The circulating levels of CTRP5 and the ratio of CTRP1 to CTRP5 plasma levels are significant predictors for cIMT value in patients with type 2 diabetes

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Abstract

Background

There is growing evidence that C1qTNF-related protein (CTRP) family has crucial role in physiology and pathophysiology of metabolic disorders such as Type 2 Diabetes (T2D) and obesity. We sought to identify the association of CTRP1 and CTRP5 circulating levels with various obesity parameters such as visceral adipose tissue (VAT) thickness, visceral adiposity index (VAI) and with carotid intima-media thickness (cIMT) in patients with T2D and healthy subjects.

Methods

This case- control study recruited 42 T2D patients and 42 healthy adults (all men). cIMT and VAT thickness measurement were performed using an Accuvix XQ ultrasound. Circulating CTRP1 and CTRP5 concentrations were measured by enzyme-linked immunosorbent assay (ELISA).

Results

CTRP-1 and CTRP1/CTRP5 ratio were markedly higher in patients with T2D compared to controls ($p < 0001$ and $p < 0004$ respectively). Interestingly, binominal logistic regression revealed that higher circulating level of CTRP1 was associated with presence of T2D (odds ratio [OR]: 13203.554 [95% CI: 65.186-2674407.708]; P=.000). When considering the study population as a whole, CTRP1 circulating levels were correlated with WHR, VAT and HOMA-IR. In addition, we observed that the ratio of CTRP1 to CTRP5 plasma levels ($\beta = 0.648$, P=0.005) and CTRP5 circulating levels ($\beta = 0.4\ 44$, P=0.049) are significant predictors for cIMT value.

Conclusions

Our results indicated that CTRP1 and CTRP5 concentrations were correlated with atherosclerosis in human subjects and these adipokines might have a causal role for cardiometabolic risk in type 2 diabetes disease

1. Background

Type 2 Diabetes (T2D) is one of the most common diseases worldwide affecting about 9% of the world population. (1) As a complex disease, it affects the function of many organs, which implies the possible connection it has with many other diseases.(2–4) Obesity and cardiovascular disease (CVD) which are in the context of this study, are two of the most well-known examples of these connections with confirmed links to diabetes.(5–7)

Obesity is a leading cause of insulin resistance thus, it is considered as one of the major risk factors for diabetes. Moreover, it is generally accepted that CVD is the leading cause of mortality among T2D patients, which arise from several abnormalities in cellular metabolism and energy homeostasis. Since

the connection among these conditions is becoming more and more evident through recent studies, identifying the possible molecules and the their underlying mechanism seem to be important in this regard.(8)

Adipose tissue plays a major role in regulating the overall metabolism of the body by using, secreting a wide range of adipocytes. Adiponectin and their parallogues, the family of C1q/TNF-related proteins (CTRPs), seems to be the crucial molecules in the cross-talk among metabolic disorders.(9)

There is growing evidence that adiponectins levels are inversely associated with insulin resistance. Adiponectin acts as an anti-inflammatory agent in the adipose tissue and can improve insulin sensitivity in peripheral tissues.(10, 11) More importantly, accumulating evidence points toward the association between hypoadiponectinemia and increased risk of cardiovascular problems.(12, 13)

The family of CTRPs has 15 protein members that plays key roles in physiological and pathological metabolic conditions.(14, 15) The alteration in circulating levels of CTRPs has been reported in various metabolic diseases such as T2D, obesity, CVD, fatty liver disease and metabolic syndrome.(16–19)

CTRP1 is expressed in various tissues including adipose tissue, liver, muscles, kidneys, and heart.(14) Muscles are primary targets for CTRP1 as it activates AMPK and MAPK signaling pathways and promotes glucose uptake, ameliorates insulin resistance and increases fat oxidation.(20) Studies have shown increased levels of CTRP1 in T2D, prediabetes, coronary artery disease, congestive heart failure and atherosclerosis.(21, 22) Although there is evidence on the protective role of CTRP1 in murine heart injuries, the exact role of CTRP1 in these conditions is still not fully understood and requires further studies.(23)

CTRP5, another member of CTRPs family also expressed in a wide range of tissues including adipose tissue, eye, testis, skeletal muscle, brain, spleen, uterus, and ciliary epithelium but like CTRP1, adipose tissue is considered as the main secretor.(21) CTRP5 increases glucose uptake via stimulating plasma membrane incorporation of the glucose transporter 4 (GLUT4) into plasma membrane by a mechanism dependent on AMPK phosphorylation. In addition, Phosphorylation of acetyl-CoA carboxylase (ACC) is mediated by CTRP5 that results in fatty acid oxidation in rat myocytes. (14, 24, 25) According to recent studies, decreased levels of CTRP5 have been observed in metabolic syndrome, and T2D and increased levels were reported in coronary artery disease. Studies about the exact association between CTRP5 and metabolic disorders are rare with contradicting results, either suggesting a role against insulin resistant or a role promoting insulin resistance and atherosclerosis.

Given the importance of CVD as one of the most common cause of death in T2D patients as well as a close association among T2D, obesity and an increased occurrence of CVD risk factors, it has been of great importance to detect the possible molecules which links between aforementioned conditions.

Up to date, there is no study to evaluate CTRP1 and CTRP5 correlation with various obesity indices including body mass index (BMI), waist, hip, waist-to-hip ratio (WHR), visceral adipose tissue (VAT), and

visceral adiposity index (VAI) in T2D patients compared to healthy group. In this study, we intended to address the association of circulating CTRP1 and CTRP5 with obesity indices and carotid intima-media thickness (cIMT) in patients with T2D and healthy subjects.

2. Methods

2.1. Study population

A total of 84 subjects participated in the study (all man), including 42 type 2 diabetes and 42 healthy people. All subjects were recruited from Shariati Hospital, Tehran, Iran. Outpatient clinic from March 2012 until November 2013. Informed written consents were obtained prior to study, and study was approved by Ethnics Committee of the Tehran University of Medical Sciences (TUMS). To diagnosis the T2DM, the basis of American Diabetes Association (ADA) criteria was used as: fasting blood glucose (FBG) ≥ 126 mg/dl (7.0 mmol/l) or 2 hours plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test (OGTT) or random plasma glucose ≥ 200 mg/dl (11.1 mmol/l) (26). VAI was calculated as a novel sex-specific index, based on waist circumference (WC), BMI, triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C), indirectly expressing visceral adipose function in all participants as described previously (27)

2.2. Ultrasound methods

Ultrasound examinations for measurement of the cIMT and visceral adipose tissue thickness (VAT) were performed using an Accuvix XQ ultrasound unit (Medison, Seoul, Korea) equipped with a 3–7 MHZ curved-array and a 5–12 MHz linear-array transducer. The technique for measuring cIMT and VAT has been previously described (28, 29). In brief, cIMT measured at its thickest point on the distal wall of the carotid arteries, along a 1.5-2 cm proximal to the carotid bulb. cIMT on the left and right sides was evaluated and mean values of both sides were determined as carotid IMT. Also, VAT (in millimeter) was measured as the distance between the anterior wall of the aorta and the internal face of the rectus abdominis muscle perpendicular to the aorta.

2.3. Anthropometric and clinical characterization

Anthropometric indices of all participants including age, weight, height, BMI, WC, hip, WHR, and blood pressure were examined. BMI was measured based on the ratio of weight in kg divided by height in m^2 to assess participants' obesity. WC using flexible inch strip in the middle between the lowest rib and the iliac crest was calculated. Furthermore, hip was measured at the maximum circumference of the buttocks. WHR based on the ratio of WC in centimeters divided by hip circumference in centimeters was measured. After a 15-minute rest in sitting position, systolic and diastolic blood pressures were measured by a manual sphygmomanometer. VAI, as a gender-specific mathematical index was calculated based on simple anthropometric [BMI and WC] and metabolic [TG and HDL Cholesterol (HDL)] parameters.

$$\text{Females}: \text{VAI} = \left(\frac{WC}{36.58+(1.89 \times BMI)}\right) \times \left(\frac{TG}{0.81}\right) \times \frac{1.52}{HDL}$$

$$\text{Males}: \text{VAI} = \left(\frac{WC}{39.68+(1.88 \times BMI)}\right) \times \left(\frac{TG}{1.03}\right) \times \frac{1.31}{HDL}$$

2.4. Biochemical and laboratory measurements

Fresh venous blood samples were collected into sterile tubes containing the EDTA-K2 after an overnight fasting, in order to biochemical analyses. Fasting blood glucose (FBG), urea, creatinine, TG, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), HDL-C, aspartate amino transferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP), and gamma glutamyl transferase (γ-GT) were measured by auto analyzer using commercial kits (Pars Azmoon, Tehran, Iran). Additionally, fasting plasma insulin was calculated by enzyme linked immunosorbent assay (ELISA) kit (Monobind Inc., USA). To examine the IR, homeostasis model assessment of IR (HOMA-IR) was calculated with the equation of: fasting blood glucose (mg/dL) × fasting blood insulin (μU/mL) / 405.

2.5. Plasma adiponectin measurement

Plasma levels of adiponectin were determined by using the ELISA Kit (Elabscience, Wuhan, China) according to manufacturer's protocol. Intra-assay and inter-assay Coefficients of Variability (CV) were < 10%.

2.6. Plasma CTRP5 and CTRP1 measurement

CTRP1 concentration were measured by ELISA kit (Biovendor research and diagnostic products) with a minimum detectable concentration of 0.016 ng/ml, Intra assay Coefficients of Variability (CV) was 2.7% and Inter assay CV was 8.5%. Plasma levels of CTRP5 were measured by immunoassay using Cayman system kit according to manufacturer's protocol. The inter-assay variability and intra-assay variability were 6.975 and 6.3%, respectively.

2.7. Statistical analysis

Continuous variable with normal distribution is presented as mean ± standard deviation (SD) and variables with non-normal distribution are presented as median (interquartile ranges (IQR)). Descriptive analysis was applied and normality was tested for all quantitative variables by means of the Shapiro-Wilk test. For data with normal distribution, comparisons of anthropometric, biochemical, and laboratory parameters between two groups were done by the student's t-test and by Mann-Whitney U test when we have non-normal distribution. A p-value < 0.05 was applied to interpret all achieved data from analysis. All data analysis was performed using SPSS 20 (SPSS, Chicago, IL, USA).

3. Results

Anthropometric, clinical and laboratory data of T2D patients, and control subjects are shown in Table 1. All subjects were men and there is no statistically difference between two studied groups in term of age (P = 0.622). However, T2D group had increased values of WC and WHR compared to controls (P = 0.039 and P = 0.012, respectively). However, other obesity parameters including hip, VAT and VAI were not comparable between two study groups. We should be noted that BMI was higher in T2D in comparison with the control group but did not reach our threshold of statistically significant difference.

Table 1

Anthropometric and laboratory characteristics of study population.

Characteristics	Healthy subjects (n = 42)	T2DM (n = 42)	P value
Age, years	51(48-57.25)	55(46.50-59.25)	0.622
Waist, cm	99.52 ± 10.21	104.45 ± 11.30	0.039*
Hips, cm	102.43 ± 6.417	103.79 ± 7.15	0.363
WHR, -	0.97 ± 0.05	1.004 ± 0.06	0.012*
Height, cm	169.48 ± 5.70	168.13 ± 5.65	0.281
Weight, kg	78.01 ± 11.89	81.31 ± 12.10	0.212
BMI, kg/m2	27.13 ± 3.72	28.78 ± 4.33	0.064
FBG, mg/dL	93.50(87.01–99.17)	146(123.45-183.07)	0.000*
Insulin, µU/mL	8(3.50–10.10)	7.10(4.35–9.55)	0.906
HOMA-IR, -	1.79(0.83–2.43)	2.61(1.58–3.77)	0.009*
Triglycerides, mg/dL	129.10(93.85–160.30)	142.30(108.28–184.40)	0.214
Cholesterol, mg/dL	196.50 (167.85–213.90)	202.60 (167.88-221.45)	0.545
HDL, mg/Dl	50.10 (44.45–55.90)	55.90 (44.23–64.25)	0.225
LDL, mg/dL	113.71 ± 32.23	115.73 ± 37.56	0.796
LDL to HDL, -	2.26 ± 0.67	2.152 ± 0.63	0.451
Urea, mg/dL	30.46 ± 7.58	32.20 ± 6.55	0.272
Creatinine, mg/dL	1.27 ± 0.18	1.21 ± 0.18	0.164
AST, U/L	18.70 (16.20-23.93)	20.20 (15.98–26.15)	0.679
ALT, U/L	20.50 (14.30-29.65)	22.80 (14.98–40.20)	0.255
ALP, U/L	227 (196.50–263)	220 (185.75–285)	0.810
γ-GT, U/L	24.33 (19.58–32.10)	28.34 (21.69–43.91)	0.045*
SBP, mmHg	122 (113.75–140)	132 (120–150)	0.081
DBP, mmHg	80(70–90)	80 (74.25-90)	0.876
Visceral Fat, %	60.76 ± 22.35	66.26 ± 21.90	0.258

*Continuous variables with normal distribution were described as mean ± SD and with non-normal distribution were described as Median (IQR)

Characteristics	Healthy subjects (n = 42)	T2DM (n = 42)	P value
WBC, $\times 10^9$/L	5.40 (1.9)	6.70 (2)	0.029*
cIMT, mm	0.79 ± 0.10	0.83 ± 0.12	0.086
VAI	1.60 (1.11–2.05)	1.67 (1.25–2.27)	0.577
*Continuous variables with normal distribution were described as mean ± SD and with non-normal distribution were described as Median (IQR)			

As expected, patients with T2D had higher FBG concentration, insulin levels and HOMA-IR in comparison with controls. The concentration of TG, HDL-C, LDL- C showed no significant difference between patients and controls.

All liver function related tests including AST and ALT with expect to GGT, showed higher levels in T2D group compared to controls. Moreover, cIMT as a measurement of subclinical atherosclerosis was significantly increased in T2D patients compared to controls but did not reach our threshold of statistically significant difference (P = 0.086).

The comparison of CTRP-5, CTRP-1, adiponectin circulating levels and ratio of CTRP-1 to CTRP-5 between T2D patients and controls **(Fig. 1)** revealed that CTRP-1 and CTRP1/CTRP5 ratio were significantly higher in patients with T2D rather than in controls ($p < 0001$ and $p < 0004$ respectively). While, plasma levels of both CTRP5 and adiponectin with a borderline significant, was lower in T2D patients in comparison with controls ($p < 0.0928$ and $p < 0.0941$ respectively).

We also performed binomial logistic regression to investigate whether ratio of CTRP1 to CTRP5 and plasma levels of CTRP1, CTRP5 and adiponectin might predict the presence of T2D (Table 2). When all afore-mentioned items were inserted, we found only higher circulating level of CTRP1 was associated with presence of T2D (odds ratio [OR]: 13203.554 [95% CI: 65.186-2674407.708]; P = .000).

Table 2
Binomial logistic regression for odds ratio of T2D according to ratio of CTRP1 to CTRP5 and plasma levels of CTRP1, CTRP5 and adiponectin.

	B	S.E.	Wald	Sig.	Exp(B)	95% CI. for EXP(B)	
						Lower	Upper
CTRP1	9.488	2.710	12.261	.000	13203.554	65.186	2674407.708
CTRP5	-3.099	2.293	1.826	.177	.045	.001	4.037
Adiponectin	-2.320	1.792	1.675	.196	.098	.003	3.296
CTRP1/CTRP5	− .105	.131	.650	.420	.900	.697	1.163

To identify independent predictors of CTRP1 circulating levels, we performed multivariate stepwise linear regression analysis with age, BMI, WC, hip, WHR, VAI, and VAT as independent variables. Our results showed that WHR (β = 0.273, P = 0.014) is the only predictor for CTRP1 concentration in all participants.

In addition, we performed multivariate stepwise linear regression analysis with cIMAT as dependent variable and ratio of CTRP1 to CTRP5 and plasma levels of CTRP1, CTRP5 and adiponectin as independent variables. Our results showed that the ratio of CTRP1 to CTRP5 plasma levels (β = 0.648, P = 0.005) and CTRP5 circulating levels (β = 0.4 44, P = 0.049) are significant predictors for cIMT value.

The ROC curves analysis of CTRP1, CTRP5 and CTRP1/CTRP5 circulating levels in discriminating T2D from controls showed an area under the curve (AUC) of 0.75 (p < 0.0001, 95% CI 0.65–0.85), 0.60 (p < 0.0945, 95% CI 0.48–0.73) and of 0.73 (p < 0.0945, 95% CI 0.61–0.83) in T2DM, respectively (Fig. 2).

The results of correlation analysis of CTRP1/CTRP5 and circulating levels of CTRP1 and CTRP5 with anthropometric, and biochemical characteristics in all participants and in T2D patients and controls are depicted in Table 3 and Table 4. We found a positive significant correlation between CTRP1 levels with WHR, VAT and HOMA-IR in the whole population study. Moreover, there was a significant correlation between CTRP1 circulating levels with cIMT (P = 0.062), VAI (P = 0.093) and visceral fat (P = 0.051) with a borderline significance. Moreover, CTRP5 circulating levels inversely correlated with HOMA-IR index (p = 0.008). Furthermore, the ratio of CTRP1 to CTRP5 was positively and significantly correlated with cIMT (P = 0.020) and HOMA-IR (P = 0.015) in all participants.

Due to technical limitations, Tables 3-4 are provided in the Supplementary Files section.

4. Discussion

A grown body of evidence highlight the crucial role of adiponectin and CTRP family in metabolic disorders (30, 31), but few studies have ever attempted to associate the CTRP1, CTRP5 and adiponectin circulating levels with unfavorable obesity indices including VAI, VAT, HOMA-IR, and also carotid intima-media thickness in T2D patients. In our study, we have demonstrated that circulating levels of CTRP1 were higher in T2D patients compared to those in healthy groups, in contrast to the reduced trend of adiponectin serum levels. Moreover, binominal logistic regression investigation revealed that elevated CTRP1 plasma levels were direct indicator of T2D; suggesting the hypothesis that CTRP1 might be involved in the pathogenesis of T2D. Our results are consistent with observations reported by Bai B et al and Shanaki M et al (31, 32). They found that plasma levels of CTRP1 increased in T2D and NAFLD patients relative to healthy participants. One possible explanation regarding elevation of CTRP1 concentrations in T2D patients might be a self-protective or compensatory mechanism in response to abnormal glucose metabolism. Inconsistent with the above results, it was reported that CTRP1 levels did not significantly higher in diabetic subjects(33). The main reason for this discrepancy could be due to different samples as human and animal models (DIO or *ob/ob* mice) investigated. Also, in a previous study, it has been indicated that circulating CTRP1 in adiponectin- null mice were significantly enhanced relative to controls that confirms our finding concerning different serum pattern of CTRP1 and

adiponectin(34). In addition, CTRP1 may have specified overlapping roles as adiponectin. For instance, overexpression of recombinant CTRP1 could efficiently diminish serum levels of glucose in mice (34). Our data indicated that the differential pattern of CTRP1 and adiponectin in T2D condition might reflect an effective function in modulating glucose homeostasis; and the paradoxical elevation of CTRP1 circulating levels in T2DM subjects might exert a compensatory response to the abnormal glucose and lipid metabolism, which demands further clinical studies.

Interestingly, we found that CTRP1 markedly correlated with WHR and HOMA-IR and with VAI and VAT with a borderline significance. In line with our results, previous data reported that CTRP1 levels significantly increased in obese condition and associated with metabolic indices such as BMI and HOMA-IR (35–38). Moreover, in line with current literature, Bai *et al*. observed higher circulating levels of CTRP1 were significantly correlated with hyperglycemia and HOMA-IR in T2D patients (39). However, contrary to this result, another study indicated that CTRP1 circulating levels significantly decreased in diet-induced obese mice relative to normal diet mice (36, 40). Also, there is evidence that inhibition of CTRP1 impairs glucose homeostasis and insulin signaling which points into possible contribution of CTRP1 in regulating energy metabolism and systemic insulin sensitivity (41, 42). Moreover, it has been noted that CTRP1 likely correlated with sex hormones and may affect systemic metabolism in a sex-dependent manner (41). Based on discrepancy results of different pattern of CTRP1 in the context of obesity, future studies are needed to unravel underlying mechanisms in which CTRP1 regulates energy metabolism.

In the present study, a ROC curve analysis showed that circulating CTRP1 discriminated with high accuracy between T2D patients and healthy controls. These findings points toward a contributory role of CTRP1 as a potential marker in patients with T2D. However, future study with higher sample size is necessary to establish this concept.

There is also ample evidence about possible role of CTRP1 in coronary artery disease and atherosclerosis (43–45). In addition, it has been shown that circulating level of CTRP1 was associated with several diseased coronary arteries and the atherosclerotic extent index. Also, the close associations of CTRP1 with unfavorable metabolic profile may have contributed to the significant linkage between CTRP1 and cardiovascular incidence risk. Here, we reported a positive correlation of CTRP1 with cIMT with a borderline significance. It has been noted that adiponectin (a paralogue of CTRP1) has potential anti-atherogenic properties and might be an independent factor correlated with atherosclerosis. So it is tempting to speculate that high level of CTRP1 is independently associated with subclinical atherosclerosis and vascular injury.

Taken together, our results along with others suggest that measurement of circulating CTRP1 concentrations may be valuable for assessment of cardiovascular risk. However, future researches are required to elucidate the impact of CTRP1 on cardiovascular homeostasis.

Recently, CTRP5 has been found as a mediator of metabolic pathways involved in T2D, insulin resistance and also obesity-related cardiovascular risk(47). Nevertheless, the previous results are inconsistent. There is report about the low levels of circulating CTRP5 in type 2 diabetes subjects, whereas another study

argued that circulating levels of CTRP5 were significantly higher in obese and diabetic mice rather than lean group (47, 48). An *in vivo* study by Lei et al revealed that CTRP5 circulating levels were not significantly changed in ob/ob mice (49). In addition, we previously showed that plasma CTRP5 levels were significantly lower in NAFLD and T2D patients in comparison with healthy subjects (50). In the present study, circulating CTRP5 concentrations were lower in T2D patients with a borderline significant level. As mentioned above, there is a discrepancy between animal model studies and human surveys that are might be due to the different functions of CTRP5 in humans and mice; just as resistin plays different roles in humans and mice(51). Another reason might be due to different genetic background that affects phenotype, which type 2 diabetes in humans is a heterogeneous disease that associated with environmental factors, whereas ob/ob and db/db mice are only caused by leptin deficiency(52). Also, it is noteworthy that we observed a negative correlation between CTRP5 and HOMA-IR, which suggests a link between CTRP5 and insulin resistance. It has been shown that inhibition of CTRP5 action may result in the alleviation of insulin resistance associated with obesity and diabetes (49). However, data are lacking on the correlation between CTRP5 and type 2 diabetes in humans and future clinical studies are demanded.

As an important finding, we also found that CTRP5 circulating levels and CTRP1/CTRP5 ratio might be two independent predictors for the cIMT index. It has been demonstrated that serum CTRP5 levels were significantly increased and are positively correlated with the extent and severity of atherosclerosis in patients with CAD(53). It seems that decreased levels of CTRP5 may be linked to cardiovascular complications in T2D patients. However, more research on this subject needs to be undertaken. It is tempting to speculate that the enhancement of CTRP1 levels along with reduced CTRP5 circulating levels were associated with an increase in the risk of T2D. Therefore, these adipokines can be considered as a possible metabolic mediator in the context of T2D and cardiovascular complications. It is also worth mentioning that the detailed mechanism associating with CTRP1 and CTRP5 alterations cannot be elucidated based on current study, although we provided a novel finding regarding the association of CTRP1 and CTRP5 with T2D and cardiovascular risk. Several limitations of the study should be considered. The main limitation is the relatively small number of patients. In this regard, the low number of T2D patients precluded any definitive conclusions on the relationship between CTRP1, CTRP5, obesity indices, T2D and cardiometabolic risk factors. In addition, we were able to recruit only men. Therefore, considering the sex-dependent manner of CTRP1 and CTRP5, it remains to be investigated the circulating levels of these adipokines in both genders.

5. Conclusions

In summary, we showed that circulating CTRP1 levels markedly elevated in T2D patients and significantly correlated with the cIMT index in all participants. Also, we revealed that CTRP5 may be a mediator of metabolic pathways that affects glucose and insulin metabolism in humans. We also noted that CTRP1 and CTRP5 concentrations were associated with atherosclerosis in human subjects and alteration in adipokines levels might be considered as an emerging cardiometabolic risk factor in patients with type 2 diabetes. However, more investigations are needed to confirm this concept.

Abbreviations

CTRP
C1qTNF-related protein
T2D
Type 2 Diabetes
VAT
Visceral adipose tissue
SAT
Subcutaneous adipose tissue
VAI
Visceral adiposity index
cIMT
Carotid intima-media thickness
ELISA
Enzyme-linked immunosorbent assay
CVD
Cardiovascular disease
ACC
Acetyl-CoA carboxylase
BMI
Body mass index
WHR
Waist-to-hip ratio
TG
Triglycerides
HDL-C
High-density lipoprotein cholesterol
LDL-C
Low-density lipoprotein cholesterol
AST
Aspartate amino transferase
ALT
Alanine amino transferase
ALP
Alkaline phosphatase
γ-GT
Gamma glutamyl transferase
HOMA-IR
Homeostasis model assessment for insulin resistance

OGTT
Oral glucose tolerance test

Declarations

Ethics approval and consent to participate

The procedures, used in the study, were approved by the Ethical Committee of the Tehran University of Medical Sciences (TUMS) and fully informed, written consent was obtained from the patients.

Consent for publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Figure 2

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