

# Different measurements of the obesity, adiponectin and coronary heart disease: a single-center study from Isfahan

Zahra Pourmoghaddas<sup>1</sup>, Masoumeh Sadeghi<sup>2</sup>, Ali Hekmatnia<sup>3</sup>, Hamid Sanei<sup>4</sup>, Babak Tavakoli<sup>5</sup>, Hamidreza Roohafza<sup>6</sup>, Nizal Sarrafzadegan<sup>7</sup>

<sup>1</sup> Assistant Researcher, Cardiovascular Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran. <sup>2</sup> Associate Professor, Cardiac Rehabilitation Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical sciences, Isfahan, Iran. <sup>3</sup> Assistant Professor, Department of Radiology, Isfahan University of Medical Sciences, Isfahan, Iran. <sup>4</sup> Assistant Professor, Department of Cardiology, Isfahan University of Medical sciences, Isfahan, Iran. <sup>5</sup> Resident, Department of Radiology, Student Research Committee, Isfahan University of Medical sciences, Isfahan, Iran. <sup>6</sup> Psychiatrist, Cardiovascular Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran. <sup>7</sup> Professor, Cardiovascular Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical sciences, Isfahan, Iran.

**BACKGROUND:** Adipose tissue as an endocrine organ secretes adiponectin that is a cardiovascular atherosclerosis-modulating factor. However, some studies showed that adiponectin reduces obesity. In the present study, adiponectin association with body mass index (BMI), waist circumference (WC), visceral adipose tissue (VAT) and subcutaneous visceral tissue (SAT) as different measurements of obesity were evaluated in patients with coronary heart disease (CHD). **METHODS:** Sixty-eight patients with CHD were chosen using simple random sampling. Body weight, height, WC and blood pressure were measured. Fasting blood samples were taken to assess fasting blood sugar, total cholesterol, triglyceride, low and high-density lipoproteins cholesterol. Patients underwent an abdominal computerized scan (CTS) to detect VAT and SAT. Linear regression test used to assess the relation of different measurements of the obesity with adiponectin adjusting for age, sex, hypertension, dyslipidemia, and diabetes mellitus. **RESULTS:** The mean age of the study population was  $50.5 \pm 7.0$ . Females were 67.6% of study population. Multivariate analyses showed the inverse association of waist-to-height ratio (WHtR) ( $\beta = -0.25$ ,  $p = 0.03$ ), WC ( $\beta = -0.24$ ,  $p = 0.24$ ) and visceral fat ( $\beta = -0.32$ ,  $p = 0.01$ ) with adiponectin. **CONCLUSIONS:** WC and WHtR are simple proxy measures of obesity that better showed adverse metabolic effect of visceral fat in patients with CHD.

**KEYWORDS:** Adiponectin, Coronary Heart Disease, Obesity, Intra-abdominal Fat, Waist Circumference, Waist-to-height Ratio

## BACKGROUND

Coronary atherosclerosis causes coronary heart disease (CHD) which known as one of the global cause of myocardial infarction and mortality.<sup>[1]</sup> Many metabolic risk factors such as dyslipidemia, impaired glucose level, and obesity are known as the underlying cause of the atherosclerosis.<sup>[2]</sup> Obesity, as an excess body fat, is traditionally measured by body mass index (BMI). This measurement indicated the overall adiposity.<sup>[3]</sup> Waist circumference and waist-to-height ratio (WHtR) are another indicators of obesity which evaluate the abdominal visceral and subcutaneous adipose tissue.<sup>[4]</sup> Many studies showed different adverse metabolic effects of different kinds of fat accumulation, i.e. evidences suggesting visceral adipose tissue (VAT) have stronger association with CHD risk factors compared to subcutaneous adipose tissue (SAT).<sup>[5]</sup>

Adipose tissue, as an active endocrine organ, secretes adipokines which influences many metabolic

processes.<sup>[6-8]</sup> Adiponectin is one of the adipokines which plays an anti-atherogenic role. <sup>[9,10]</sup> Recent studies showed the effects of these proteins in cardiovascular atherosclerosis and represented the relation of the adiponectin to insulin resistance, glucose and lipid metabolism which are causes of this atherosclerosis.<sup>[11-16]</sup>

Studies which evaluated the adiponectin concentration relation to different types of adiposity showed the controversial findings according to different types<sup>[3,17]</sup> and measurements of the adipose tissue. For instance, Nakamura et al.<sup>[17]</sup> showed the inverse correlation of adiponectin with VAT and direct association with SAT while Staiger et al.<sup>[18]</sup> in their study found that adiponectin concentration did not have any relation with waist circumference. Considering the important role of the adipokines in CHD and some controversy about this concept, this study was designed to investigate the association of adiponectin and different types and measurements of the obesity in Iranian patients with CHD.

**Address for correspondence:** Masoumeh Sadeghi, Associate Professor, Cardiac Rehabilitation Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical sciences, Isfahan, Iran. E-mail: sadeghimasoumeh@gmail.com

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## METHODS

### Study population

This cross-sectional study conducted on 68 CHD positive patients who were 35-75 years old in Isfahan Cardiovascular Research Center from 2007 to 2010. The participants were selected through convenient sampling method among patients who were referred for coronary angiography to Chamran Hospital, a university referral hospital. If patients signed informed consent form, demographic, past medical and drug history data of them were collected.

Patients who referred for coronary angiography with diagnosis of stable angina and had at least one significant major epicardial coronary artery diseases were included. Patients with history of chronic renal failure, chronic or acute hepatitis, congenital and valvular heart disease and also those with the history of myocardial infarction, heart failure, participating in any weight reducing programs (including diet) and pregnant women were excluded from the study. The protocol of this study was reviewed and approved by Ethical Committee of Isfahan University of Medical Sciences (Research project Number: 86131).

### Anthropometrics and laboratory data Measurements

A trained nurse measured the patients' weight and height, while they wore light indoor clothing without shoes. Waist circumference (WC) measured by tape at 1cm above their navel horizontally.<sup>[19]</sup> A physician examined patients' blood pressure (BP), two times with 5 minutes intervals. Mean of these two measurements was used for analyzing the data.

Fasting blood sample of the patients were used in order to measure cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C) and Adiponectin level. Enzymatic method was used for detecting level of the TC, TG, HDL-C, and LDL-C. Adiponectin level was assessed by EII-SA method (BioVendor Research and Diagnostic Product Kits).

### Determination of the coronary artery involvement and body composition

Coronary angiography conducted by JUDKINS method.<sup>[20]</sup> Angiography films were separately reviewed by two cardiologists and if they agreed about more than 50% stenosis of at least one vessel, subjects were considered as patients with CHD.

After 3 days, patient underwent CT scan using a Philips Medical Systems CT (TOMO SCAN AV). A scout view was taken in addition to four cuts just distal to the L4 inferior end-plate, tangential to it, with a collimation of 5mm and no overlap. Scan parameters included kV: 120, mA: 250, slice thickness: 5mm, field of view: 500mm, window width: 500, window center: 40. Images were transfused to the DICOM (Digital Imaging and Communications in Medicine) workstation and analyzed with freeware Image J Software version 1.36. Adipose tissue area was measured as mm<sup>2</sup> in different compartments. The measurements were performed in four images for each patient and the average (means) were used for the analysis.

### Statistical Analysis

SPSS software (version 15, Chicago, IL, USA) was used for statistical analysis. To examine the association between different measurements of the obesity and adiponectin, Pearson correlation test was used as well as age and sex adjusted multiple linear regression tests. In addition, the same test was used for adjusting the association for hypertension (a history of high blood pressure or using any hypertensive drugs, systolic BP  $\geq$  140 mmHg, diastolic BP  $\geq$  90 mmHg), dyslipidemia (history of dyslipidemia or TC  $\geq$  200 mg/dl, TG  $\geq$  150 mg/dl, LDL-C  $\geq$  100 mg/dl, HDL-C  $\leq$  40 mg/dl in men and  $\leq$  50 mg/dl in women) and diabetes (FBS  $\geq$  126 mg/dl, anti-diabetic drug usage or history of the diabetes mellitus). P-value of equal or less than 0.05 was considered as statistically significant.

## RESULTS

Sixty-eight subjects aged 35-75 years were recruited. Forty-six of the subjects were females (67.6%). Mean age of the study population was  $50.5 \pm 7.0$ . Table 1 shows the basic characteristics of the study population. Pearson correlation test only indicated the negative correlation of WC with adiponectin ( $r = 0.23$ ,  $p = 0.023$ ).

**Table 1. Basic characteristics of the study populations**

	Mean $\pm$ SD
Age (years)	50.5 $\pm$ 7.0
BMI (kg/m <sup>2</sup> )	27.8 $\pm$ 3.8
Waist circumference (cm)	100.4 $\pm$ 9.2
Waist-to-height ratio	0.619 $\pm$ 0.068
Visceral fat (mm <sup>2</sup> )	11538 $\pm$ 5546
Superficial subcutaneous fat (mm <sup>2</sup> )	1111 $\pm$ 6597
Deep subcutaneous fat (mm <sup>2</sup> )	14112 $\pm$ 6163
Total subcutaneous fat (mm <sup>2</sup> )	25230 $\pm$ 11654
Adiponectin (mg/l)	11.3 $\pm$ 9.5

Linear regression test was used in two steps to evaluate the association of adiponectin and different measurements of obesity (Table 2). In, Analyses in step one was age and sex adjusted showing the inverse association of WC ( $\beta = -0.20$ ,  $p = 0.04$ ). Age and sex in addition to hypertension (history of the high blood pressure or using any hypertensive drugs, systolic BP  $\geq 140$  mmHg, diastolic BP  $\geq 90$  mmHg), dyslipidemia (history of dyslipidemia or TC  $\geq 200$  mg/dl, TG  $\geq 150$  mg/dl, LDL-C  $\geq 100$  mg/dl, HDL-C  $\leq 40$  mg/dl in male and  $\leq 50$  mg/dl in female), diabetes mellitus (FBS  $\geq 126$  mg/dl or anti diabetic drug consumption or history of the diabetes mellitus) were used for adjusting in the second step. The results of the second step showed WHtR ( $\beta = -0.25$ ,  $p = 0.03$ ), waist circumference ( $\beta = -0.24$ ,  $p = 0.03$ ) and visceral fat ( $\beta = -0.32$ ,  $p = 0.01$ ) inversely associated with adiponectin.

**Table 2. Association of adiponectin and body fat distributions indicators in coronary heart disease**

	Adiponectin level		
	Unadjusted	Adjusted†	Adjusted‡
BMI (kg/m <sup>2</sup> )	-0.14	-0.15	-0.12
Waist circumference (cm)	-0.23*	-0.20*	-0.24*
Waist-to-height ratio	-0.18	-0.24	-0.25*
Visceral fat (mm <sup>2</sup> )	-0.28	-0.23	-0.31*
Superficial subcutaneous fat (mm <sup>2</sup> )	-0.14	-0.11	-0.11
Deep subcutaneous fat (mm <sup>2</sup> )	-0.17	-0.14	-0.11
Total subcutaneous fat (mm <sup>2</sup> )	-0.18	-0.16	-0.13

Data are expressed by standardized coefficients (beta) obtained from linear regression models.

BMI: Body Mass Index, CHD: Coronary Heart Disease, WC: Waist circumference, VSF: Visceral fat, SSQF: Superficial subcutaneous fat, DSQF: Deep subcutaneous fat, TSQF: Total subcutaneous fat.

\* P-value < 0.05

† Age and sex adjusted

‡ Age and sex, history of high blood pressure or using any hypertensive drugs or SBP  $\geq 140$  mmHg or DBP  $\geq 90$  mmHg, history of dyslipidemia or TC  $\geq 200$  mg/dl or TG  $\geq 150$  mg/dl or LDL-C  $\geq 100$  mg/dl or HDL-C  $\leq 40$  mg/dl in men and  $\leq 50$  mg/dl in women, FBS  $\geq 126$  mg/dl or history of antidiabetic drug consumption or history of the diabetes mellitus

## DISCUSSION

The present study demonstrated adiponectin concentration inverse associated with visceral fat, WC, and WHtR in 68 patients with CHD aged 35-57 years old. The inverse association of adiponectin with WC is in accordance with study of Yang et al.<sup>[21]</sup> and Schober et al.,<sup>[22]</sup> while Staiger et al.<sup>[18]</sup> did not show any association between adiponectin and waist circumference.

Different types of adjusting could be a reason for these various results. We adjusted with age, sex, history of hypertension, dyslipidemia and diabetes mellitus, but Staiger et al. used sex and percentage of the body fat for adjusting. On the other hand, we showed negative association of adiponectin with WHtR; this association may be due to the inverse association of adiponectin with WC.

Multivariate linear regression test, after adjusting for all factors, indicated a significant inverse association of the visceral fat with adiponectin. This result was also found in other studies,<sup>[3,17]</sup> while this association could not be found with different types of subcutaneous adipose tissue in the current study. Various studies such as study of Nakamura et al.<sup>[17]</sup> showed different association of visceral and subcutaneous fat with adiponectin concentration and documented a strong inverse correlation of visceral fat with adiponectin. As mentioned before, the only organ which secretes the adiponectin is the adipose tissue, but inverse association of the adiponectin with visceral and waist circumference suggests a negative feedback on the adiponectin production in visceral fat and our results were in accordance with other studies which suggested that the visceral fat was more active producer of adiponectin than subcutaneous fat.

In spite of the inverse association of the BMI with adiponectin, no significant association was observed between this indicator of overall obesity and adiponectin. This finding was in contrast with study of Milewicz et al.<sup>[23]</sup> that showed this association in menopause woman. Some studies indicated different level of adiponectin in men and women and various ages.<sup>[3]</sup> Our study evaluated adiponectin level in 35-57 males and females; hence, we adjusted our data for sex and age. BMI is the indicator of the overall obesity and contains VAT, SAT and peripheral fat. In many surveys, it was documented that SAT and peripheral fat had positive association with adiponectin concentration.<sup>[17,18]</sup> Thus, BMI is an indicator which includes all of these adipose tissue indicators with different correlations to adiponectin. This may be the reason for absence of association with adiponectin in BMI. In addition, small sample size of our study population might have caused this finding.

In one study by Sanjari and coworkers, adiponectin was negatively associated with metabolic syndrome.<sup>[25]</sup> In other study, obesity and type II diabetes were associated with low serum adiponectin concentration.<sup>[24]</sup>

Adiponectin anti-inflammatory role is demonstrated via decreased level of TNF- $\alpha$  which induced an attachment of macrophage to endothelial cell. On the other hand, other studies showed adiponectin was detectable in catheter-injured vessel wall in animals compared to normal vessel. These two mechanism suggested possible participation of this protein to the pathogenesis of the atherosclerosis.

### Strength and Limitations

Recruiting patients with CHD in both genders with wide range of age was the main strength of the present study. Cross-sectional design of this study that could not indicate causal relations between adiponectin and different measurements of the obesity, small sample size and questionable power of the computerized scan results for detecting visceral and subcutaneous fat due to respiratory movements were the limitations of this study.

## CONCLUSIONS

WC, WHtR and visceral fat are the obesity indicators that had significant inverse association with adiponectin in patients with CHD. This correlation might be due to visceral fat that had a stronger adverse metabolic effect. BMI as an indicator that includes visceral and peripheral obesity, probably could not reflect the association with adiponectin, so WC and WHtR as simply measurable obesity indicators must be considered in patients with CHD.

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