

# Association of apolipoprotein B, apolipoprotein A, and the its ratio with body fat distribution

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**Background:** To evaluate the association of apolipoprotein B (apoB), apolipoprotein A (apoA), and apoB/apoA ratio with the body fat indicators in patients with stable angina pectoris (SA). **Materials and Methods:** One hundred and twenty two participants aged 40-60 years old, with a mean age of  $52.1 \pm 7.2$  years and SA, were recruited for the present study. Body weight, height, and waist circumference (WC) were measured, and waist to height ratio (WHtR) was calculated. After 12 hours of fasting, a blood sample was obtained and serum levels of apoB and apoA were measured and the apoB/apoA ratio was calculated. These patients underwent an abdominal computerized tomography scan (CTS) to assess visceral and subcutaneous adipose tissue (VAT, SAT). Linear regressions were computed to assess the relation of apoB, apoA, and their ratio with various measurements of adiposity (VAT, SAT, WC, and WHtR), with adjustment for age, sex, and  $BMI \geq 25$ ,  $WC \geq 80$  in women and  $WC \geq 90$  in men and  $WHtR \geq 0.59$ . **Results:** From totally 123 patients with SA with a mean age of  $52.1 \pm 7.2$  years, 44.7% male and 55.3% women were entered. Significant positive associations were found between visceral fat area and the apoB/apoA ratio ( $P = 0.02$ ,  $\beta = 0.2$ ), and significant negative correlations were observed between visceral fat area and apoA concentrations ( $P = 0.04$ ,  $\beta = -0.2$ ). **Conclusion:** As abdominal fat accumulation is associated with other risk factors such as apolipoproteins in ischemic patients, then we most focus on control of these factors.

**Key words:** Apolipoprotein A, apolipoprotein B, apolipoprotein B/apolipoprotein A, cardiovascular disease, intra-abdominal fat

## INTRODUCTION

At the beginning of this new decade, considerable research has focused on novel cardiovascular risk factors, among which were apolipoproteins.<sup>[1]</sup> Apolipoprotein B (apoB), which indicates the number of potentially atherogenic lipoprotein particles, and apolipoprotein A (apoA), which associates with anti-atherogenic HDL particles, were two main apolipoproteins which have shown significant associations with coronary artery disease (CAD).<sup>[2]</sup> The predictive value of the apoB/apoA ratio, which is thought to reflect the balance between atherogenic and anti-atherogenic particles, is also well-documented.<sup>[3]</sup>

Traditionally, obesity and higher body mass index (BMI) values have been recognized as CAD risk factors.<sup>[4]</sup> However, the contribution of regional fat distribution is increasingly recognized in the association between obesity and CAD.<sup>[5]</sup> Anthropometric measurements such as waist circumference (WC) and waist to height ratio (WHtR) have been used to measure body fat distribution, but investigators also based their research on imaging techniques such as computerized tomography (CT) assessments of regional fat distribution as visceral and superficial fat.<sup>[6-8]</sup>

The association between regional body fat distribution and CAD risk factors has been widely documented in normal populations.<sup>[9-11]</sup> However, in populations with established CAD, the association of body fat distribution with apolipoproteins is not well-documented. In this study, we examined the association of body fat distribution indicators and apolipoproteins in patients with stable angina pectoris (SA).

## MATERIALS AND METHODS

This cross-sectional study was performed in Isfahan Cardiovascular Research Institute in 2009. One hundred and twenty two patients with documented diagnosis of stable angina who agreed to participate and signed the informed consent form were included in this study. Patients with a history of chronic renal failure, chronic or acute hepatitis, congenital and valvular heart diseases, myocardial infarction, and heart failure were excluded. Patients participating in any weight reduction program (including diet) and pregnant women were also excluded. The ethical Committee of Isfahan University of Medical Sciences reviewed and approved this study.

### Anthropometrics and laboratory data measurements

At the beginning of this study, weight and height of

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the patients were measured when they wear light indoor clothing without shoes. BMI was calculated by dividing weight by the square of height. Horizontal tape measures at the umbilical level (1 cm above the navel) were used to determine waist circumference.<sup>[12]</sup>

Twelve hours fasting blood samples were obtained for measuring total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL-C), low-density lipoprotein (LDL-C), apolipoproteins A and B. Measurement of TC, TG, HDL-C, and LDL-C levels was carried out by the enzymatic method. Immunoturbidimetric method was used to measure the levels of apo A and apo B. Pars Azmoon Kits accredited by Bioactiva Diagnostica (Germany) was used for all the above-mentioned biochemical measures.<sup>[13]</sup>

Each patient underwent an abdominal CT scan using a Philips Medical Systems CT (TOMO SCAN AV). With a collimation of 5 mm and no overlap, a scout view and four cuts tangentially at the distal of the L4 inferior end-plate were taken. Scan parameters were: 120 kV, 250 mA, slice thickness: 5 mm, field of view: 500 mm, window width: 500, window center: 40. Images were transferred to the DICOM (Digital Imaging and Communications in Medicine) workstation and analyzed with freeware ImageJ software version 1.36. Adipose tissue area was measured in mm<sup>2</sup> in the abdominal compartments of interest. For each patient, the measurements were performed on four images, and the averages were used in the analyzes.<sup>[14]</sup>

### Statistical analysis

SPSS software (version 15.0, Chicago, IL, USA) was used for Statistical analyzes. We evaluated the possible correlation between body fat distribution indicators and circulating concentrations of apolipoproteins using Pearson correlation coefficients. To compare the association between body fat distribution indicators and circulating concentrations of apolipoproteins in patients with stable angina, multiple linear regression tests were performed separately. At first, unadjusted data are recorded, then the data were adjusted for age and sex, and then data were analyzed by adjusting for age and sex as well as BMI  $\geq 25$ , WC  $\geq 80$  in women, and WC  $\geq 90$  in men.

## RESULTS

Basic characteristics of the patients are presented in Table 1. From 132 cases, 123 consecutive SA patients with mean age of  $52.12 \pm 7.2$  years entered the study. From nine excluded participants, seven had myocardial infarction and two had heart failure.

Mean levels of apoA, apoB, and apoB/apoA level were, respectively,  $156.3 \pm 25.8$  mg/dL,  $100.8 \pm 26.4$  mg/dL, and  $0.66 \pm 0.19$ .

Correlations between adiposity indicators and apolipoprotein concentrations are shown in Table 2. The apoB/apoA ratio only correlated significantly with visceral fat area ( $P = 0.00$   $r = 0.24$ ). Statistical adjustment for age and sex revealed a negative association between apoA and visceral fat area ( $P = 0.03$ ,  $\beta = -0.19$ ) and WC ( $P = 0.00$ ,  $\beta = -0.19$ ) as well as a positive association between visceral fat area and the apoB/apoA ratio ( $P = 0.00$ ,  $\beta = 0.27$ ).

Adjusted data for BMI, WC, and WHtR were presented in Table 2; these data documented positive ( $P = 0.02$ ,  $\beta = 0.26$ ) and negative ( $P = 0.04$ ,  $\beta = -0.22$ ) association of apoB/apoA ratio and apoA with VAT, respectively. As it is shown in Table 2, there were no significant associations between circulating concentrations of apoA, apoB or the apoB/apoA ratio and BMI, total subcutaneous (SC) fat, superficial SC fat, and deep SC fat.

## DISCUSSION

In the present study, we evaluated the association of apoA, apoB, and apoB/apoA ratio as non-traditional CAD risk factors and body fat distribution indicators in patients with SA and found that the apoB/apoA ratio was a significant positive correlate of visceral fat area. We also observed significant negative associations of apoA with visceral fat area and WC.

Many studies have shown that visceral fat area is a strong predictor of metabolic risk factors such as hypertriglyceridemia and low high-density lipoproteins cholesterol (HDL-C). On the other hand, the associations of subcutaneous fat tissue indicators with these metabolic

**Table 1: Basic characteristics of study population (n=123)**

	Mean $\pm$ SD	Minimum	Maximum
Age (years)	52.12 $\pm$ 7.2	33.00	70.00
BMI (kg/m <sup>2</sup> )	28.39 $\pm$ 4.5	18.00	42.60
WC (cm)	101.29 $\pm$ 9.7	76	130
WHtR	0.63 $\pm$ 0.07	0.44	0.85
Visceral fat (mm <sup>2</sup> )	11488.14 $\pm$ 5696.79	1559.11	27644.01
Deep SC fat (mm <sup>2</sup> )	14694.74 $\pm$ 6639.11	480.67	35559.27
Superficial SC fat (mm <sup>2</sup> )	12636.24 $\pm$ 7320.11	621.53	36801.45
Total SC fat (mm <sup>2</sup> )	27330.98 $\pm$ 12565.22	1102.20	55140.99
ApoA (mg/dL)	156.25 $\pm$ 25.76	112.0	227
ApoB (mg/dL)	100.78 $\pm$ 26.38	51.0	192.0
ApoB/apoA (mg/dL)	0.66 $\pm$ 0.19	0.34	1.27
Total cholesterol (mg/dL)	190.78 $\pm$ 42.55	99.00	322
LDL-C (mg/dL)	109.07 $\pm$ 29.97	53.00	201.00
HDL-C (mg/dL)	34.07 $\pm$ 11.50	12.00	78.00
Glucose level	123.07 $\pm$ 50.22	58.00	401.00

Apo=Apolipoprotein; BMI=Body mass index; WC=Waist circumference; WHtR=Waist to height ratio; SC=Subcutaneous; LDL-C=Low-density lipoprotein; HDL-C=High-density lipoprotein

**Table 2: Association of apolipoprotein B, apolipoprotein A, and apolipoprotein B/apolipoprotein A ratio and body fat indicators**

	Apo B (mg/dl)			Apo A (mg/dl)			Apo B/apo A		
	Crude	Adjusted <sup>†</sup>	Adjusted <sup>††</sup>	Crude	Adjusted <sup>†</sup>	Adjusted <sup>††</sup>	Crude	Adjusted <sup>†</sup>	Adjusted <sup>††</sup>
BMI	0.07	0.14	-	0.62	-0.06	-	0.14	0.18	-
Waist	0.56	0.19	-	0.41	-0.19*	-	0.13	0.13	-
Visceral fat	0.03	0.15	0.14	0.41	-0.19*	-0.22*	0.24*	0.27*	0.26*
Total SC fat	0.06	0.15	0.08	0.33	-0.14	-0.19	0.06	0.26	0.22
Superficial SC fat	0.12	0.14	0.31	0.02	-0.02	0.00	0.03	0.00	0.05
Deep SC fat	0.31	0.05	0.00	0.49	-0.7	-0.08	0.08	0.13	0.05

\* $P \leq 0.05$ , Adjusted<sup>†</sup>=Age and sex adjusted; Adjusted<sup>††</sup>=Age and sex plus BMI $\geq 25$ ; WC $\geq 80$  in women and WC $\geq 90$  in men and WHtR;  $\geq 0.59$  were adjusted; Apo=Apolipoprotein; SC=Subcutaneous; BMI=Body mass index

risk factors were lost after adjusting data.<sup>[7,15]</sup> These studies' results are consistent with our findings. The pathogenic role of visceral fat tissue may be due to its smaller adipocyte size, higher rate of fatty acid absorption, higher protein content, secretion of anti-inflammatory mediators and vasoactive substances, and its communication with liver via portal circulation, which may contribute to its role in insulin resistance.<sup>[16]</sup> It may also represent a marker of the inability of fat tissues to efficiently manage excess dietary fat.<sup>[17,18]</sup>

Our study showed that BMI, WC, and WHtR were not significantly associated with apoB and the apoB/apoA ratio. As mentioned above, the correlation of subcutaneous fat tissue with metabolic risk factors had not been documented in previous research<sup>[7,15]</sup> since BMI is an obesity indicator which reflects overall adiposity,<sup>[16]</sup> while WC and WHtR are two obesity indicators which indirectly reflect visceral and subcutaneous fat tissue in abdominal region.<sup>[19,20]</sup> It is logical that these indicators did not show any significant correlation with these two non-traditional CAD risk factors.

Available literature has shown that associations of low-density lipoprotein cholesterol (LDL-C) with visceral fat area are generally weak and non-significant.<sup>[7,15]</sup> Our findings did not show an association of visceral fat area with apoB, but strong association with the apoB/apoA ratio was found. Many studies have documented that the risk relationship was stronger for the apoB/apoA ratio than other lipid-related measurements like apoB. It has been suggested that the predictive value of this ratio is better than that of other CAD risk factors.<sup>[19]</sup> This may be due to the fact that this fraction reflects the ratio of atherogenic LDL\_C to non-atherogenic HDL particles.<sup>[3]</sup>

The correlation of apoA level within HDL\_C with visceral fat area is in consistent with other studies, which reported the negative association of HDL with visceral fat tissue.<sup>[7,15]</sup> Other groups could not show the relation between visceral fat tissue to coronary artery involvement.<sup>[12,13]</sup> Our results show the association of three non-traditional risk factors with visceral fat in patients with stable angina. Thus,

even patients who show symptoms of CAD are similar to a normal population where intra-abdominal fat is also associated with CAD risk factors.

In spite of the strengths of this study, which evaluated visceral and subcutaneous fat tissue in association with non-traditional risk factors in patients with stable angina, some limitations must be taken into consideration. The cross-sectional design and the relatively small sample size could limit our analyzes. On the other hand, although several adjustments were performed, it is possible that unmeasured confounders may explain part of the associations between visceral fat area and non-traditional CAD risk factors.

## CONCLUSION

Visceral fat tissue accumulation was associated with a mount of apolipoproteins in patients with stable angina. This reinforces the notion that patients with higher intra-abdominal fat have higher risk factors of CAD. Then, we most focus on controlling body fat via life style modification especially.

## LIMITATION

Some patients after angiography didn't come to CT scan unit; then, we must replace these patients. This project appraises in Isfahan Cardiovascular Research Institute with number 86131 and in collaboration with MC Gill University, Mike Rosen bloom Lab for cardiovascular Research, Montreal, Quebec.

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