with normal groups (Table 4; Fig. 6A), but, H-FABP (AUC ± SE (95 % CI): 1.0 ± 0.00 (1.0–1.0): $P < 0.0001$) and CD36 (AUC ± SE (95 % CI): 0.982 ± 0.02 (0.947–1.0), $P < 0.0001$) showed more accuracy with higher sensitivity and Specificity compared to Troponin I (AUC ± SE (95 % CI): 0.946 ± 0.04 (0.867–1.0), $P < 0.0001$) and CK-MB (AUC ± SE (95 % CI): 0.906 ± 0.04 (0.822–0.990), $P < 0.0001$) in comparison between coronary artery occlusion in different groups (Table 4; Fig. 6B). The cutoffs were used to classify the biomarker's quality. The detection rate of all biomarkers for each comparison was shown in Table 4 Collectively, based on ROC curve analysis, H-FABP and CD36 were suggested as new biomarkers for myocardial injury and coronary artery occlusion detection and prediction.

4. Discussion

CVD is a major cause of morbidity and mortality in Asian countries, particularly in Iran, where hyperlipidemia and underlying conditions such as diabetes are prevalent contributing factors [42,43]. Recent surveys in the past five years indicate that blood pressure has been increasing, particularly among men who often go undiagnosed and untreated [44].

CAD is the most prevalent type of CVD and atherosclerosis is the underlying mechanism for this disease [45]. Regarding the high prevalence of CAD, finding a biomarker for this disease is a necessity.

Multiple studies have demonstrated that BPA directly affects myocardial cells and coronary arteries, as well as its impact on the cardiovascular system through the endocrine system. Recent studies have consistently reported a link between BPA concentration and CVD [22,46,47]. Our findings demonstrate a direct correlation between BPA serum levels and the presence of coronary artery stenosis. In the United States, a study conducted between 2003 and 2012 identified a correlation between environmental phenols and CVD, specifically implicating BPA among the three main phenol pollutants [48]. Furthermore, analysis of national health and nutrition examination surveys conducted between 2003 and 2016 revealed a dose-dependent relationship between BPA exposure and CVD, with potential influences of age and sex on CVD prevalence [49]. Additionally, exposure to BPA was suggested to correlate with the expression of pro-inflammatory genes and inflammation biomarkers associated with CVD, thereby increasing the risk of CVD development in young individuals [47]. This study further established a significant relationship between BPA and various risk factors associated with CAD. Notably, BPA exhibited a strong correlation with the severity of CAD, suggesting a potential role in the development of this condition. Previous research has also indicated that BPA levels increase in the presence of cardiometabolic diseases, and experimental studies have linked BPA to the progression of atherosclerosis. Specifically, BPA acts as a potent activator of PXR, contributing to increased atherosclerosis in mice lacking the apoE gene. Furthermore, BPA has been found to enhance the expression of CD36 in mice, potentially leading to increased cholesterol uptake by macrophages and the progression of atherosclerosis. The present study supports a significant association between BPA and CD36 levels, suggesting that BPA's impact on CD36 expression may contribute to this relationship. CD36 serves as a scavenger receptor that promotes the unregulated uptake of oxidized LDL, thereby facilitating the progression of atherosclerosis [50,51].

Biochemical blood biomarkers have long been employed for disease detection, with the development of specific organ-specific markers enabling accurate identification of organ-related issues and the prevention of chronic and incurable diseases. Troponin I and CK-MB have served as primary myocardial biomarkers for assessing heart function [23,24,27]. However, the present study reveals CD36 and H-FABP as novel biomarkers that outperform troponin I and CK-MB in detecting different classes of coronary artery occlusion.

H-FABP has been utilized in the detection of acute coronary syndrome, with enhanced test accuracy observed when radio-labeled antibodies are employed for in vivo assessment [52,53]. Similar to myoglobin, plasma levels of H-FABP increase within 3 h following an acute myocardial infarction but return to normal after 24 h [54]. However, H-FABP is not recommended as a valuable biomarker for monitoring patients after Cryoablation treatment for atrial fibrillation [55].

ROC curve analysis results confirmed that new and conventional biomarkers measured in the current research could distinguish healthy subjects from patients with CAD, but H-FABP and CD-36 with high sensitivity and specificity compared to Troponin I and CK-Mb can distinguish 1-VD patients from healthy individuals (It may be said that this result is the main finding of the present study); also, according to Table 4, the diagnostic value of H-FABP and CD-36 in identifying patients with 1,2 & 3-VD from each other and healthy subjects is more than CK-MB and Troponin I. Therefore, it seems that H-FABP and CD-36 have high diagnostic values.

Considering the aforementioned study and our findings, CD36 and H-FABP emerge as promising biomarkers for assessing myocardial function and injuries, particularly in the early stages. This discovery holds potential for the prevention and reduction of cardiovascular disease (CVD) within the population, particularly among older individuals.

5. Conclusion

This study assessed traditional serum myocardial biomarkers (troponin I, CK-MB) and newer biomarkers (CD36, H-FABP) for early detection of myocardial infarction. BPA concentration correlated with various diseases, including CVD, as observed in previous literature. Our findings revealed significant prognostic value for all serum biomarkers in myocardial injuries, with CD36 and H-FABP exhibiting higher accuracy, particularly in distinguishing between different levels of coronary artery occlusion. Moreover, our data confirmed the association between BPA concentration and myocardial necrosis, and certain degrees of coronary artery occlusion, highlighting the detrimental impact of BPA on the general population's health.

Future scope

In this study, for the first time, the diagnostic value of H-FABP and CD-36 in the diagnosis of myocardial infarction caused by BPA was evaluated in comparison to Troponin I and CK-MB. The results confirmed that H-FABP and CD-36 not only have high sensitivity and accuracy in diagnosing coronary artery stenosis, but also enter the blood in the early hours of myocardial infarction and can be detected easily, so it seems that they are suitable diagnostic tools to identify CAD as quickly as possible. Therefore, future studies should confirm these findings to use them as routine diagnostic tests in medical laboratories. For this purpose, it is necessary to increase the study population and evaluate the H-FABP and CD-36 serum levels and their diagnostic value in different ages and races.

Study limitations

Some constraints of the current research should be elucidated. Significant restriction of the present study was the small sample size that obtained results should be confirmed in a larger sample size with further analytical results. Other hypothesized limitations include Severe financial constraints to use advanced techniques with high sensitivity and specificity for assessing biomarkers, which could affect the confidence level of our study. Another limitation of this present research was a failure to assess the amounts of involved stenosed vessels and their relationship with diagnostic biomarkers and BPA. Another limitation of human studies can be the lack of proper cooperation of some patients, nurses, and doctors with researchers. Other hypothesized limitations of our results are variations between individuals in terms of social and socioeconomic status that could be considered in interpreting results. Therefore, further studies are needed to elucidate the precise role and function of H-FABP and CD36 as myocardial infarction biomarkers for quick and timely diagnosis of CAD.

Author Contributions

Masoumeh Karami: Conceptualization, Data curation, Formal analysis, Supervision, Validation, Writing – review & editing. Forogh Mohammadi: Formal analysis, Software. Ghorban Khodayar: Data curation, Writing – review & editing. Siamak Asri: Conceptualization, Investigation, Methodology, Software, Supervision, Validation. Seyyed Hosein Mousavi: Conceptualization, Supervision, Validation, Writing – review & editing. Shahin Alizadeh-Fanalou: Conceptualization, Data curation, Formal analysis, Methodology, Software, Writing – original draft, Writing – review & editing. Sara Mehdipour: Data curation, Methodology, Software, Writing – original draft. Shirin Rokhsartalb-Azar: Formal analysis, Software, Writing – original draft

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Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Masoumeh Karami reports financial support was provided by AJA University of Medical Sciences, Iran. there is nothing If there are other authors, they 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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