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Research Article

Serum CTRP1 Levels in Candidates for Coronary Artery Bypass Graft

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ABSTRACT

Objectives: C1q/tumor necrosis factor-related protein 1 (CTRP1) is an adipokine that plays crucial roles in the cardiovascular system, and its dysregulation has been reported in patients with coronary artery disease (CAD). In this study, our aim was to measure the level of CTRP1 in patients who were candidates for cardiac bypass surgery.

Methods: The participants consisted of 30 candidates for coronary artery bypass graft (CABG) surgery and an additional 30 controls. Inflammatory parameters and the level of CTRP1 were assessed using enzyme-linked immunosorbent assay (ELISA) kits.

Results: Serum CTRP1 levels significantly increased in the patient group compared to the control group (p-value < 0.0001). Furthermore, CTRP1 level was positively correlated with the inflammatory parameters.

Conclusion: Elevated levels of CTRP1, along with inflammation in CAD, suggest the involvement of CTRP1 in inflammatory responses. However, this finding needs to be confirmed in further studies including a larger population.

Keywords: Coronary artery bypass graft; CTRP1; IL-6; TNF-α; hs-CRP

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Introduction

Coronary artery disease (CAD) is a common heart problem caused by the narrowing of blood vessels due to plaque formation, thereby restricting the flow of blood, nutrients, and oxygen to the heart muscle. It is among the primary reasons for mortality and morbidity and accounts for 17.8 million deaths annually [1]. Atherosclerotic plaques begin to form in the context of hypercholesterolemia, inflammation, and oxidative stress, with hypercholesterolemia playing a crucial role in their development. Research indicates the complexity of CAD pathophysiology and elucidates additional factors such as lipid peroxidation, inflammatory signals, endothelial dysfunction, hyperglycemic stress, immune dysregulation, aging, and more [2]. Nevertheless, the mechanisms underlying atherosclerosis development remain poorly understood, highlighting the necessity to identify new markers for both diagnosis and therapeutic interventions.

C1q/TNF-related protein 1 (CTRP1) is an adipokine belonging to a family of proteins that share a modular organization with adiponectin. It includes collagen-like and globular C1q-like domains, similar to adiponectin. CTRP1 participates in the regulation of energy homeostasis and insulin sensitivity, and elevated levels of CTRP1 are associated with metabolic disorders such as type 2 diabetes [3]. Moreover, CTRP1 plays modulatory roles in inflammation, lipid metabolism, and endothelial cells. It hinders collagen-stimulated platelet aggregation by disrupting the interaction between collagen and von Willebrand factor [4]. The levels of CTRP1 in the serum of patients with CAD were notably increased, and this elevation correlated with the severity of CAD [5]. Moreover, the acute myocardial infarction group exhibited significantly higher CTRP1 levels compared to both stable/unstable angina and non-CAD groups [6]. Furthermore, in Chinese male CAD patients who underwent coronary angiography, it was observed that serum CTRP1 levels were higher compared to the control group [7]. It has been demonstrated that oxidized low-density lipoprotein (ox-LDL), a major contributing factor in atherosclerosis, increases CTRP1 and triggers inflammatory responses through proliferator-activated receptor γ (PPAR-γ) in human macrophages [8].

The primary treatment strategies for individuals with CAD encompass a blend of lifestyle adjustments, such as dietary modifications and exercise, in conjunction with medical interventions. In cases where the initial treatments prove ineffective and symptoms persist or worsen, coronary artery bypass graft (CABG) surgery is usually advised to improve blood supply to the heart. The procedure includes separating a blood vessel from the arms, chest, or legs and using it to create a bypass around the obstruction in the coronary artery, supplying blood to the heart [9]. Focusing on the significant association between CTRP1 and atherosclerosis, the main aim of this study was to assess the CTRP1 levels and its relation with inflammatory markers in individuals eligible for cardiac bypass surgery.

Methods

The study adhered to the guidelines outlined in the Declaration of Helsinki and obtained approval from the Ethics Committee at Kerman University of Medical Sciences in Kerman, Iran (Approval ID: IR.KMU.AH.REC.1403.033). Each participant provided written informed consent. The study comprised 30 participants slated for CABG surgery, along with an additional 30 control participants. Individuals with a body mass index (BMI) below 30 kg/m², who abstained from alcohol consumption and were identified as candidates for CABG surgery by a specialist, were enrolled in the study. Patients with cancer, liver, and cardiovascular diseases, as well as individuals who consume drugs or decline to participate, were excluded from the study. For this research, 30 individuals diagnosed with CAD were chosen from those referred to Shafa Hospital in Kerman. Blood samples were then gathered from those who fulfilled the inclusion criteria before undergoing surgery. The control group comprised individuals with no prior history of CAD who also met the specified entry criteria. After a 12-hour fasting period, a 5 ml blood sample was drawn from each participant to measure the levels of lipids, triglyceride (TG) and total cholesterol (TC), fasting blood glucose (FBG) levels, inflammatory parameters, and CTRP1.

Anthropometrics and biochemical measurements

Demographic and anthropometric information was obtained for each individual, comprising age, weight, and height. BMI was calculated using the formula kg/m², where "kg" represents weight and "m" stands for height. The collected blood sample was left for 30 minutes to allow clot formation. Subsequently, it was centrifuged at 1500g for 10 minutes to separate the serum from the clot. Biochemical parameters such as TC, TG, and FBG were assessed using kits.

Measurement of inflammatory indicators

Serum samples underwent analysis for C-reactive protein (CRP), high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and tumor necrosis factor α (TNF-α) levels utilizing enzyme-linked immunosorbent assay (ELISA) kits (Karmania Pars Gene, Kerman, Iran), following the manufacturer's guidelines. Absorbance measurements were acquired at 450 nm utilizing an ELISA reader (BioTek, Winooski, Vermont, USA). The lowest detection limits of the kits were 10 ng/mL for hs-CRP, 2 pg/mL for TNF-α, and 3 pg/mL for IL-6. The intra- and inter-assay precision (coefficients of variation) were 10% and 12% for hs-CRP, 3% and 9% for IL-6,

and 3% and 8% for TNF-α, respectively.

CTRP1 assay

Serum CTRP1 concentration was determined using a commercially accessible ELISA kit, following the manufacturer's protocol. Intra-assay and inter-assay precision were 4–6% and 8–12%, respectively.

Statistical analyses

SPSS 22 software was utilized for data analysis (SPSS, Chicago, IL, USA). Initially, the Kolmogorov-Smirnov test was employed to assess the distribution of various variables within the two studied groups. To statistically compare the two studied groups, the Student's t-test was employed for variables exhibiting a normal distribution, while the Mann-Whitney test was utilized for variables displaying a non-normal distribution. Pearson correlation analysis was conducted to evaluate the degree of association between two variables, as indicated by the correlation coefficient.

Results

As indicated in Table 1, there are no significant differences in age and BMI between the patient and control groups. Moreover, the patient group exhibited higher levels of inflammation due to elevated circulating levels of inflammatory indicators such as IL-6, TNF-α, CRP, and hs-CRP compared to the control group. A part of these data has been documented in our previous study [9].

As depicted in Figure 1, the circulating CTRP1 levels were 37.12 ng/mL in the patient group and 13.34 ng/mL in the control group. This difference in CTRP1 levels was found to be statistically significant in the studied groups ($P < 0.001$). Moreover, correlation analysis revealed a strong positive correlation between CTRP1 levels and inflammatory markers: CRP ($r = 0.461$, $P < 0.001$), hs-CRP ($r = 0.741$, $P < 0.001$), IL-6 ($r = 0.759$, $P < 0.001$), and TNF-α ($r = 0.543$, $P < 0.001$).

Discussion

The findings of this study indicated that there was no significant difference between the two groups in terms of age, BMI, and TC. However, the patient group exhibited higher levels of TG compared to the control group. Additionally, inflammatory markers such as IL-6, TNF-α, CRP, and hs-CRP were found to be elevated in the patient group compared to the control group. Furthermore, the levels of CTRP1 were also higher in the patient group and positively correlated with inflammatory parameters.

CTRP1, an adipose tissue-derived adipokine, serves multiple functions in various pathways, encompassing inflammation, lipid, and glucose metabolism. Consequently, the dysregulation of CTRP1 is implicated in the development of metabolic disorders, tumor progression, renal, and cardiovascular diseases [10]. Our results demonstrate that serum CTRP1 levels are elevated in patients undergoing cardiac bypass surgery. Both animal and human studies have indicated the involvement of CTRP1 in cardiovascular homeostasis [11, 12]. For instance, CTRP1 levels were found to increase in plasma and heart tissue four weeks after myocardial infarction in mice [13]. Additionally, in

Table 1. Clinical characteristics of the study population.

Variables	Control (n = 30)	Patient (n = 30)	P-value
Gender (sex) w/m	15/15	11/19	0.234
Age (years)	57.3 ± 1.2	60.4 ± 1.0	0.057
BMI (kg/m^2)	25.7 ± 4.6	26.1 ± 2.6	0.706
FBG (mg/dL)	116 ± 15.3	133± 10.2	0.024
TG (mg/dL)	99 ± 7.5	142± 7.7	< 0.001
TC (mg/dL)	147± 5.7	155± 7.7	0.43
IL-6 (pg/dL)	2.00 ± 0.59	3.93 ± 0.99	< 0.001
TNF-α (pg/dL)	2.80 ± 0.61	4.45± 1.18	< 0.001
CRP (mg/dL)	7.2 ± 0.77	34.2 ± 7.38	< 0.001
hs-CRP (mg/dL)	0.70± 0.05	1.96± 0.10	< 0.001

BMI: Body mass index; FBG: Fasting blood glucose; CR: Creatinine; TG: Triglyceride; TC: Total cholesterol

Table 2. Correlation of serum CTRP1 with the inflammatory parameters

	CRP (mg/dl)	hs-CRP (mg/dl)	IL6 (pg/mL)	TNF-α (pg/mL)
Correlation Coefficient	0.461	0.741	0.759	0.543
P value	0.000	0.000	0.000	0.000

CRP: c-reactive protein, hs-CRP: High-Sensitivity C-Reactive Protein, IL-6: Interleukin-6, TNF-α: Tumor necrosis factor alpha

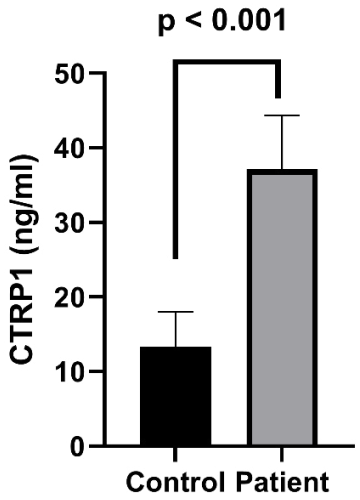

Figure 1. Serum levels of CTRP1 in patients and control groups

men with CAD, elevated CTRP1 levels were correlated with systolic blood pressure [7]. Furthermore, CTRP1 levels are increased in peripheral blood mononuclear cells, aortic atherosclerotic plaques, endarterectomy specimens, and serum of CAD patients compared with controls, and are associated with CAD severity [14]. Indeed, our data, along with the results from other studies, indicate that the levels of CTRP1 in the bloodstream rise among patients with CAD. This elevation can serve as an indicator of the severity of vessel lesions [5].

The precise role of CTRP1 in the cardiovascular system remains uncertain. CTRP1 demonstrates antithrombotic activity by inhibiting collagen-stimulated platelet aggregation through the suppression of the interaction between VWF (von Willebrand factor) and collagen [4]. Additionally, Han et al. reported that CTRP1 regulates blood pressure homeostasis by modulating angiotensin II receptor 1 membrane trafficking via the AKT/AS160 pathway, thus preventing hypotension in dehydrated conditions [15]. However, some of the beneficial effects of CTRP1 on the cardiovascular system stem directly or indirectly from its impact on glucose and lipid metabolism, as well as its ability to enhance insulin sensitivity [16]. Therefore, regarding the positive effects of CTRP1 in the cardiovascular system, it may be inferred that the increase in CTRP1 levels in CAD patients could be a compensatory response to the pathological conditions present in these patients or could be due to potential resistance to CTRP1. Nonetheless, this hypothesis necessitates validation through further research studies.

Our data also reveal a positive correlation between CTRP1 and inflammatory factors such as CRP, hs-CRP, IL-6, and TNF-α. The interaction between CTRP1 and inflammation has been investigated in several studies, indicating the potential role of CTRP1 in the progression of inflammation. In this regard, Shen et al. demonstrated a positive correlation between CTRP1 levels and the concentrations of IL-6 and TNF-α in CAD patients [17]. Additionally, Wang et al. showed that stimulating primary human macrophages with CTRP1 in the presence of oxLDL resulted in a notable increase in the secretion of pro-atherogenic and inflammatory factors, such as MCP-1, TNF-α, IL-1β, and IL-6. Conversely, treatment with a CTRP1 neutralizing antibody significantly reduced their production [8]. Similarly, the injection of CTRP1 significantly promoted inflammation and atherogenesis in apoE$^{-/-}$ mice, whereas its deletion substantially ameliorated atherosclerosis [14]. It seems that the inflammatory markers and CTRP1 have mutual effects on each other. It was found that the inflammatory factors, as well as ox-LDL, induce the production of CTRP1 in monocytic THP1 cells and HUVEC endothelial cells [14]. This evidence suggests that the involvement of CTRP1 in CAD may coincide with a low-grade chronic inflammatory condition.

Conclusion

Our data demonstrated higher circulating levels of CTRP1 in patients who were candidates for cardiac bypass surgery. Furthermore, inflammatory markers such as TNF-α, IL-6, CRP, and hs-CRP showed a positive correlation with CTRP1. However, further investigation is necessary to fully elucidate the roles of CTRP1 in coronary artery disease.

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Conflict of Interest

The authors declared that they have no conflict of interest.

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References

1. Tangjitgamol S, Udayachalerm W, Wanishsawad C, Kaewwanna W, Ativanichayapong N. Association of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio and Coronary Artery Disease Among the Physicians. J Inflamm Res. 2024:59-66. https://doi.org/10.2147/jir.s447750
2. Salekeen R, Haider AN, Akhter F, Billah MM, Islam ME, Islam KMD. Lipid oxidation in pathophysiology of atherosclerosis: Current understanding and therapeutic strategies. Int J Cardiol Cardiovasc Risk Prev. 2022:200143. https://doi.org/10.1016/j.ijcrp.2022.200143
3. Pan X, Lu T, Wu F, Jin L, Zhang Y, Shi L, et al. Circulating complement-C1q TNF-related protein 1 levels are increased in patients with type 2 diabetes and are associated with insulin sensitivity in Chinese subjects. PloS one. 2014;9(5):e94478. https://doi.org/10.1371/journal.pone.0094478
4. Lasser G, Guchhait P, Ellsworth JL, Sheppard P, Lewis K, Bishop P, et al. C1qTNF–related protein-1 (CTRP-1): a vascular wall protein that inhibits collagen-induced platelet aggregation by blocking VWF binding to collagen.

Blood. 2006;107(2):423-30. https://doi.org/10.1182/blood-2005-04-1425
5. Zhang Y, Liu C, Liu J, Guo R, Yan Z, Liu W, et al. Implications of C1q/TNF-related protein superfamily in patients with coronary artery disease. Sci Rep. 2020;10(1):878. https://doi.org/10.1038/s41598-020-57877-z
6. Wang H, Wang R, Du D, Li F, Li Y. Serum levels of C1q/TNF-related protein-1 (CTRP-1) are closely associated with coronary artery disease. BMC Cardiovasc Disord. 2016;16:1-5. https://doi.org/BMC Cardiovasc. Disord
7. Yuasa D, Ohashi K, Shibata R, Takeshita K, Kikuchi R, Takahashi R, et al. Association of circulating C1q/TNF-related protein 1 levels with coronary artery disease in men. PLoS One. 2014;9(6):e99846. https://doi.org/10.1371/journal.pone.0099846
8. Wang XQ, Liu ZH, Xue L, Lu L, Gao J, Shen Y, et al. C1q/TNF-related protein 1 links macrophage lipid metabolism to inflammation and atherosclerosis. Atherosclerosis. 2016;250:38-45. https://doi.org/10.1016/j.atherosclerosis.2016.04.024
9. Pourghadamyari H, Moghadam ES, Eghbali M, Borji H, Dialamy M, Sadeghi A. Inflammatory indices IL-6, TNF-α, CRP, and hs-CRP in candidates for coronary artery bypass graft surgery. Acta Biochim Iran. 2023;1(3):126-32. https://doi.org/10.18502/abi.v1i3.14548
10. Janowska JD. C1q/TNF-related protein 1, a multifunctional adipokine: an overview of current data. Am J Med Sci. 2020;360(3):222-8. https://doi.org/10.1016/j.amjms.2020.05.036
11. Fadaei R. Adipokines as a link between adipose tissue with inflammation and insulin resistance in cardiometabolic diseases. Acta Biochim Iran. 2023. https://doi.org/10.18502/abi.v1i3.14546
12. Barmoudeh Z, Shahraki MH, Pourghadamyari H, Borj MR, Doustimotlagh AH, Abbaszadeh-Goudarzi K. C1q tumor necrosis factor related proteins (CTRPs) in patients with cardiovascular diseases. Acta Biochim Iran. 2023. https://doi.org/10.18502/abi.v1i1.14060
13. Gu Y, Hu X, Ge P-B, Chen Y, Wu S, Zhang X-W. CTRP1 aggravates cardiac dysfunction post myocardial infarction by modulating TLR4 in macrophages. Front Immunol 2021;12:635267. https://doi.org/10.3389/fimmu.2021.635267
14. Lu L, Zhang RY, Wang XQ, Liu ZH, Shen Y, Ding FH, et al. C1q/TNF-related protein-1: an adipokine marking and promoting atherosclerosis. Eur Heart J 2016;37(22):1762-71. https://doi.org/10.1093/eurheartj/ehv649
15. Han S, Jeong AL, Lee S, Park JS, Buyanravjikh S, Kang W, et al. C1q/TNF-α–related protein 1 (CTRP1) maintains blood pressure under dehydration conditions. Circ Res. 2018;123(5):e5-e19. https://doi.org/10.1161/circresaha.118.312871
16. Rodriguez S, Lei X, Petersen PS, Tan SY, Little HC, Wong GW. Loss of CTRP1 disrupts glucose and lipid homeostasis. Am J Physiol Endocrinol Metab. 2016;311(4):E678-E97. https://doi.org/10.1152/ajpendo.00087.2016
17. Shen L, Wang S, Ling Y, Liang W. Association of C1q/TNF-related protein-1 (CTRP1) serum levels with coronary artery disease. J Int Med Res. 2019;47(6):2571-9. https://doi.org/10.1177/0300060519847372