Original article

Association of the waist-hip ratio with plasma adiponectin related to coronary artery disease

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Abstract

Objective: By enrolling a prospective study of 82 patients that underwent non-urgent coronary angiography for coronary artery disease (CAD), it is aimed to investigate the correlation between adiponectin and waist-hip-ratio with severity of CAD. ***Materials and methods*:** The results of the angiography, divided the patients into two groups, patients admitted with a diagnosis of CAD and non-CAD. In the conducted hospital based research, two groups were involved: the study group with documented angiographically CAD and control group without angiographic evidence of CAD. Some of the baseline adiponectin levels in stored serum samples of all patients, anthropometric and biochemical risk factors were assessed in both groups. ***Result and discussion*:** As the result, we have seen the presence of CAD that was associated with current smoking, male gender, waist–hip ratio (WHR).While, no significant difference between median adiponectin levels at baseline were observed between cases and controls. ***Conclusion*:** There is a significant positive correlation between waist - hip ratio and presence of severity of coronary artery disease.

Keywords: adiponectin, waist - hip ratio, coronary artery disease,

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Introduction

More than two decades have passed since researchers[1,2] have discovered a 247-amino acid peptide known as Adiponectin (ARCP 30, AdipoQ, apM1 or GBP28), secreted by adipose tissue. In the total plasma protein, the amount of the adiponectin accounted for 0.01% while the concentration of adiponectin circulating in plasma is very high (2 to 20 μg/ml)[3]. Some populations have bigger levels of adiponectin such in the Japanese population, were it is about 5 to 10 μg/ml[4] and in some other populations such as in Indo-Asians when compared with Caucasians (median 3.3 vs. 4.9 μg/ml)[5] is lower. The adiponectin has gained interest especially since it is related to insulin sensitivity, atherosclerosis and inflammation[6] and that high adiponectin concentration is an independent predictor of mortality in chronic heart failure patients that are at high risk for cardiovascular events[7-11]. It is also interesting to mention that women have about 40% higher circulating levels of adiponectin than men[3].

One proven independent risk factor for CAD in both genders is obesity. It is a growing health problem in most developed and some developing countries[12-14]. Some of the primary methods to determine the obesity were body weight, body mass index (BMI), waist circumference (WC) and WHR. According to some studies it is presented that the central obesity (determined by WC and WHR) is more relevant in CAD risk compared to general obesity (determined by BMI)[15-17]. In other cases, waist circumference is shown to have a better correlation with abdominal fat localization[18-21].

Authors in[22] explain that adiponectin protects against the development of disease and once the disease is established, adiponectin concentrations are elevated

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as a counter-regulatory response to protect against further inflammation and atherosclerosis. Other authors in[23] suggest that in order to find positive correlation between adiponectin and culprit lesion necrotic core(NC) content is consistent with the hypothesis that in advanced CAD, serum adiponectin levels are elevated in a counter-regulatory response. Another paradoxical relation stating that high serum adiponectin levels, instead of being protective, have been shown to be associated with increased mortality and adverse event rates is further supported by study that included patients undergoing PCI for symptomatic CAD[24]. Some of the studies have demonstrated beneficial effects in relations between heart failure and high plasma adiponectin and some other have showed a potential association between heart failure and high plasma adiponectin. Elevated plasma levels of adiponectin among patients with heart failure can be a reflection of accompanying renal dysfunction or "adiponectin resistance" including impaired adiponectin signal transduction in myocardium. Furthermore, several statins are also efective for elevating plasma adiponectin[25,26].

Methodology

In the following we will describe the methodology of the study, including the subject, measurements and the statistics.

Subject of the study

Before initiating the study, it was approved by the Ethical Committee of the Faculty of Medicine, in the University of Prishtina, in accordance with the Declaration of Helsinki Guidelines. In line with that, a written consent was obtained from all the participants of the study. The prospective study consisted of 82 patients who underwent coronary angiography for suspected or known coronary atherosclerosis. They had to present in a stable clinical condition without major concomitant non-cardiovascular disease at the University Clinical Center of Kosovo. Patients with acute coronary syndrome, valvular heart disease, elevated serum troponin, severe heart failure, chronic renal failure and chronic inflammatory disease were excluded from study population.

Coronary angiography

The definition of the coronary angiography in the case of single vessel involvementwas more than 50% luminal stenosis identified in a minimum of two views. On the other hand, two experienced observers have scored the angiograms. They were not aware of the diagnosis.According to the Gensini[27] the narrowing of the lumen of coronary artery has a score. That score is 1 1-25% narrowing, 2 for 26-50% narrowing, 4 for 51-75%, 8 for 76-90%, 16 for 91-99% and 32 for a completely occluded artery. After the determination of the score, we multiply it by a factor of the lesion location. For example, 1.5 is the factor for a mid left anterior descending artery (LAD) lesion, 1 for distal LAD, 2.5 for proximal LAD and 5 for left main stem. Gensini score was expressed as the sum of the scores for all three coronary arteries to evaluate the entire extent of coronary artery disease[27].

Measurements

Before measuring the patients, their upper clothes was removed, as well as shoes and the examination dress was worn. In order to have the exact measurements, we have performed each measurement twice and the average was considered for the analysis. We used nearest 0.1 unit of the measurement as for height and weight. In the other hand, body mass index (BMI) and waist height ratio (WHtR) were expressed in the corresponding units, weight (kg) divided by the square of height (m^2) and division of weight circumference by their height. As the above mentioned, as well the waist circumference (WC), were categorized according to the World Health Organization (WHO) criteria[28]. Other measurements included WHR. In the WHR, the waist is measured between the lowest rib and iliac crest, and the hip circumference is taken at the widest area of the hips at the greatest protuberance of the buttocks. After that, we simply divided the waist measurement by the hip measurement. For the decisive benchmark of metabolic syndrome, the definition of the WHO is the ratio of >9.0 in men and >8.5 in women.

In the other hand the laboratory measurements such as blood samples were taken in the morning after night fast and were stored immediately at -70 C after centrifugation until being assayed. The serum of adiponectin concentrations were determinedby ELISA. It is understood that the technicians had no information on the patient characteristics.

Statistics

Using the Chi squared test we have evaluated the binary data. The cut p value of 0.1 was used as a criterion to identify the variables which need to be included in the Binary Logistic Regression Models. Using the t-test we have evaluated the continues variables, which are presented in the tables with the standard deviation (SD). The pearson correlation was used to analyze the relation of adiponectin with other variables. It should be mentioned that regaldless of the statistical significance of the adiponectin, it was involved in the model since it represents the focusing variable. Other variables included diastolic blood

pressure, WHR, gender and if the subject smokes or not. Everything was done and analyzed by the help of the statistics software SPSS.

Results

As mentioned before, our study involved eighty-two patients. From them, half comprised the study subject group CAD and other half the control subject non-CAD. The mean age of the study group was 66.76+9.12, while of the control group it was 64.80 ± 8.30.

In the Table 1 we have laid out the demographic and clinical characteristics of all participants. We see from Table 1 that while as mentioned CAD patients were older, they had also a tendency to be of male gender and a smoker. So from 41 patients in CAD group, 29 of them were male, while in non CAD group the number of male patients was 17. Besides that, the smokers consisted of 27 of patients in CAD group and only 13 in non-CAD group.

Table 1. Demographic and clinical characteristics of non-CAD and CAD groups. BMI:basal metabolic index,WC, WHtR, WHR.

Variables	Group I Non CAD (n=41)			Group II CAD (n=41)			P value*
Age (mean ± SD)	64.80	±	8.30	66.76	±	9.12	0.31
BMI (kg/m2) (mean ± SD)	28.76	±	4.68	28.17	±	3.32	0.51
WC (cm)	95.13	±	11,52	96.97	±	8.63	0.44
WHtR (mean ± SD)	0.57	±	0.08	1.76	±	7.56	0.32
WHR (mean ± SD)	0.88	±	0.07	0.93	±	0.06	0.000
Sex (M), n (%)	17		41.5%	29		70.7%	0.008
Smokers, n (%)	13		31.7%	27		65.9%	0.002

Other than that, fifteen patients (18.2%) had normal BMI (mean 23.22±1.4), 37 patients (45%) were overweight, 30 patients (43.4%) were obese, in all patients. From that, the BMI in case group had mean of 28.17± 3.32, while in control group the mean was 28.76±4.68. Also in the case group, WC was 96.97±8.63, in regards to the control group that had 95.13±11.52. Continuing, from Table 1, we see that WHtR in case patients is 1.76 ±7.56 and in control is 0.57±0.08, while the WHR is significant between case and control (0.93±0.06) versus (0.88±0.07) (p-value: 0.0001).

In the Table 2, we have presented some other measurements such as for example the Gensini score between the groups. CAD patients had higher mean Gensini scores than non-CAD patients (53.16 ± 33.46 versus 1.21 ±5.66, P<0.0001), but there was no statistically significant difference detected between CAD and non CAD for plasma adiponectin levels. In other hand the cholesterol in the populations averaged from 3.58 ± 1.07 mmol/l in cases and 3.59 ± 1.19 mmol/l in the control groups. Also, worth mentioning the Plasma HDL-cholesterol levels which were 0.93 ± 0.24mmol/l and 1.02±0.26mmol/l, respectively.

Discussion and conclusion

In this study, we have presented the association of the waist-hip ratio with plasma adiponectin related to coronary artery disease. The study suggests that there is a strong association between adiponectin and coronary artery disease. These findings provide further evidence for an “adiponectin paradox” in which higher levels of adiponectin may be secreted as a protective or a compensatory response to worsening cardiovascular disease.

In the study performed by[29], authors have concluded that there were no significant differences in plasma concentrations of adiponectin between patients with stable angina pectoris (SAP) and control patients, which has had similar findings to our study where plasma concentrations of adiponectin between patients with SAP and control group (3.45 v 3.49

Table 2. Biochemical characteristics of the two groups. CAD, AST: Aspartate aminotransferase, CRP:C reactive protein, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol.

Variables	Group I Non CAD (n=41)			Group II CAD (n=41)			P value*
	mean	±	SD	mean	±	SD	
Adiponectin (µg/ml)	3.49	±	1.93	3.45	±	2.75	0.94
AST (U/L)	24.06	±	6.69	23.04	±	8.49	0.55
CRP (mg/l)	7.30	±	25.33	5.28	±	11.25	0.64
Urea(mmol/L)	5.02	±	1.45	5.41	±	2.45	0.38
Creatinine(µmol/L)	60.44	±	16.74	66.71	±	31.99	0.27
Total Cholesterol(mmol/L)	3.58	±	1.07	3.59	±	1.19	0.97
Triglyceride(mmol/L)	1.15	±	0.75	1.05	±	0.47	0.47
HDL-C(mmol/L)	1.02	±	0.26	0.93	±	0.24	0.13
LDL-C(mmol/L)	2.04	±	0.90	2.26	±	1.00	0.30
10^{-12} Erythrocyte/L	4.39	±	0.52	4.37	±	0.45	0.86
10^{-9}Leukocyte/L	7.56	±	2.30	7.43	±	2.11	0.79
Hematocrit (%)	38.76	±	6.39	39.34	±	4.79	0.64
Hemoglobin g/L	132.68	±	15.76	132.49	±	16.38	0.96
10^{-9} Platelet/L	263.37	±	75.43	257.37	±	61.15	0.69
Glucose(mmol/L)	6.40	±	2.62	6.67	±	2.52	0.65
Gensini score	1.21	±	5.66	53.16	±	33.46	0.000

Baseline adiponectin concentrations correlated significantly in terms of the lipid parameters, positively with HDL cholesterol concentrations (r= 0.327, P=0.028) as presented in Figure 1 and serum triglyceride concentrations were correlated negatively (r=-0.513, P<0.001) as presented in Figure 2.

Significant differences were seen in Binary Logistic Regression models for CAD analysis for adiponectin, WHR, DBP, male gender and for smoker. WHR (OR 14; 95% CI 0.94-207.60; p=0.06), smoking (OR 4.15; 95% CI 1.65-10.44; p=0.001), male patients (OR 3.41, 95% CI 1.37-8.52; p=0.01), all presented in Table 3.

Table 3. Binary Logistic Regression Models for CAD (Unadjusted and Adjusted),WHR, LVEF.

	Unadjusted Odds Ratio (95% CI)	P value		Adjusted Odds Ratio (95% CI)	P value
Adiponectin < 2 µg/mL	1.28 (0.48-3.42)	0.62		1.06 (0.29-3.84)	0.93
WHR < 0.8	1.00 (Reference)	0.13		1.00 (Reference)	0.67
0.8 - 0.99	3.77 (0.40-35.51)	0.25		3.42 (0.23-50.38)	0.37
≥ 1	14 (0.94-207.60)	0.06		3.03 (0.13-71.20)	0.49
Sex (Male)	3.41 (1.37-8.52)	0.01		2.9 (0.81-10.35)	0.10
Smoker	4.15 (1.65-10.44)	0.00		3.51 (0.98-12.52)	0.05

µg/ml) had no significant differences.It should be noted that patients in our SAP group had already been receiving some treatment with antianginal and antiatherosclerotic drugs.

Furthermore, in[29], researchers found an important clinical finding, showing that plasma concentrations of adiponectin were considerably increased in older and female patients with CAD. Their suggestion was that unstable plaque may stabilize as the patient grows older or it is the case due to the accumulation of adiponectin in atherosclerotic vascular walls. That could suppress its elimination from plasma, resulting

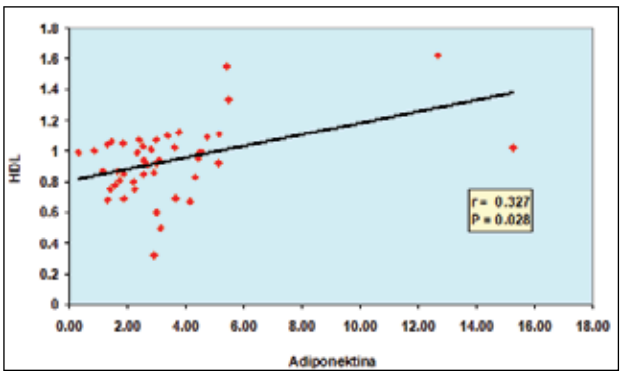

Fig 1. Correlation between Adiponectin and HDL

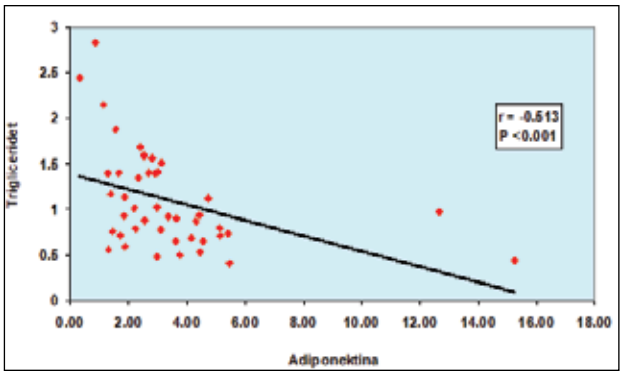

Fig 2. Correlation between adiponectin and triglyceride

in an increase of adiponectin plasma concentrations in older patients with CAD. Other researchers[30] as well back up the claim that age has an effect on serum adiponectin levels and there is a relation between the two, even though that could not be verified by our study. But a relation that was similar to our study as well involved several other research studies before. One of them suggest that including both individuals with and without cardiovascular disease, higher adiponectin has protecting role in those without cardiovascular disease and predictive of worse outcomes in those with existing disease[31]. Furthermore, in another research study it was suggested that normal and even higher serum adiponectin levels could prevent the development of cardiovascular diseases and complications in healthy individuals[32]. While the other study shows that male patients with hypoadiponectinemia (<4.0 µg/ml) had a two-fold increase in CAD prevalence, independent of well-known CAD risk factors[34], which as well Similar to our study in male gender withhypoadiponectinemia (<2.0 µg/ml) presented in Table 3.

According to the results, we can conclude that there is a positive association between waist - hip ratio and severity of coronary artery disease. For other more reliable investigations, we would need to increase the sample size. Moreover, they should stimulate for other studies either epidemiological either experimental ones to further evaluate the role of adiponectin in CAD.

Conflic of interest: None declared

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