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RESEARCH ARTICLE

Circulating levels of C1q/TNF-α-related protein 6 (CTRP6) in coronary artery disease and its correlation with inflammatory markers

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Abstract

Introduction Circulating levels of C1q/TNF-α-related protein 6 (CTRP6) is an adipokine that is involved in regulation of glucose and lipid metabolism, inflammation, and insulin sensitivity. However, the exact role of CTRP6 in metabolic processes remains unclear due to conflicting findings. To address current gap, we aimed to investigate the serum levels of CTRP6 in patients with coronary artery disease (CAD) and its association with inflammatory cytokines.

Method In this case-control study, the serum levels of CTRP6, interlukin-6 (IL-6), tumor necrosis factor- α (TNF-α), adiponectin, and fasting insulin were measured using enzyme-linked immunosorbent assay (ELISA) kits in a total of 176 participants, consisting of 88 CAD patients and 88 control subjects. Additionally, various anthropometric and biochemical measurements were measured and compared between cases and controls.

Results The present study found that serum levels of CTRP6 were significantly higher in the CAD group (561.3 ± 15.14) compared to the control group (429.3 ± 12.85, $p < 0.001$). After adjusting for age, sex, and body mass index (BMI), CTRP6 levels were found to be positively associated with the risk of CAD ($p < 0.001$). Correlation analysis in CAD subjects revealed a positive correlation between CTRP6 levels and BMI, systolic blood pressure (SBP), malondialdehyde (MDA), TNF-α, and IL-6, as well as a negative correlation with creatinine and total anti-oxidant capacity.

Conclusion The findings of this study provide novel evidence that elevated serum levels of CTRP6 are significantly associated with an increased risk of developing CAD. Moreover, our results indicate a correlation between CTRP6 and various risk factors for atherosclerosis.

Keywords Coronary artery disease · CTRP6 · Inflammation · Insulin resistance · Lipid profile · Obesity

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Introduction

Coronary artery disease (CAD) is a prevalent form of cardiovascular disease (CVD) and remains a leading cause of death globally [1]. This disease is characterized by the formation of atherosclerotic plaques caused by the accumulation of cholesterol and lipids in the walls of the coronary arteries [2]. There is compelling evidence to suggest that inflammation and obesity have a significant and independent impact on the prognosis of atherosclerosis [1, 3]. In obesity, there is a persistent inflammatory state characterized by increased infiltration of macrophages in adipose tissue. These macrophages can alter the secretory profile of adipocytes, resulting in various metabolic and inflammatory processes that can affect the body [4]. In addition, being overweight or obese is associated with not only heightened systemic inflammation but also increased oxidative stress.

Excessive caloric intake leads to an increase in substrate-induced tricarboxylic acid cycle activity, resulting in the overproduction of mitochondrial NADH and reactive oxygen species (ROS). Oxidative stress is recognized as a shared underlying factor in insulin resistance, type 2 diabetes, and cardiovascular disease, linking inflammation with these conditions [5, 6].

Adipose tissue releases secretory cytokines known as adipokines, which have a significant impact on whole-body metabolism, endocrine functions, and inflammation [1]. Research has demonstrated that adipokines, such as resistin, leptin, chemerin, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and adiponectin, play significant roles in both the development and progression of atherosclerosis. These adipokines can also impact diabetes, insulin resistance, coagulation, fibrinolysis, and lipid levels [1, 7]. Adiponectin has anti-inflammatory, anti-diabetic, and anti-atherogenic properties. Low circulating levels of adiponectin are associated with various cardiovascular diseases, including CAD [8, 9]. C1q/TNF-related proteins (CTRP) are a family of adipokines that have been identified as adiponectin paralogs with a significant impact on several metabolic pathways [10]. The CTRP family consists of 15 members, ranging from CTRP1 to CTRP15, which act as metabolic regulators [11], The CTRP family of adipokines regulates several metabolic pathways, including lipid and glucose metabolism and inflammation. They also play a significant role in the association between obesity and inflammation, as well as the modulation of inflammation in adipose tissue [12].. CTRP6 is a member of the CTRP family, primarily expressed in adipose tissue, brain, heart, and placenta. Reports have suggested that CTRP6 has a distinct function in comparison to other well-known CTRPs [13, 14].. A growing body of evidence has shown that CTRP6 can regulate the differentiation of adipocytes and myofibroblasts, as well as angiotensin II-induced hypertension, cardiac fibrosis, fibrogenesis, and the function of endothelial cells [13]. Furthermore, CTRP6 is associated with the regulation of glucose and lipid metabolism, inflammation, and insulin sensitivity [12, 13]. In conditions of obesity and diabetes, the expression of CTRP6 adipokine is significantly increased in adipose tissue, with stromal vascular cells and macrophages being the primary source of CTRP6 [12, 13]. In addition, an increase in CTRP6 levels has been reported in patients with rheumatoid arthritis [15]. Furthermore, CTRP6 has been shown to increase the expression of interleukin-10 in macrophages, indicating its anti-inflammatory effect [16]. Lei et al. [17]. and Wei et al. [18] have shown CTRP6 cardioprotective effects. They demonstrated that elevated levels of CTRP6 may mitigate postinfarct cardiac fibrosis and lower the incidence of acute coronary syndrome (ACS). Nevertheless, the existing literature presents contrasting evidence regarding the function of CTRP6 in metabolic processes, and no definitive findings have emerged regarding the connection between CTRP6 and risk factors for coronary artery disease (CAD). Against this backdrop, the present study was undertaken to assess the serum concentrations of CTRP6 in patients with CAD and to investigate its association with anthropometric and biochemical parameters, as well as inflammatory cytokines.

Materials and methods

Study population

A total of 176 participants were recruited, including 88 CAD patients (55 males and 33 females) and 88 controls (46 males and 42 females) aged between 45 and 75 years. All participants underwent angiography in Shariati Hospital (Tehran, Iran) to determine the extent of coronary artery stenosis. CAD was identified by a cardiologist, and patients with more than 50% stenosis in at least one coronary artery were classified as CAD patients. The control group consisted of subjects whose coronary vessel stenosis was less than 30%. Subjects with underlying diseases, such as unstable angina, carotid artery stenosis, cerebrovascular disease, peripheral and coronary vascular disease, myocardial infarction, diabetes, and those being treated with thiazolidinedione drugs, were excluded from the control category. Additionally, none of the participants had used alcohol or cigarettes in the past three months. The study adhered to the Helsinki Declaration and was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.SHARIATI.REC.1401.017). All study participants provided written consent.

Anthropometric and laboratory assessment

The body mass index (BMI) was estimated using the standard formula of weight (in kilograms) divided by height (in square meters). Systolic and diastolic blood pressures were measured in the seated position following 15 min of rest, utilizing a standard sphygmomanometer. After overnight fasting, venous blood samples were collected, and laboratory parameters such as triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), creatinine (Cr), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) were measured via commercially available kits (Pars Azmoon; Iran) with an auto analyzer. Additionally, malondialdehyde (MDA) and total antioxidant capacity (TAC) were measured following the provided instructions of a commercially

available kit (Kia zist; Iran). Fasting insulin levels were measured using an Enzyme-linked immunosorbent assay (ELISA) kit (Monobind; U.S.A.). The homeostasis model of insulin resistance (HOMA-IR) was calculated using the standard formula of [fasting blood glucose (mg/dL)] multiplied by [fasting blood insulin (μU)] divided by 405.

Cytokine and adipokine measurement

To evaluate serum levels of TNF-α (Cat# DTA00C) and IL-6 (Cat# HS600B), ELISA kits (R & D Systems; USA) were employed. The least detectable range for IL-6 was 0.11 pg/mL and for TNF-α was 0.5 pg/mL. Intra-assay and inter-assay coefficients of variation (CV) for IL-6 and TNF-α were 6.9 and 9.6, and 5.2 and 7.4, respectively. Adiponectin serum levels were measured with an ELISA kit (Adipogen; South Korea; Cat# AG-45 A-0001YEKKI01), and the least detectable range was 0.1 pg/mL, with intra- and inter-assay CV of 3.4% and 4.3%, respectively. CTRP6 levels were measured using an ELISA kit (Aviscera Bioscience; USA; Cat# SK00392-06) with an intra-assay CV of 7%, an inter-assay CV of 6%, and a detection limit of 10 pg/mL.

Table 1 Anthropometric and biochemical measurements of study population

Variables	Non-CAD	CAD	P
Age	57.5 ± 0.85	57.92 ± 0.80	0.720
BMI (kg/m2)	26.33 ± 0.4	26.56 ± 0.4	0.686
SBP (mmHg)	124 (115, 135)	130 (120, 143)	0.009
DBP (mmHg)	80 (70, 83.5)	80 (78, 90.5)	0.005
FBG (mg/dl)	95.22 ± 1.23	95.15 ± 1.12	0.966
Insulin (μU/ml)	3.26 (2.25, 5.4)	8.22 (4.3, 11.26)	< 0.001
HOMA-IR	0.8 (0.48, 1.26)	1.89 ± (1.01, 2.65)	< 0.001
TG (mg/dl)	126.17 ± 5.16	151.24 ± 4.5	< 0.001
TC (mg/dl)	164.49 ± 4.48	189.42 ± 4.54	< 0.001
LDL-C (mg/dl)	97.92 ± 3.53	113.77 ± 3.47	0.002
HDL-C (mg/dl)	45.02 ± 0.96	40.86 ± 0.75	0.001
Creatinine (mg/dl)	1.15 ± 0.02	1.2 ± 0.01	0.068
AST (U/l)	19.71 ± 0.64	21.57 ± 0.67	0.047
ALT (U/l)	20.19 ± 0.9	22.11 ± 0.87	0.131
Adiponectin (μg/ml)	10.36 ± 0.4	8.54 ± 0.3	< 0.001
MDA (nmol/ml)	6.69 (5.32, 9.1)	9.27 (8.23, 11.45)	< 0.001
TAC (nmol/ml)	93.77 ± 1.8	80.27 ± 1.37	< 0.001
TNF-alpha (pg/ml)	24.8 (16.95, 28.35)	26.65 (23.4, 33.35)	0.004
IL-6 (pg/ml)	6.2 (4.3, 7.8)	7.9 (5.4, 12.35)	< 0.001

Normal distributed data are expressed as mean ± SEM and non-normal distributed data are expressed as median (IQR)

Statistical analysis

The categorical data were analyzed using the chi-square test and presented as frequency and percentage. The normality of variables was assessed using the Kolmogorov–Smirnov test. Variables with normal distribution were expressed as mean ± standard Error of mean (SEM), while those with non-normal distribution were presented as median ± interquartile range (IQR). Student t-test and Mann-Whitney U test were employed for data analysis with normal and non-normal distribution, respectively. The analysis of covariance (ANCOVA) test was utilized to eliminate any possible influence of covariates on CTRP6 levels. Pearson correlation analysis was used to assess the correlation of CTRP6 with biochemical and anthropometric variables. Binary logistic regression was performed to predict CAD risk based on the circulating level of CTRP6. Logarithmic transformation was performed for non-normally distributed data before correlation and regression analysis. The CTRP6 cut-off value was determined based on the receiver operating characteristic (ROC) curve to differentiate between the CAD and control groups. The statistical analysis was performed using SPSS21 (SPSS, Chicago, IL, USA), and a p-value < 0.05 was considered statistically significant.

Results

Anthropometric and biochemical measurements

Table 1 presents the descriptive statistics of study variables for the CAD and control groups. The mean age for the CAD and control groups were 57.92 and 57.5 years, respectively, and did not differ significantly ($P = 0.720$). The mean BMI also did not differ significantly between the CAD and control groups ($P = 0.686$). The CAD patients had higher levels of TG, TC, and LDL-C, and lower levels of HDL-C, compared to the control group, with significant differences observed for TG, TC, HDL-C, and LDL-C ($P < 0.001$, $P < 0.001$, $P = 0.002$, and $P = 0.001$, respectively).

MDA levels were significantly higher in CAD patients [9.27 (8.23, 11.45)] compared to controls [6.69 (5.32, 9.1), ($p < 0.001$)], while TAC levels were markedly lower in CAD group [93.77 ± 1.80 vs. 80.27 ± 1.37, ($P < 0.001$)]. No significant differences were observed for ALT ($P = 0.131$), FBG ($P = 0.966$), and creatinine ($P = 0.068$), while significant differences were observed for AST ($P = 0.047$), insulin ($P < 0.001$) (Fig. 1a), HOMA-IR ($P < 0.001$), (Fig. 1b), DBP ($P = 0.005$), and SBP ($P = 0.009$) between the groups.

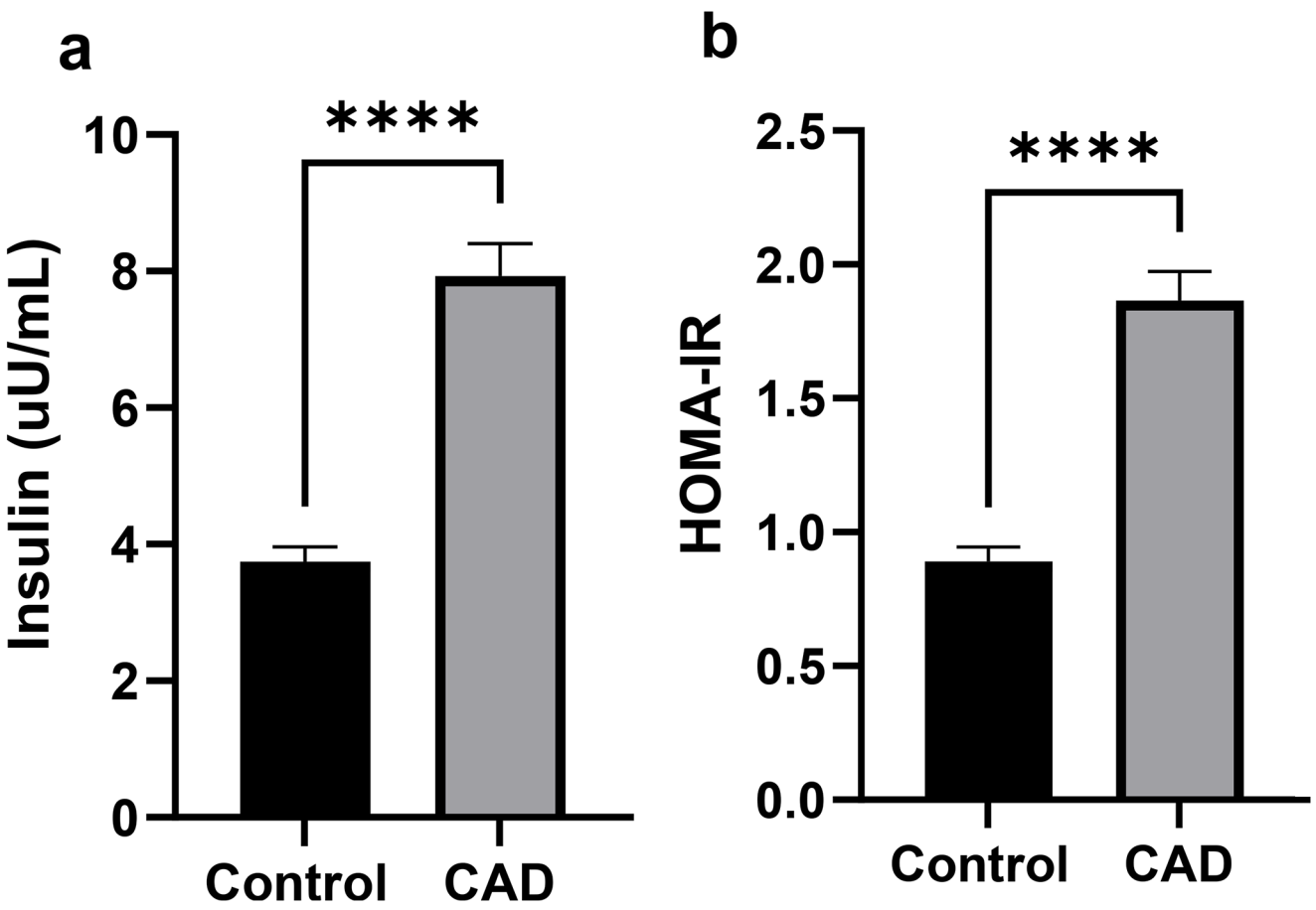

Fig. 1 Serum levels of Insulin and HOMA-IR in control and CAD patients

Cytokine and adipokine serum levels

The study found that CAD patients had higher serum levels of IL-6 [7.9 (5.4, 12.35) pg/mL] and TNF-α [26.65 (23.4, 33.35) pg/mL] than controls [6.2 (4.3, 7.8) pg/mL and 24.8 (16.95, 28.35) pg/mL, respectively] (Table 1). In contrast, Adiponectin serum levels were significantly lower in the CAD group than in the control group [8.54 ± 0.30 µg/mL vs. 10.36 ± 0.40 µg/mL, ($P < 0.001$)] (Table 1). Moreover, the study observed a higher level of CTRP6 in CAD patients compared with the controls ($P < 0.001$, Fig. 2a).

Additionally, CTRP6 serum levels were higher in the 3-vessel disease group compared to the 1-vessel disease group, and in the 2-vessel disease group compared to the 1-vessel disease group ($P < 0.001$). However, no significant difference was observed between the 3-vessel disease and 2-vessel disease groups ($P > 0.05$), Fig. 2b).

Furthermore, we analyzed CTRP6 levels according to gender and BMI in each group. In the control group, females had higher significant levels of CTRP6 compared to males ($P < 0.001$), while no significant difference was observed between males and females in the CAD group ($P > 0.05$, Fig. 2c). We have further compared male and female CAD patients to their control counterparts. There was a significant higher CTRP6 levels in female CAD patients than controls females ($P < 0.01$). Similar result was found for male participants; CTRP6 levels was higher in male CAD patients compared to control males ($P < 0.001$, Fig. 2c).

Moreover, in both CAD and control subjects, serum levels of CTRP6 differed significantly between BMI < 25 and BMI > 25 groups ($P < 0.001$ and $P < 0.01$, respectively), with higher levels in those with BMI > 25 (Fig. 2d).

The association of CTRP6 levels with biochemical and anthropometric parameters

The results of the correlation analysis between CTRP6 levels and other parameters in both the control and CAD groups are presented in Table 2. In the control group, serum CTRP6 levels were positively correlated with BMI, SBP, insulin, HOMA-IR, ALT, and MDA, while showing a negative correlation with HDL-C and TAC. Similarly, in the CAD group, CTRP6 levels were positively correlated with BMI, SBP, MDA, IL-6, and TNF-α, and negatively correlated with creatinine and TAC (Table 2).

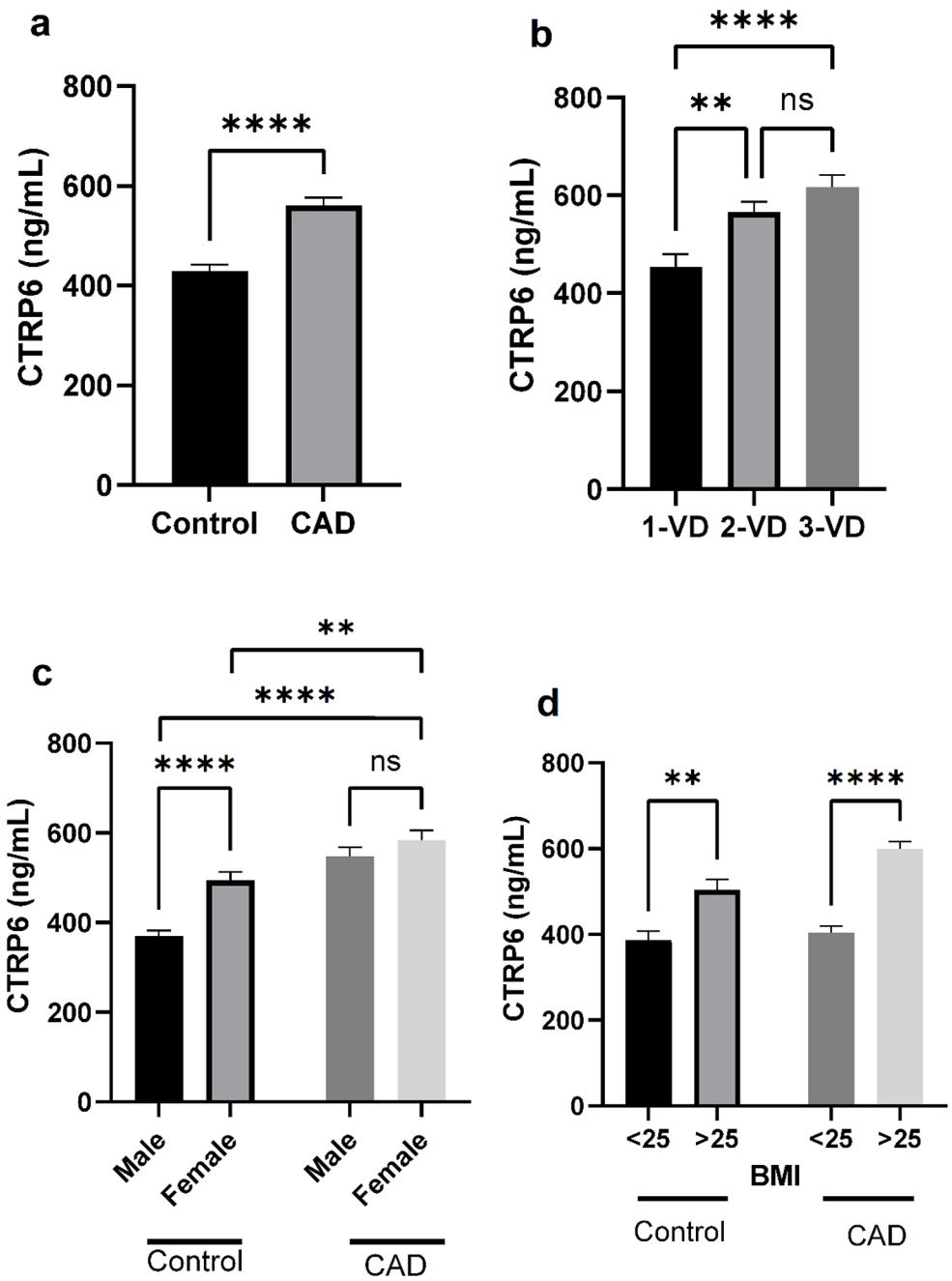

Fig. 2 Serum levels of CTRP6 in study population. (**a**) Serum levels of CTRP6 were found to be higher in CAD patients compared to controls ($p < 0.001$). (**b**) CTRP6 serum levels demonstrated higher level in 3-VD and 2-VD groups than 1-VD group ($p < 0.001$). (**C**) Serum levels of CTRP6 were higher in females compared with males in control group. (**d**) CTRP6 serum levels were significantly higher in groups with BMI > 25 ($p < 0.001$)

The association of CTRP6 with CAD

A logistic regression analysis was conducted to explore the potential relationship between serum CTRP6 levels and the likelihood of CAD. The results of this analysis are summarized in Table 3. Specifically, the odds ratio (OR) of CAD status per 10-unit increase in CTRP6 was examined. In the unadjusted model, higher serum levels of CTRP6 were significantly associated with an increased risk of CAD (OR [95% confidence interval (CI)] = 1.078 [1. 049–1.108]; $p < 0.0001$). Furthermore, after controlling for the effects of BMI, sex, and age, CTRP6 remained significantly correlated with the risk of CAD (OR [95% CI] = 1.123 [1.079–1.169]; $p < 0.0001$).

Receiver operating characteristic (ROC) curve analysis was employed to evaluate the diagnostic ability of CTRP6 to discriminate between the CAD and control groups (area under the curve (AUC): 0.745 [95% CI: 0.674–0.816] and $p < 0.0001$), indicating moderate accuracy of CTRP6 in distinguishing between CAD and control subjects (Fig. 3).

Table 2 The correlation analysis in both control and CAD groups

Variables	Control (r)	B (95%CI)	CAD (r)	B (95%CI)
Age (Years)	0.018	-	−0.088	-
BMI (kg/m2)	0.423**	5.51 (-0.9, 11.92)	0.412**	8.14 (0.8, 15.48) *
SBP (mmHg)	0.234*	316.35 (-87.77, 720.46)	0.313**	524.09 (16.18, 1032.01) *
DBP (mmHg)	0.034	-	0.104	-
FBG (mg/dl)	0.157	-	−0.009	-
Insulin (µU/ml)	0.306**	-	0.025	-
HOMA-IR	0.314**	115.4 (40.7, 190.12) **	0.024	-
TG (mg/dl)	−0.002	-	−0.040	-
TC (mg/dl)	−0.169	-	0.168	-
LDL-C (mg/dl)	−0.179	-	0.092	-
HDL-C (mg/dl)	−0.223*	-1.91 (-4.24, 0.43)	0.148	-
Creatinine (mg/dl)	−0.138	-	−0.225*	-82.69 (-232.06, 66.67)
AST (U/l)	0.082	-	−0.137	-
ALT (U/l)	0.283**	1.49 (-1.1, 4.08)	−0.055	-
Adiponectin (µg/ml)	−0.195	-	0.019	-
MDA (nmol/ml)	0.419**	155.99 (10.34, 301.65) *	0.413**	231.52 (-38.44, 501.47)
TAC (nmol/ml)	−0.324**	-1.62 (-2.97, -0.32) *	−0.390**	-1.46 (-3.63, 0.71)
TNF-alpha (pg/ml)	0.182	-	0.373**	269.27 (46.47, 492.07) *
IL6 (pg/ml)	0.175	-	0.286**	31.82 (-100.39, 164.04)

Pearson correlation analyses were performed to determine if an association exists between the variables

B: Regression coefficients, CI: Confidence Interval

*$P < 0.05$

**$P < 0.01$

Table 3 Odd ratio of the CAD status according to 10 unit change in CTRP6.

Model	OR	95% CI	P
Crude	1.078	1.049–1.108	< 0.0001
Adjusted*	1.123	1.079–1.169	< 0.0001

OR: Odd ratio. CI: Confidence Interval

* Adjustment was performed for age, sex and BMI

Discussion

The current study represents a novel investigation into the association between CTRP6 and the risk factors of CAD. While prior research has explored the expression levels of various members of the CTRP family in different metabolic disorders such as metabolic syndrome, non-alcoholic fatty liver disease, and diabetes [19–22] this study provides unique insights into the specific relationship between CTRP6 and CAD risk factors. Among them, CTRP13, CTRP9, CTRP12, CTRP3 and CTRP1 have been stated to be linked with CAD [10, 20, 23, 24]. Previous research has suggested a correlation between CTRP6 and inflammatory markers, lipid oxidation, and glucose metabolism, among other metabolic disorders [12, 13, 25–27]. While there is evidence for relation of CTRP6 with risk factors of atherosclerosis in cardiometabolic diseases, there is limited data on the relationship between CTRP6 and the CAD. Given the similar structure and biological activities of the CTRP family, along with CTRP6's role as a metabolic and immune regulator, we hypothesized that CTRP6 may play a significant role in the development of CAD.

Based on our findings, we observed that the levels of CTRP6 were higher in CAD patients and exhibited a positive correlation with the severity of the disease. Contrary to the results of the present study, in 2022, Wei et al. [18]. investigated the association of serum CTRP6 with the development and exacerbation of ACS. They indicated that the levels of CTRP6 were markedly lower in the ACS group than the control group, and the risk of developing ACS reduced with high levels of CTRP6. The reasons behind the differences between the present study and their reports may be related to the study population. In this context, cases of unstable angina were excluded in our study, while not in Wei *et al*'s study. Also, patient with less than 50% stenosis in coronary artery were included in the control group, but in our study, people with less than 30% stenosis in coronary artery were classified in control group. The racial differences of the participants in both studies can also have an effect on the dissimilarity in the consequences.

Several studies have reported comparable results to our findings in the context of cardiometabolic diseases, including type 2 diabetes, metabolic syndrome, and non-alcoholic fatty liver disease. Sadeghi and colleagues demonstrated a statistically significant elevation in the concentration of CTRP6, among patients diagnosed with polycystic ovary syndrome (PCOS). On the other hand, an independent study has reported similar findings, documenting a higher concentration of CTRP6 in a cohort of obese individuals [28, 29]. In addition, in 2017, Lei et al. [12]. conducted a study in mouse and human models with diabetes and obesity, demonstrating a significant up-regulation of CTRP6 expression

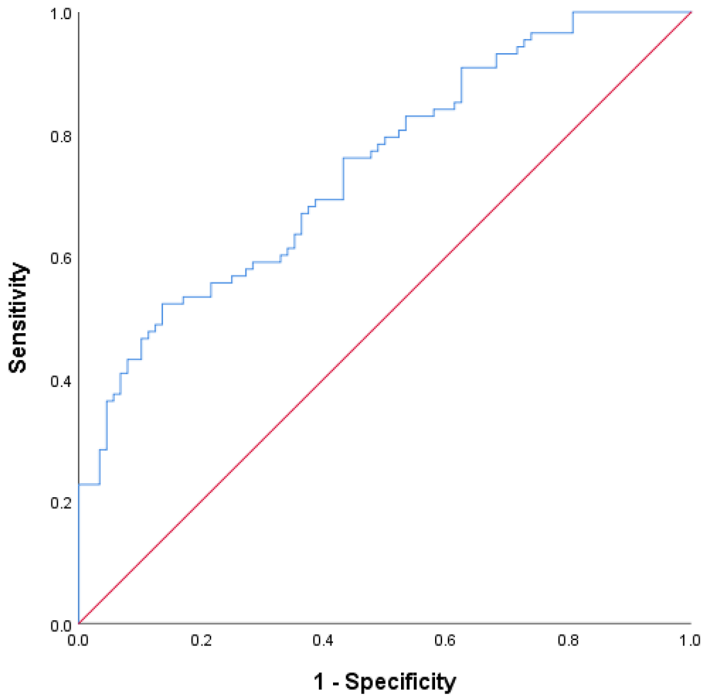

Fig. 3 ROC curve for CTRP6. A CTRP6 < 475.5500 pg/mL (area under curve [CI] = 0.745 [0.674–0.816]; $p < 0.0001$) was the cut-off values to differentiating between CAD and control groups

in adipose tissue. In line with these finding, there was a positive association between circulating CTRP6 with BMI in the recent study. A number of studies have shown the regulatory mechanism of CTRP6 in lipid metabolism. Knockout of CTRP6 resulted in inhibition of adipogenesis in adipocytes by suppression of lipogenic and adipogenic markers like CCAAT/enhancer binding proteins (C/EBPs), extracellular signal-regulated kinase 1/2 (Erk1/2) signaling pathway and peroxisome proliferator-activated receptor gamma (PPARγ) [30] as well as prevented inappropriate lipogenesis in myoblasts by reducing the AdipoR1/Erk/PPARγ signaling pathway [31]. This mechanism might be a causative explanation for the relation of CTRP6 with obesity and adipose tissue.

Furthermore, the overexpression of CTRP6 has been shown to increase the levels of circulating inflammatory cytokines and pro-inflammatory macrophages in adipose tissue. Conversely, the loss of CTRP6 has been found to decrease the serum levels of TNF-α and MCP1 in mice under a high-fat diet [12]. Consistent with these findings, our study has shown a positive correlation between CTRP6 and IL-6 and TNF-α in patients with CAD. Additionally, our study found a positive correlation between CTRP6 and MDA, a marker of lipid peroxidation, and a negative correlation with total antioxidant capacity. The impact of CTRP6 on oxidative stress is inconsistent; while there is evidence for a favorable impact of CTRP6 on MDA levels and ROS production [32], there are also studies that show CTRP6 leads to an increase in oxidative stress, and loss of CTRP6 is protective against oxidative stress [33]. These studies utilized various cell types, implying that the impact of CTRP6 on oxidative stress may be specific to certain tissues. Our findings have demonstrated a correlation between CTRP6 and oxidative stress in patients with CAD, but not in healthy controls. These results collectively suggest a complex relationship between CTRP6 and oxidative stress, indicating the need for further studies in this regard.

While relation of CTRP6 and oxidative stress was limited to CAD patients, the relation of CTRP6 and insulin levels and insulin resistance was limited to controls. In 2018, Wang et al. [13]. investigated the serum levels of CTRP6 in patients with type 2 diabetes for the first time. Their results showed that CTRP6 level was higher in diabetic group than healthy group, and its serum levels had a positive correlation with BMI, fat%, WHR, fasting insulin, FBG, HOMA-IR as well as TNF-α and a negative association with adiponectin [34, 35].

Chi et al. [36]. in 2017 showed that CTRP6 serum levels were notably decreased in spontaneously hypertensive rats (SHR), and conversely overexpression of CTRP6 significantly reduced angiotensinII-mediated hypertension and inflammation of vascular endothelial. CTRP6 can reduce hypertension caused by angiotensin II and dysfunction of vascular endothelial in SHR by activating the Erk1/2 signaling pathway and PPARγ expression, which negatively regulates angiotensin II [36]. These findings are contrary to our results that show a positive correlation of CTRP6 with SBP in CAD patients. The reason for these discrepancies can be attributed to the different CTRP6 mechanism of action in humans and mice. On the other hand, it can be assumed that

the body increases circulating CTPP6 levels as a compensatory response to hypertension.

Conclusion

In conclusion, the study provides unique insights into the specific relationship between CTRP6 and CAD risk factors. The findings indicate that the levels of CTRP6 were higher in CAD patients and exhibited a positive correlation with the severity of the disease. Our study has also shown a positive correlation between CTRP6 and circulating inflammatory cytokines, oxidative stress, and insulin resistance. However, the impact of CTRP6 on oxidative stress may be specific to certain tissues, indicating the need for further studies. The regulatory mechanism of CTRP6 in lipid metabolism may be a causative explanation for the relationship of CTRP6 with obesity and adipose tissue.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40200-024-01415-5.

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Data availability The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate This investigation was performed according to the Helsinki Declaration as well as was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.SHARIATI.REC.1401.017). All study contributors signed forms of written and informed consent.

Consent for publication Not applicable.

Competing interests The authors announce that they have no competing interests.

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