doi: 10.4183/aeb.2023.19

SERUM OMENTIN-1 LEVEL IS ASSOCIATED WITH THE AGGREGATION OF CARDIOVASCULAR RISK FACTORS IN ADOLESCENTS

Y. Chen, J. Zhang, L. Li, C. Liu, P. Li*

Shengjing Hospital of China Medical University, Department of Endocrinology, Shenyang, China

Abstract

Objective. The existing studies involving omentin-1 have mainly focused on relationships with single cardiovascular risk factor. Whether omentin-1 is associated with the aggregation of cardiovascular risk factors has not been reported. We investigate the relationship between the serum omentin-1 level and aggregation of cardiovascular risk factors in adolescents.

Subjects and Methods. A total of 741 young students, 11–16 years of age, were enrolled using a stratified cluster sampling method. The participants were given a questionnaire survey and underwent a physical examination. The aggregation of cardiovascular risk factors was defined as two or more cardiovascular risk factors occurring simultaneously in the same individual.

Results. Partial correlation analysis suggested that serum omentin-1 level was significantly correlated with waist circumference (R=-0.086, P=0.019) and Body Mass Index (R=-0.096, P=0.009). Logistic regression analysis showed that as the serum omentin-1 level increased, the risk of aggregation of cardiovascular risk factors decreased. Cardiovascular risk factors which were most closely associated with a decrease in the serum omentin-1 level were obesity calculated by Body Mass Index (OR=0.988, P=0.043) and central obesity calculated by waist circumference (OR=0.993, P=0.012).

Conclusions. The serum omentin-1 level in adolescents is inversely associated with the aggregation of cardiovascular risk factors. Waist circumference and Body Mass Index are factors most closely associated with a decrease in the serum omentin-1 level.

Keywords: Omentin-1, aggregation of cardiovascular risk factors, adolescent, obesity.

INTRODUCTION

Cardiovascular diseases are a major group of diseases that threaten human health. Moreover, more than 200 risk factors for cardiovascular diseases have been identified. The phenomenon that multiple risk factors occur in an individual simultaneously is referred to as an aggregation of risk factors (1, 2), which significantly increases the risk of cardiovascular diseases. Omentin-1 is an adipokine that functions as an insulin sensitizer, anti-inflammatory, and anti- atherosclerosis. The existing studies involving omentin-1 have mainly focused on relationships with single risk factor (3, 4). Indeed, the correlation between omentin-1 and the aggregation of cardiovascular risk factors has rarely been reported. In addition, previous studies have involved adults as study subjects (5-7). The metabolic characteristics during growth and development differ between adolescents and adults; however, whether or not omentin-1 is associated with the aggregation of cardiovascular risk factors in adolescents has not been reported. We recruited young people, 11-16 years of age, from a medium-sized city in northeast China as study subjects and analyzed the relationship between omentin-1 level and the aggregation of cardiovascular risk factors. The study will not only help better understand the role of omentin-1 in metabolic diseases, but also provide evidence for screening novel serum biomarkers for the aggregation of cardiovascular risk factors in adolescents.

MATERIALS AND METHODS

Study subjects

From January 2010 to January 2011, a total of 1,368 junior and senior high school students from Liaoyang City were selected using a random stratified cluster sampling method. The participants completed a questionnaire survey. Informed consent

*Correspondence to: Ping Li MD, Shengjing Hospital of China Medical University, Department of Endocrinology, Shenyang, 110004, China, E-mail: scizhong@163.com

was obtained from 781 students or their parents or guardians prior to blood testing. There were 741 participants with complete data for analysis. The study subjects denied a history of diabetes, hypertension, and hyperlipidemia, as well as administration of hypoglycemic, antihypertensive, and lipid-lowering agents and weight-loss agents. All study subjects received a detailed explanation of the study protocol. The study was approved by the Ethics Committee of Shengjing Hospital of China Medical University, and the study was conducted in accordance with the Helsinki Declaration.

Sample collection

All subjects completed a questionnaire, including questions pertaining to the medical history and medications. The subjects were required to fast after 8PM the day before obtaining blood samples, which was done between 7:00 and 8:00 AM. Before blood samples were obtained, trained physicians measured the subjects' height, weight, and waist circumference. Blood pressure was measured twice using a benchtop mercury sphygmomanometer. The subjects rested for at least 10 min before blood pressure measurement and there was at least a 2-min interval between the two measurements. The recorded systolic and diastolic blood pressures were the average value of the two measurements. Fasting venous blood samples were sent to the Diabetes Hospital of Liaoyang City for testing. The fasting plasma glucose level was determined by the glucose oxidase assay. A routine enzymatic method was used to determine serum total cholesterol, low-density lipoprotein-cholesterol, high-density lipoprotein-cholesterol, and triglycerides levels (Olympus 400; Olympus Optical Company, Tokyo, Japan). Serum was isolated and samples were stored at -80°C. The fasting insulin level was measured by radioimmunoassay (China Institute of Atomic Energy, Beijing, China) and the serum omentin-1 level was measured by ELISA (R&D Company, city, state, USA) with an intra-batch variation < 9% and an inter-batch variation < 15%. Serum insulin and omentin-1 testing were performed in the Central Laboratory of Shengjing Hospital affiliated with China Medical University. The Body Mass Index was calculated as follows: body weight in kg/height in m2. The homeostasis model assessment-insulin resistance (HOMA-IR) was calculated as follows: fasting blood glucose (mmol/L)× fasting insulin (μU/ml)/22.5.

Diagnostic criteria and definitions

Cardiovascular risk factors were divided into four components: (1) high blood pressure, systolic blood pressure ≥ 130 mmHg and/or diastolic blood pressure ≥ 85 mmHg (8); (2) hyperglycemia, fasting plasma glucose ≥ 5.6 mmol/L(2) ; (3) dyslipidemia, high-density lipoprotein-cholesterol < 1.03 mmol/L, non-high-density lipoprotein cholesterol ≥ 3.76 mmol/L, or triglycerides ≥ 1.47 mmol/L(2) ; (4) general obesity (Body Mass Index ≥ 95% of adolescents of the same age and sex) and central obesity (waist circumference ≥ 90% of adolescents of the same age and sex) (2), either of which exceeded the standard value for obesity. Aggregation of cardiovascular risk factors was defined as any two or more of the following conditions in one individual: high blood pressure; hyperglycemia; dyslipidemia; and obesity.

Statistical analyses

Data processing and statistical analyses were performed using SPSS 19.0 software. Normally distributed data were tested with the Kolmogorov-Smirnov test. Non-normally distributed data were analyzed after being logarithmically transformed to approximate a normal distribution. Continuous data with a normal distribution are expressed as the mean ± standard deviation and continuous data with a non-normal distribution are expressed as the median (interquartile range). Categorical data are expressed as a percentage and analyzed by a $\chi 2$ test. ANOVA was used for multi-group comparisons of normally distributed data and the Kruskal-Wallis H test was used for multi-group comparisons of non-normally distributed data. Partial correlation analysis after adjusting confounding factors was used to calculate the correlation coefficient between the omentin-1 level and cardiovascular risk factors. Logistic multivariate regression analysis was used to evaluate the effect of the omentin-1 level on associated risk factors and the aggregation of these factors. $P < 0.05$ was considered statistically significant.

RESULTS

Distribution of omentin-1 level in the study subjects

A total of 741 adolescents, 11–16 years of age, were enrolled in the study. The subjects were divided into three tertiles (T1, T2, and T3) based on increasing serum omentin-1 levels. There were significant differences in age, sex, and SBP among the groups.

Table 1. Clinical characteristics of the study subjects stratified by the omentin-1 level

Indicators	Omentin-1 level tertiles			*P*
	T1 (n=247)	T2 (n=247)	T3 (n=247)	
Omentin-1(ng/L)	57.54(46.77-65.23)	94.85(83.28-104.46)	236.38(149.08-473.20)	<0.001*
Age (years)	13.71±1.49	13.68±1.49	14.05±1.47	0.01*
Sex (male,%)	144 (58.3)	130 (52.8)	113(45.7)	0.02*
Waist circumference (cm)	77.44±11.25	76.61±10.61	76.72±10.50	0.654
BMI (kg/m²)	22.18±4.45	21.30±4.00	21.45±4.39	0.051
SBP (mmHg)	120±13	116±13	118±14	0.031*
DBP (mmHg)	73±10	72±11	74±11	0.179
HDL (mmol/L)	1.06(0.86-1.26)	1.01(0.86-1.24)	1.01(0.84-1.25)	0.300
non-HDL (mmol/L)	3.35±0.80	3.45±0.82	3.50±0.77	0.098
TG (mmol/L)	0.99(0.70-1.35)	0.94(0.68-1.30)	0.91(0.67-1.28)	0.510
FPG (mmol/L)	4.80(4.40-5.00)	4.80(4.50-5.10)	4.70(4.30-5.00)	0.174
FINS (uIU/mL)	18.00(14.00-25.00)	18.00(14.00-25.00)	18.00(13.00-24.00)	0.872
HOMA-IR	3.84(2.74-5.23)	3.78(2.90-5.27)	3.79(2.61-5.35)	0.792

Study subjects were divided into three groups with increasing omentin-1 levels according to serum omentin-1 level tertiles. Data are expressed as the mean ± standard deviation or median (interquartile range);Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein-cholesterol; non-HDL-C, non-high-density lipoprotein cholesterol; TG, triglycerides; FINS, fasting insulin; HOMA-IR, homoeostatic model assessment of insulin resistance.*P < 0.05.

Table 2. Comparison of the positive rates of cardiovascular risk factors in three groups with various omentin-1 levels

Risk factors	Tertile interval			*P*
	T1 (n=247)	T2 (n=247)	T3 (n=247)	
Obesity (%)	20.24	12.20	14.98	0.045*
Central obesity (%)	46.96	43.90	42.91	0.641
High blood pressure (%)	27.13	21.05	29.15	0.101
Dyslipidemia (%)	67.61	70.85	70.45	0.759
High fasting blood glucose (%)	4.45	9.31	5.67	0.074
Aggregation of cardiovascular risk factors (%)	48.58	46.34	45.34	0.761

Categorical data are expressed as percentages and compared by a $\chi 2$ test. * p< 0.05.
Obesity: BMI ≥ 95% of BMI of adolescents of the same age and sex; central obesity: waist circumference ≥ 90% of adolescents of the same age and sex.

Table 3. Partial correlation analysis between omentin-1 and Cardiovascular diseases risk factors

Omentin-1	R	*P*
Waist circumference	-0.086	0.019*
BMI	-0.096	0.009*
SBP	-0.031	0.398
DBP	0.008	0.830
HDL	-0.057	0.119
non-HDL	0.046	0.212
TG	-0.009	0.797
FPG	-0.034	0.355
FINS	0.011	0.762
HOMA-IR	0.004	0.909

Abbreviation: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein-cholesterol; non-HDL-C, non-high-density lipoprotein cholesterol; TG, triglycerides; FINS, fasting insulin; HOMA-IR, homoeostatic model assessment of insulin resistance. Partial correlation analysis after adjusting for age and sex.*P<0.05.

Comparisons between groups showed that the age of the subjects in the T3 group, which had the highest omentin-1 level, was significantly greater than the T1 and T2 groups. The SBP of the subjects in T1 group was higher than the T2 group (Table 1).

Comparison of the positive rates of the aggregation of cardiovascular risk factors and individual components in different groups stratified by the omentin-1 level

The obesity rate based on Body Mass Index was significantly different in the groups with various omentin-1 levels. The positive rates of other components did not show significant differences between the groups (Table 2).

Partial correlation between the omentin-1 level and cardiovascular risk factors

After controlling for age and sex, the omentin-1 level was significantly negatively correlated with waist circumference (R=-0.086, P=0.019) and Body Mass Index (R=-0.096, P=0.009), but not correlated with blood pressure, HOMA-IR, fasting blood-glucose (FPG), lipid, and insulin levels (Table 3).

Difference in omentin-1 levels in groups with (cases) and without (controls) various cardiovascular risk components

The study subjects were further grouped based on the presence of corresponding risk components. The case group refers to the group with individual risk components (component-positive) and the control group refers to the group without risk components. The omentin-1 levels in the case and control groups were compared. As shown in the results, the omentin-1 level in the obesity (case group) was significantly lower than the omentin-1 level in the normal (control group) [81.38 (55.04-142.73) *vs*. 96.37 (67.64-159.05) (ng/L), P=0.004]. The omentin-1 level in the group with the aggregation of cardiovascular risk factors was significantly lower than the corresponding control group [90.49 (62.32-141.86) *vs*. 96.77 (67.15-172.71) (ng/L), P=0.033] (Table 4).

Correlation between omentin-1 level and the aggregation of cardiovascular risk factors and its component individual risk factors

Logistic regression analysis showed that as the serum omentin-1 level increased, the risk of aggregation of cardiovascular risk factors decreased. Statistical significance was maintained after adjusting for confounding factors including age, sex, and HOMA-IR. Omentin-1 was a protective factor for the aggregation of cardiovascular risk factors (OR=0.987, P=0.001). Logistic regression analysis of the model after adjusting for confounding factors showed that the risk factors most closely related to a decreased omentin-1 level were obesity based on BMI (OR=0.988, P=0.043) and central obesity based on waist circumference (OR = 0.993, P = 0.012) (Table 5).

DISCUSSION

By analyzing the association between omentin-1 and aggregation of cardiovascular risk factors in adolescents in northern China, we showed that the serum omentin-1 level was negatively correlated with the aggregation of cardiovascular risk factors independent of sex, age, and insulin resistance. Obesity was the risk factor most closely associated with decreased omentin-1 levels.

Current research indicates that omentin-1 has a variety of important biological functions, including insulin sensitization, blood glucose regulation, anti-inflammation, and anti-atherosclerosis (9). Our study, for the first time, investigated the association between the serum omentin-1 level and cardiovascular risk factors in healthy adolescents. We showed that the serum omentin-1 level was independently and negatively correlated with the aggregation of

Table 4. Comparison of omentin-1 level between groups stratified by cardiovascular risk factors

	Omentin-1 level (ng/L)		
	Case group	Control group	*P*
Obesity	81.38(55.04-142.73)	96.37(67.64-159.05)	0.004*
Central Obesity	91.40(61.58-141.38)	95.85(67.92-172.15)	0.07
High blood pressure	90.88(64.46-150.22)	95.23(65.23-147.54)	0.523
Dyslipidemia	94.86(65.52-152.37)	94.47(64.27-141.24)	0.683
High fasting blood glucose	94.55(78.32-127.55)	94.77(64.75-150.70)	0.967
Aggregation of cardiovascular risk factors	90.49(62.32-141.86)	96.77(67.15-172.71)	0.033*

The patients were grouped according to their risk status (positive or negative). The case group refers to the corresponding factor-positive group and the control group refers to the in corresponding factor-negative group. Obesity: BMI ≥ 95% of the BMI of adolescents of the same age and sex. Central obesity: waist circumference ≥ 90% of the waist circumference of adolescents of the same age and sex. *P<0.05.

Table 5. Correlation between the omentin-1 level and the aggregation of cardiovascular risk factors as well as individual risk factors

	95% CI for EXP(B)		OR	*P*
	Lower	Upper		
Correlation between the omentin-1 level and the aggregation of cardiovascular risk factors				
MODEL 1	0.998	0.999	0.999	0.002*
MODEL 2	0.898	0.999	0.946	0.002*
MODEL 3	0.977	0.999	0.987	0.001*
Correlation between the omentin-1 level and individual cardiovascular risk factors (based on MODEL 3)				
Obesity	0.977	0.999	0.988	0.043*
Central obesity	0.988	0.999	0.993	0.012*
High blood pressure	0.998	1.000	0.999	0.119
Dyslipidemia	0.999	1.001	1.000	0.550
High fasting blood glucose	0.996	1.001	0.999	0.223

MODEL 1. Before adjustment; MODEL 2. Adjustment for age and sex; MODEL 3. Adjustment for MODEL 2+HOMA-IR.*P<0.05.

cardiovascular risk factors in healthy adolescents. Previous studies have reported that the omentin-1 level is significantly reduced in obese patients and patients with type 2 diabetes (10). In a cohort of obese women, a low level of omentin-1 was closely related to metabolic syndrome (11). In patients with metabolic syndrome, the omentin-1 level was also negatively associated with the presence and severity of cardiovascular diseases (5). In a study involving young people and children as study subjects, it was observed that the omentin-1 level is negatively correlated with waist circumference and BMI (12). Consistent with the previous study, we also found that the omentin-1 level was significantly negatively correlated with waist circumference and BMI. Additionally, the aggregation of cardiovascular risk factors which was investigated in our study reflects the risk status of the study subjects more comprehensively than individual factors. Using the aggregation of cardiovascular risk factors as an indicator for cardiovascular diseases risk to evaluate the applicable potential of the omentin-1 level has not been previously reported. Our study showed that after controlling for age, sex, and the insulin resistance index, each rise in units -of the omentin-1 level predicted a 1.3% decrease in risk for the aggregation of cardiovascular risk factors.

Some scholars even found that omentum-1 was negatively correlated with FPG, blood pressure, triglycerides, and low-density lipoprotein-cholesterol in some case-control studies and baseline of prospective studies (13, 14). But our study did not demonstrate a significant correlation, and it was consistent with previous population(15) and prospective studies(16). Our study was a population study in which the majority of subjects were healthy. The sample size of our study was also larger than those case-control studies. Therefore, the results we obtained may be different from those obtained from most case-control studies. The above results suggested that the association between the omentin-1 level and blood pressure, blood glucose and lipid levels would gradually become apparent with the development of disease.

Our study showed that obesity was the risk component most closely associated with a low level of omentin-1. It is generally believed that omentin-1 is involved in obesity. The omentin-1 level is generally low in obese individuals, particularly those with metabolic syndrome (14), and is negatively correlated with BMI, waist circumference (14, 17), and the waist-to-hip ratio (18). It was also shown that the omentin-1 level was significantly decreased in obese children, and among all study subjects the omentin-1 level was negatively correlated with BMI (12). After lifestyle intervention and weight loss, the omentin-1 level increased (14). These results are in agreement with our findings.

The mechanism by which omentin-1 affects the development of cardiovascular diseases is not well understood. Omentin-1 may reduce some key cardiovascular diseases associated processes, such as chronic inflammatory responses, endothelial damage, arterial calcification, and oxidative stress. A study showed that omentin-1 inhibits tumor necrosis factor-alpha (TNF-α)-induced vascular adhesion factor expression by inhibiting P38 and JNK phosphorylation in smooth muscle cells (19). In addition, omentin-1 has an anti-inflammatory role by inhibiting TNF-α-induced cyclooxygenase-2 (COX-2) expression in endothelial cells (20). By interfering with the ERK/NF-KB signaling pathway, omentin-1 also inhibits the expression of ICAM-1, VCAM-1, and adhesion of monocytes to TNF-α, and activates endothelial cells (21). By activating the Akt signaling pathway, omentin-1 regulates the synthesis of nitric oxide and affects endothelial cell function, which is a crucial step in the pathogenesis of arteriosclerosis (22). By inhibiting the JNK signaling pathway, omentin-1 suppresses the expression of COX-2 induced by TNF-α, suggesting that omentin-1 can prevent the progression of arteriosclerosis by regulating vascular endothelial inflammation (20). In addition, adenovirus-mediated overexpression of omentin-1 reduced arterial calcification via the PI3K-Akt signaling pathway (23). What's more, omentin-1 released the cardiotoxic effects of drugs by inhibiting oxidative stress in mitochondria (24).

The novelty of our study was determining the effect of omentin-1 on the aggregation of cardiovascular risk factors. Moreover, our study was conducted in healthy adolescents instead of adults; data involving adolescents are limited in previous studies. There were some limitations in our study. First, the scope of cardiovascular risk factors is rather extensive, and we only chose several relatively important factors to study. Therefore, the results may not be comprehensive. Second, as a cross-sectional study, our study only revealed the correlation between the serum omentin-1 level and the aggregation of cardiovascular risk factors, as well as individual components. Thus, the causal relationship between factors warrants further studies. Finally, the detailed mechanisms underlying omentin-1 function on obesity and cardiovascular risk factors

were not addressed in our study.

In conclusion, our study showed serum omentin-1 level was negatively correlated with the aggregation of cardiovascular risk factors in healthy adolescents. The most closely correlated factor was obesity, including general obesity based on Body Mass Index and central obesity based on waist circumference.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Wilson PW. Established risk factors and coronary artery disease: the Framingham Study. American Journal of Hypertension. 1994;7(7 Pt 2):7S-12S.
2. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents; National Heart, Lung, and Blood Institute. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics.2011;128 Suppl 5:S213-256.
3. Herder C, Kannenberg JM, Niersmann C, Huth C, Carstensen-Kirberg M, Wittenbecher C, Schulze M, Bluher M, Rathmann W, Peters A, Roden M, Meisinger C, Thorand B. Independent and opposite associations of serum levels of omentin-1 and adiponectin with increases of glycaemia and incident type 2 diabetes in an older population: KORA F4/FF4 study. European journal of endocrinology. 2017;177(4):277-286.
4. Franz M, Polterauer M, Springer S, Kuessel L, Haslinger P, Worda C, Worda K. Maternal and neonatal omentin-1 levels in gestational diabetes. Archives of gynecology and obstetrics. 2018;297(4):885-889.
5. Shang FJ, Wang JP, Liu XT, Zheng QS, Xue YS, Wang B, Zhao LY. Serum omentin-1 levels are inversely associated with the presence and severity of coronary artery disease in patients with metabolic syndrome. Biomarkers: biochemical indicators of exposure, response, and susceptibility to chemicals. 2011;16(8):657-662.
6. Onur I, Oz F, Yildiz S, Oflaz H, Sigirci S, Elitok A, Pilten S, Karaayvaz EB, Cizgici AY, Kaya MG, Onur ST, Sahin I, Dinckal HM. Serum omentin 1 level is associated with coronary artery disease and its severity in postmenopausal women. Angiology. 2014;65(10):896-900.
7. Pourbehi MR, Zahedi T, Darabi H, Ostovar A, Assadi M, Nabipour I. Omentin-1 and Nonfatal Ischemic Heart Disease in Postmenopausal Women: A Population-Based Study. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2016;22(7):780-785.
8. Zimmet P, Alberti G, Kaufman F, Tajima N, Silink M, Arslanian S, Wong G, Bennett P, Shaw J, Caprio S, International Diabetes Federation Task Force on E, Prevention of D. The metabolic syndrome in children and adolescents. Lancet. 2007;369(9579):2059-2061.
9. Zhou JY, Chan L, Zhou SW. Omentin: linking metabolic syndrome and cardiovascular disease. Current vascular pharmacology. 2014;12(1):136-143.
10. Yoo HJ, Hwang SY, Hong HC, Choi HY, Yang SJ, Seo JA, Kim SG, Kim NH, Choi KM, Choi DS, Baik SH. Association of circulating omentin-1 level with arterial stiffness and carotid plaque in type 2 diabetes. Cardiovascular Diabetology 2011; 10(1):103.
11. Auguet T, Quintero Y, Riesco D, Morancho B, Terra X, Crescenti A, Broch M, Aguilar C, Olona M, Porras JA, Hernandez M, Sabench F, del Castillo D, Richart C. New adipokines vaspin and omentin. Circulating levels and gene expression in adipose tissue from morbidly obese women. BMC medical genetics. 2011;12: 60.
12. Zengi S, Zengi O, Kirankaya A, Kucuk SH, Kutanis EE, Yigit O. Serum omentin-1 levels in obese children. Journal of pediatric endocrinology & metabolism. 2019;32(3):247-251.
13. Senolt L, Polanska M, Filkova M, Cerezo LA, Pavelka K, Gay S, Haluzik M, Vencovsky J. Vaspin and omentin: new adipokines differentially regulated at the site of inflammation in rheumatoid arthritis. Annals of the rheumatic diseases. 2010;69(7):1410-1411.
14. Zhang M, Tan X, Yin C, Wang L, Tie Y, Xiao Y. Serum levels of omentin-1 are increased after weight loss and are particularly associated with increases in obese children with metabolic syndrome. Acta paediatrica. 2017;106(11):1851-1856.
15. Onat A, Ademoglu E, Karadeniz Y, Can G, Uzun AO, Simsek B, Kaya A. Population-based serum omentin-1 levels: paradoxical association with cardiometabolic disorders primarily in men. Biomarkers in medicine. 2018;12(2):141-149.
16. Saely CH, Leiherer A, Muendlein A, Vonbank A, Rein P, Geiger K, Malin C, Drexel H. High plasma omentin predicts cardiovascular events independently from the presence and extent of angiographically determined atherosclerosis. Atherosclerosis. 2016;244: 38-43.
17. de Souza Batista CM, Yang RZ, Lee MJ, Glynn NM, Yu DZ, Pray J, Ndubuizu K, Patil S, Schwartz A, Kligman M, Fried SK, Gong DW, Shuldiner AR, Pollin TI, McLenithan JC. Omentin plasma levels and gene expression are decreased in obesity. Diabetes. 2007;56(6):1655-1661.
18. Tan BK, Adya R, Farhatullah S, Chen J, Lehnert H, Randeva HS. Metformin treatment may increase omentin-1 levels in women with polycystic ovary syndrome. Diabetes. 2010;59(12):3023-3031.
19. Kazama K, Usui T, Okada M, Hara Y, Yamawaki H. Omentin plays an anti-inflammatory role through inhibition of TNF-alpha-induced superoxide production in vascular smooth muscle cells. European journal of pharmacology. 2012;686(1-3):116-123.
20. Yamawaki H, Kuramoto J, Kameshima S, Usui T, Okada M, Hara Y. Omentin, a novel adipocytokine inhibits TNF-induced vascular inflammation in human endothelial cells. Biochemical and biophysical research communications. 2011;408(2):339-343.
21. Zhong X, Li X, Liu F, Tan H, Shang D. Omentin inhibits TNF-alpha-induced expression of adhesion molecules in endothelial cells via ERK/NF-kappaB pathway. Biochemical and biophysical research communications. 2012;425(2):401-406.
22. Maruyama S, Shibata R, Kikuchi R, Izumiya Y, Rokutanda T, Araki S, Kataoka Y, Ohashi K, Daida H, Kihara S, Ogawa H, Murohara T, Ouchi N. Fat-derived factor omentin stimulates endothelial cell function and ischemia-induced revascularization via endothelial nitric oxide synthase-dependent mechanism. The Journal of biological chemistry. 2012;287(1):408-417.
23. Xie H, Xie PL, Wu XP, Chen SM, Zhou HD, Yuan LQ, Sheng ZF, Tang SY, Luo XH, Liao EY. Omentin-1 attenuates arterial calcification and bone loss in osteoprotegerin-deficient mice by inhibition of RANKL expression. Cardiovascular research. 2011;92(2):296-306.
24. Lago F, Dieguez C, Gomez-Reino J, Gualillo O. Adipokines as emerging mediators of immune response and inflammation. Nature clinical practice Rheumatology. 2007;3(12):716-724.