CORRELATION BETWEEN BODY FAT DISTRIBUTION, PLASMA LIPIDS AND APOLIPOPROTEINS WITH THE SEVERITY OF CORONARY INVOLVEMENT IN PATIENTS WITH STABLE ANGINA

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Abstract

BACKGROUND: Previous studies reported that the distribution of body fat is an important risk factor for coronary artery diseases (CAD) and abdominal adipose tissue is associated with severe CAD. This study was conducted to evaluate the relationship between body fat distributions, plasma lipids and the severity of CAD in patients with stable angina.

METHODS: Ninety seven patients who underwent coronary angiography for stable angina were allocated into two groups: patients with mild or severe coronary artery involvement. Lipid profile (total cholesterol, LDL, HDL) and triglyceride (TG) and apolipoprotein A and B, were measured for all of the participants and a demographic data questionnaire was filled by the subjects. Participants underwent abdominal computed tomography (CT-Scan) for measurement of adipose tissues that was classified to visceral and superficial and deep subcutaneous fat tissue compartment.

RESULTS: Patients with severe coronary artery involvement had higher level of apo B (P = 0.02). Significant correlation was seen between visceral fat index and TG (P = 0.01), HDL-C (P < 0.01) in patients with mild coronary involvement and with total cholesterol (P = 0.02), LDL-C (P = 0.01) and apoB (P < 0.01) in patients with severe coronary involvement. No significant relationship was seen among deep cutaneous fat index and lipid profile in both groups.

CONCLUSION: Our findings showed that visceral adipose tissue is significantly associated with severe CAD and has a significant correlation with lipid profile as well as Apo B.

Keywords: Visceral Abdominal Adipose Tissue, Superficial Subcutaneous Adipose Tissue, Deep Subcutaneous Adipose Tissue, Coronary Involvement, Lipid Profile.

INTRODUCTION

Obesity is an important risk factor for cardiovascular (CVD) and metabolic diseases. Adipose tissue in human body is divided into: superficial subcutaneous, deep subcutaneous and visceral adipose tissue. Several studies have shown that visceral abdominal tissue has the most correlation with risk factors of CVD like dyslipidemia. Furthermore, visceral fat plays an important role in the developing of atherosclerosis and its multiple risk factors in particularly obese individuals. Even without obesity, visceral fat may be a risk factor for coronary artery diseases (CAD).

The relation between visceral abdominal adipose tissue and severity of CAD and associated morbidities has been reported before. However Caroline et al. study found no significant relationship among subcutaneous and visceral abdominal adipose tissue with calcification of coronary arteries.

As few studies have evaluated the correlation between body fat distribution based on superficial subcutaneous, deep or visceral ones with the severity of coronary involvement and apolipoproteins a and b, this study was designed to evaluate the relationship between body fat distribution, plasma lipids and the severity of CAD in patients with stable angina.
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Materials and Methods

This study was a cross-sectional study on patients with diagnosis of stable angina who underwent coronary angiography in Chamran hospital. Overall 97 patients were selected via simple sampling method among patients with inclusion criteria.

While inclusion criteria included: age between 35-70 years, stable angina pectoris, stenosis more than 75% in any of coronary arteries in angiography. Exclusion criteria included: myocardial infarction, unstable angina, borderline coronary stenosis in angiography or any considerable abdominal lesion in abdominal computerizing CT scan.

This study was approved by the ethical committee of Isfahan cardiovascular research center and written informed consents were obtained from all participants.

A demographic data questionnaire including sociodemographic data, behavioral factors, past medical history and all off medications as well as a 3-day 24-hour recall diet questionnaire was filled by all of the participants.

Fasting blood sample was obtained from the participants for measurement of fasting blood sugar (FBS), total cholesterol (Total-Ch), high density cholesterol (HDL-C), low density cholesterol (LDL-C), triglyceride (TG), apolipoprotein A (apo- A), apolipoprotein B (apo-B), insulin, adiponectin and leptin using autoanalyzer (Hitachi, Japan) in the laboratory of Isfahan Cardiovascular Research Center.

Coronary angiography was done using standard method via femoral artery and films were reviewed by a cardiologist and cardiology assistant. According to the results of coronary angiography participants were divided into two groups with mild or severe CAD.

Mild CAD was defined as more than 50% stenosis of coronary arteries without criteria of severe coronary artery involvement. Severe coronary artery involvement was defied as ≥ 50% stenosis of left main coronary artery, ≥ 90% stenosis in the proximal left anterior descending or in ≥ 2 coronary arteries or extensive ≥ 70% stenosis in three coronaries.

All participants underwent abdominal CT-Scan for the measurement of adipose tissues. CT-Scan was done at the level of umbilicus which is the best level for measurement of subcutaneous and visceral fats.

CT-Scan was done at supine position with the arms above the head and the amount of superficial, deep and visceral adipose tissue was measured by the radiologists using computerized planimetric method.

In this method the amount of adipose tissue is calculated according to fixed attenuation range from -30 to -190 Hansfiled. In this technique, visceral tissue is defined as intraabdominal adipose tissue which is bound to parietal peritoneum or fascia transversalis. Adipose tissue below the fascia transversalis is called deep subcutaneous adipose tissue and above the fascia transversalis is called superficial adipose tissue. Adipose tissue is measured as square centimeter in this method.

Data were analyzed using SPSS software and the following tests Chi-square and Fisher exact test to compare qualitative variables like distribution frequency of sex between two groups, Pearson correlation coefficient for determination of relationship between quantitative variables like the percent of visceral fat and age, Student t–test for the determination of quantitative variables difference between two groups like mean of age.

Results

A total of 97 participants were divided into two groups with 48 participants in the first group with mild CAD and 49 participants in the second group with severe CAD.

The mean age was 51.08 ± 7.63 and 55.42 ± 6.82 years in the first and second groups, respectively. Mean of waist circumference was 100.34 ± 9.37 cm and 100.6 ± 9.38 cm in the first and second group respectively. Mean of body mass index (BMI) was 28.0 ± 3.9 in group 1 and 27.77 ± 4.0 in group 2. A significant relationship was seen between age and severity of coronary involvement in both groups (P = 0.004).

47 patient was male that 29 (60.4%) cases were in mild CAD group and 18 (36.7%) cases were in severe CAD group and 50 patients were female that 19 (39.6%) cases were in mild CAD group and 31 (63.3%) were in severe CAD group.

Table 1 shows the frequency of smoking and history of underlying diseases was seen in both groups. According to table 1, there is a significant difference between the severity of CAD, based on the presence of diabetes (P < 0.01), dyslipidemia (P = 0.03), and smoking (P = 0.016).

Table 1. Past medical history in patients with mild and severe CAD

| Past Medical History | Mild CAD | Severe CAD | P |
|----------------------|----------|------------|---|
| History of Hypertension | 25(52.1%) | 34(69.4%) | 0.81 |
| History of Diabetes | 9(18.8%) | 22(44.9%) | 0.00 |
| History of Dyslipidemia | 17(35.4%) | 28(57.1%) | 0.03 |
| History of Myocardial infarction | 8(16.7%) | 6(12.2%) | 0.53 |
| History of Smoking | 17(35.4%) | 7(14.3%) | 0.01 |
Table 2. Plasma lipids and apolipoproteins in patients with mild and severe CAD

| Plasma lipids | Mild coronary involvement Mean ± SD | Severe coronary involvement Mean ± SD | P       |
|--------------|-------------------------------------|-------------------------------------|---------|
| Total Cholesterol (mg/dl) | 173.52 ± 39.91 | 190.46 ± 50.65 | 0.09   |
| Triglyceride (mg/dl)       | 158.76 ± 93.89 | 173.54 ± 106.77 | 0.50   |
| 1HDL-C (mg/dl)             | 35.19 ± 10.14  | 36.18 ± 11.46  | 0.67   |
| 2LDL-C (mg/dl)             | 100.69 ± 28.17 | 113.54 ± 35.16 | 0.06   |
| 3apo A (mg/dl)             | 149.07 ± 22.51 | 149.48 ± 30.39 | 0.94   |
| 4apo B (mg/dl)             | 92.45 ± 23.77  | 106 ± 31.74    | 0.02   |

HDL-C: High density lipoprotein cholesterol; LDL-C: Low density lipoprotein cholesterol; apo A: apolipoprotein A; apo B: apolipoprotein A

Table 3. Correlation between fat distribution and plasma lipids in patients with mild and severe CAD

| Fat distribution | TC (mg/dl) | TG (mg/dl) | HDL-C (mg/dl) | LDL-C (mg/dl) | apo A (mg/dl) | apo B (mg/dl) | Fat distribution |
|-----------------|-----------|-----------|---------------|---------------|---------------|---------------|-----------------|
| Visceral Fat Index (mm²) | Correlation | 0.067 | 0.441 | -0.470 | -0.111 | -0.061 | 0.004 | 0.270 |
|                 | P value   | 0.72 | 0.01 | 0.00 | 0.55 | 0.75 | 0.98 | 0.14 |
| Severe coronary involvement | Correlation | 0.486 | 0.326 | -0.324 | 0.498 | 0.423 | -0.175 | 0.631 |
|                 | P value   | 0.02 | 0.13 | 0.14 | 0.01 | 0.05 | 0.43 | 0.00 |
| Deep Subcutaneous Fat Index (mm²) | Correlation | 0.238 | 0.262 | -0.022 | -0.075 | 0.122 | 0.181 | 0.153 |
|                 | P value   | 0.19 | 0.15 | 0.90 | 0.68 | 0.52 | 0.32 | 0.41 |
| Severe coronary involvement | Correlation | 0.173 | 0.122 | 0.280 | 0.118 | 0.001 | 0.161 | 0.145 |
|                 | P value   | 0.44 | 0.58 | 0.20 | 0.60 | 0.99 | 0.47 | 0.52 |
| Superficial Subcutaneous Fat Index (mm²) | Correlation | 0.285 | 0.241 | 0.105 | -0.127 | 166 | 0.449 | 0.154 |
|                 | P value   | 0.12 | 0.19 | 0.57 | 0.49 | 0.38 | 0.38 | 0.40 |
| Severe coronary involvement | Correlation | 0.102 | -0.165 | 0.190 | 0.279 | 0.187 | -0.031 | 0.138 |
|                 | P value   | 0.65 | 0.46 | 0.39 | 0.20 | 0.41 | 0.89 | 0.54 |

According to table 2, there is a significant difference in the mean level of apo B between two groups. Patients with severe CAD have higher level of apo B (P = 0.02).

Table 3 shows a significant correlation between visceral fat index with TG (P = 0.01), HDL-C (P < 0.01) in the group with mild CAD; while the same was seen between total cholesterol (P = 0.02), LDL-C (P = 0.01) and apo-B (P < 0.01) in the group with severe CAD. No significant relationship was seen among deep cutaneous fat index and lipid profile in both groups. This table also reveals significant correlation among superficial subcutaneous fat index and apo-A in the group with mild CAD (P = 0.01).

Discussion

The results of the our study showed significant relationship among visceral adipose tissue with TG and HDL-C in patients with mild CAD and significant correlation among visceral adipose tissue and total cholesterol, LDL-C and apo B in patients with severe CAD.

Superficial adipose tissue had only significant correlation with apo-A in patients with mild CAD. Our results showed no correlation between apoproteins and deep subcutaneous adipose tissue. Seo et al. did not find any significant relationship among severity of coronary artery involvement and visceral fat tissue which is in contrast with our results. This difference may be due to using advanced software of CT scan in our study compared with Seo et al or the difference in weight and distribution of body fat among two population. Similar to our findings, Zamboni et al reported that the distribution of body fat is an important risk factor for CAD and visceral abdominal adipose tissue is associated with severe CAD and associated morbidities. Lee et al showed that increase in visceral adiposity is associated with severity of CAD.

Kelley et al reported significant relationship among deep subcutaneous and visceral adipose tissue with LDL-C, TG and apo-B which is similar to our results, however the association between deep subcutaneous adipose tissue and lipoproteins was not significant in our study. In contrast with Kelly et al. that may be related to the difference in sample size and inclusion criteria between these two studies, our results did not differ among men and women.
Porter et al showed correlation between visceral adipose tissue and hypercholesterolemia in women and hypertriglyceridemia in men. They also reported a protective role for subcutaneous abdominal adipose tissue against dyslipidemia.16

Nicklas et al reported significant relationship among abdominal subcutaneous and visceral adipose tissue with acute myocardial infarction in women.18 However in our study we excluded patients with myocardial infarction, in contrast we found such a correlation with severe CAD in angiography of patients with stable angina.

Although the current study had some limitations like its small sample size, however its strengths is using CT scan for the fat distribution measurement in angiographic documented CAD patients.

In conclusion, our study showed that visceral adipose tissue has a significant association with severe CAD and has a significant correlation with lipid profile especially apo B, which has been suggested more atherogenic than other lipoproteins.10

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Conflict of Interests
Authors have no conflict of interests.

References
1. Taguchi R, Takasu J, Itani Y, Yamamoto R, Yokoyama K, Watanabe S, et al. Pericardial fat accumulation in men as a risk factor for coronary artery disease. Atherosclerosis 2001; 157(1): 203-9.
2. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983; 67(5): 968-77.
3. Ramezani J, Sanei H, Sadeghi M, Hidari R, Haghani P. Central obesity as a predictor of coronary artery occlusion. ARYA Atherosclerosis Journal 2008; 4(1): 24-8.
4. Barrett-Connor EL. Obesity, atherosclerosis, and coronary artery disease. Ann Intern Med 1985; 103(6 ( Pt 2)): 1010-9.
5. Sniderman AD, Bhopal R, Prabhakaran D, Sarrafzadegan N, Tchernof A. Why might South Asians be so susceptible to central obesity and its atherogenic consequences? The adipose tissue overflow hypothesis. Int J Epidemiol 2007; 36(1): 220-5.
6. Sarrafzadegan N, Kelishadi R, Baghaei A, Hussein SG, Malekafzali H, MohammadiFard N, et al. Metabolic syndrome: an emerging public health problem in Iranian women: Isfahan Healthy Heart Program. Int J Cardiol 2008; 131(1): 90-6.
7. Lee YH, Lee SH, Jung ES, Kim JS, Shim CY, Ko YG, et al. Visceral adiposity and the severity of coronary artery disease in middle-aged subjects with normal waist circumference and its relation with lipopalin-2 and MCP-1. Atherosclerosis 2010; 213(2): 592-7.
8. Hayashi T, Boyko EJ, Leonetti DL, McNeely MJ, Newell-Morris L, Kahn SE, et al. Visceral adiposity and the risk of impaired glucose tolerance: a prospective study among Japanese Americans. Diabetes Care 2003; 26(3): 650-5.
9. Rosito GA, Massaro JM, Hoffmann U, Ruberg FL, Mahabadi AA, Vasan RS, et al. Pericardial fat, visceral abdominal fat, cardiovascular disease risk factors, and vascular calcification in a community-based sample: the Framingham Heart Study. Circulation 2008; 117(5): 605-13.
10. Zamboni M, Armellini F, Sheiban I, De Marchi M, Todesco T, Bergamo-Andreis IA, et al. Relation of body fat distribution in men and degree of coronary narrowings in coronary artery disease. Am J Cardiol 1992; 70(13): 1135-8.
11. Fox CS, Hwang SJ, Massaro JM, Lieb K, Vasan RS, O'Donnell CJ, et al. Relation of subcutaneous and visceral adipose tissue to coronary and abdominal aortic calcium (from the Framingham Heart Study). Am J Cardiol 2009; 104(4): 543-7.
12. Amanullah AM, Berman DS, Hachamovitch R, Kiat H, Kang X, Friedman JD. Identification of severe or extensive coronary artery disease in women by adenosine technetium-99m sestamibi SPECT. Am J Cardiol 1997; 80(2): 132-7.
13. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocr Rev 2000; 21(6): 697-738.
14. Borkan GA, Gerzof SG, Robbins AH, Hults DE, Silbert CK, Silbert JE. Assessment of abdominal fat content by computed tomography. Am J Clin Nutr 1982; 36(1): 172-7.
15. Kelley DE, Thaete FL, Troost F, Huwe T, Goodpaster BH. Subdivisions of subcutaneous abdominal adipose tissue and insulin resistance. Am J Physiol Endocrinol Metab 2000; 278(5): E941-8.
16. Porter SA, Massaro JM, Hoffmann U, Vasan RS, O'Donnell CJ, Fox CS. Abdominal subcutaneous adipose tissue: a protective fat depot? Diabetes Care 2009; 32(6): 1068-75.
17. Seo J. Severity of Coronary Artery Disease and Visceral Fat Obesity. Korean Circ J 1998; 28(7): 1176-84.
18. Nicklas BJ, Penninx BW, Cesari M, Kritchevsky SB, Newman AB, Kanaya AM, et al. Association of visceral adipose tissue with incident myocardial infarction in older men and women: the Health, Aging and Body Composition Study. Am J Epidemiol 2004; 160(8): 741-9.