Short communication

Apolipoprotein B/A-I ratio related to visceral but not to subcutaneous adipose tissue in elderly Swedes

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ABSTRACT

Objective: To investigate whether the amount of visceral (VAT) or subcutaneous adipose tissue (SAT) independently of the other can determine the apolipoprotein (apo)B/A-I ratio.

Methods: VAT and SAT areas were assessed using magnetic resonance imaging in 247 randomly selected 70-year-old men and women who did not use lipid-lowering drugs. Their adipose tissue areas were compared to their apoB and apo A-I levels and to their apoB/A-I ratios.

Results: The VAT area and the gender were significantly related to the apoB/A-I ratio whereas the SAT area was not. There was a positive relationship between the VAT area and the apoB/A-I ratio whereas there was no relationship between the amount of SAT and the apoB/A-I ratio. This observation supports the notion that VAT is metabolically active.

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1. Introduction

Various biochemical markers have been used to assess lipid levels and to estimate dyslipidemia, which constitute major risk factors for atherosclerosis and cardiovascular (CV) disease [1,2]. In recent years several studies favour plasma apolipoproteins (apo) [2–4] and the apoB/apoA-I ratio has been appointed the strongest plasma lipid predictor of CV risk [1,5].

Obesity is a well established risk factor for CV disease and dyslipidemia [6]. The distribution of the adipose tissue is, however, of importance. Several studies have proved the visceral adipose tissue (VAT) to provide the major part of the risk [7,8]. Imaging techniques, such as magnetic resonance imaging (MRI), provide a more reliable method to quantify VAT and subcutaneous adipose tissue (SAT) and discriminate between the two than anthropometric measurements such as waist circumference and waist/hip ratio [9].

The aim of this study was to investigate whether the amount of VAT or SAT, assessed with MRI, independently of the other can determine the apoB/apoA-I ratio, with the working hypothesis that the amount of VAT is the major determinant of the apoB/apoA-I ratio.

2. Materials and methods

2.1. Study population

After obtaining approval from the ethical committee and written informed consent, the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study conducted studies on 1016 randomly selected community-living subjects who were recruited at 70 years of age (participation rate 50.1%).

Magnetic resonance imaging (MRI) was performed on 293 subjects who were consecutively invited from the original cohort. Subjects using lipid-lowering drugs were excluded, and a subsample of 247 subjects (123 women, 124 men), who had assessable MRI images and biochemical measurements, constitute the population of the present study.

The basic characteristics among these subjects did not differ from those in the entire PIVUS population except that there were fewer current smokers and slightly higher LDL levels in the subjects of the present study (Table 1).

2.2. Subject data

Participants in the PIVUS study answered a questionnaire about their medical and drug histories.
2.3. Biochemical measurements

A venous blood sample was taken in the morning after an overnight fast at the time of inclusion in the study. No medication or smoking was allowed after midnight.

Apolipoprotein A-I (reagent: 9D92-01) and apolipoprotein B (reagent: 9D92-01) were analysed on an Architect Ci8200 analyser (Abbott Laboratories, Abbott Park, IL, USA) and reported using SI units with reagents from the same manufacturer. The total analytical imprecision for the apolipoprotein A1 assay was 1.8% at 2.00 g/L and the total analytical imprecision for the apolipoprotein B assay was 4.5% at 0.47 g/L and 2.4% at 1.88 g/L.

2.4. MR image acquisition and analysis

MRI was performed using a single axial slice from a gradient echo acquisition at the L4–L5 interface. Visceral (VAT) and subcutaneous tissues were manually contoured and their areas (cm²) were computed using the software package ImageJ (http://rsb.info.nih.gov/ij/). MRI and blood sampling were performed on separate occasions and at MRI there were no restrictions regarding food intake or time of day.

2.5. Statistical analysis

StatView 5.0.1 (SAS Institute, Cary, North Carolina) was used for statistical analyses. A univariate analysis was performed between VAT and SAT and apoA-I, apoB and the apoB/apoA-I ratio. A multiple regression model was used to analyse VAT and SAT and gender as independent variables and apoB/apoA-I ratio as the dependent variable. Then, VAT was analysed as the dependent variable with apoA-I, apoB and gender as independent variables. Finally, the Student’s t-test was used to test whether there were any differences in the investigated parameters between the genders. Two-tailed significance values were given. The significance level was set at 0.05 in all analyses.

3. Results

There were significant differences between gender in apoA-I levels (women 1.78 g/L, men 1.54 g/L, p < 0.0001), apoB/apoA-I ratio (women 0.62 g/L, men 0.71 g/L, p < 0.0001) and VAT area (women 93.7 cm², men 121 cm², p = 0.0003) and SAT area (women 260 cm², men 188 cm², p < 0.0001) but not in apoB levels (women 1.09 g/L, men 1.07 g/L, p = 0.42) (Table 1). In the multiple regression analysis the gender (correlation coefficient = −0.72, p = 0.004) was independently significantly related to the apoB/apoA-I ratio.

The VAT area (correlation coefficient = 0.25, p = 0.001) was independently significantly related to the apoB/apoA-I ratio in the multiple regression analysis whereas the SAT area was not (correlation coefficient = 0.029, p = 0.7) (Fig. 1). ApoA-I levels were independently related to the VAT area (correlation coefficient = −0.33, p = 0.0001) whereas the apoB levels were not (correlation coefficient = 0.102, p = 0.07) (Fig. 1). In the univariate model there was a positive relationship between the VAT area and the apoB/apoA-I ratio, whereas there was no relationship between the SAT area and the apoB/apoA-I ratio (correlation coefficient = 0.17, p = 0.02).

4. Discussion

The observation that there was a positive relationship between the VAT area and the apoB/apoA-I ratio is not surprising, but confirms our primary suspicion. The VAT [7,8] and the apoB/apoA-I ratio [2–4] are both independently related to increased CV risk and it is not unreasonable to believe that they might be involved in the same pathophysiological mechanism.

However, the observation that there was no relationship between the amount of SAT and the apoB/apoA-I ratio is somewhat more intriguing. Even though the VAT is established as being metabolically active and largely responsible for dyslipidemia [6], the SAT is usually not considered to be entirely harmless [10–12]. The results of the present study imply that SAT does not play a major part in the development of dyslipidemia.

A possible link between VAT and the apoB/apoA-I ratio may be the adipocyte-derived hormone adiponectin, supported by observations that adiponectin levels are determined by VAT [13–16] and that a positive association has been observed between the levels of adiponectin and apoA-I [17,18]. Thus, decreased adiponectin levels entail decreased apoA-I levels [17] and subsequently an elevated apoB/apoA-I ratio, which is associated with an increased CV risk [2,4]. This is consistent with the observation made in the present study that there was a stronger relationship between the VAT area and the apoA-I levels compared to the apoB levels.

This hypothesis is endorsed by the results of several studies; adiponectin has been observed to be positively related to VAT but not to SAT [13], adiponectin levels are significantly lower in VAT than in SAT [19,20], and no difference has been observed in...
adiponectin gene expression in SAT biopsies from obese and lean subjects [21].

The differences between women and men that were observed in apoA-I levels, apoB/apoA-I ratio [1] and adipose tissue distribution [7,11,22] are consistent with observations made by others. The observed relationship between the VAT area and the apoB/apoA-I ratio was independent of gender.

The present study was limited by the fact that only 70-year-old Caucasians were studied, entailing that the results may not apply to other ethnic or age groups. Furthermore, adipose tissue was quantified using a single axial MR image, which is less exact than using a full 3D volume. Planimetric measurements of VAT and SAT at the level of the umbilicus have, however, been reported to be in good correlation with volumetric adipose tissue quantification [23].

In conclusion, a positive relationship was established between the amount of VAT and the apoB/apoA-I ratio, whereas there was no relationship between the amount of SAT and the apoB/apoA-I ratio. This observation may support the notion that viscerally located adipocytes are metabolically active, possibly through decreased adiponectin levels. Surprisingly, subcutaneously located adipocytes do not seem to influence plasma lipid levels.

Conflicts of interest

Lars Johansson is employed by AstraZeneca.

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References


