

Measurements of Visceral Adiposity, Type-2 Diabetes and Risk for Cardiovascular Disease among Brazilian Men and Women

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Abstract

Background/aims: To detect a possible association between Visceral Adiposity Index (VAI), Lipid Accumulation Product Index (LAP) and equations to estimate Deep-Abdominal-Adipose-Tissue (DAAT) with type-2 diabetes mellitus and 10-year risk for cardiovascular disease among Brazilian men and women.

Methods: A cross sectional study was carried out among 99 subjects aged 30 to 80 years without cardiovascular disease. Type-2 diabetes mellitus was diagnosed according to medical records and 10-year risk for Coronary Heart Disease (CHD) was calculated from Framingham Risk Score (FSR). Anthropometric measurements [weight, height and Waist Circumference (WC)] were made according to standard protocols and biochemical data (total cholesterol, HDL-cholesterol and serum triglycerides) were obtained by colorimetric enzymatic method from a certified laboratory. BMI, VAI, LAP and DAAT were calculated and Analysis of Covariance Models (ANCOVA) was performed to detect independent associations.

Results: A total of 14 men's and 85 women's with an average of 57.4 ±11.9 years were enrolled in the study. Prevalence of type 2-diabetes mellitus was 33.3% according to FSR, 22.2% of the subjects were classified at a higher risk for CHD. After adjustment for confounding factors, type-2 diabetes was associated with DAAT ($p = 0.03$) and a trend for LAP ($p = 0.05$). On the other hand, VAI index was significantly higher among subjects with higher risk for CHD ($p = 0.01$).

Conclusions: A positive relation between DAAT and LAP with type-2 diabetes, as well as VAI with risk for cardiovascular disease was found independent of overall obesity. These simple tools for assessment of visceral fat tissue should be considered for clinical practice.

Keywords: Abdominal obesity; Diabetes mellitus; Risk factors; Cardiovascular diseases; Body mass index; Intra-abdominal fat; Anthropometry

Introduction

Obesity is a well-known risk factor for type-2 Diabetes Mellitus (DM) and Cardiovascular Disease (CVD) [1], and the fat accumulated on the abdominal region is strongly associated with

both conditions [2,3]. Abdominal fat includes compartments from the Subcutaneous Adipose Tissue (SAT) and Visceral Adipose Tissue (VAT). Traditional anthropometric indicators such as Body Mass Index (BMI) and Waist Circumference (WC) do not distinguish VAT from SAT compartments [4,5].

Anthropometric indices with an easy applicability and low cost have been proposed as an alternative to imaging methods for visceral fat detection. The Visceral Adiposity Index (VAI) has significant correlation with insulin sensitivity and its increase is strongly associated with cardiometabolic risk [6-8]. The Lipid Accumulation Product Index (LAP Index) is also correlated with VAT and has been associated with insulin resistance [9] and type-2 diabetes mellitus in general population [10,11]. Mathematical models to estimate Deep-Abdominal-Adipose-Tissue (DAAT) area were validated among Indian men and women [12], but not tested in Brazilian subjects.

Some of these visceral adiposity measurements have been evaluated among specific populations, but the results regarding type-2 diabetes and cardiovascular risk are inconclusive [13-15]. Besides, Brazilian population – which is composed of different ethnicities – does not have a specific cutoff for abdominal obesity, such as WC. Thus, values suggested by the World Health Organization are frequently used to detect higher risk for cardiovascular disease [16]. Therefore, the aim of this study is to detect a possible association of VAI, LAP and DAAT with type-2 diabetes mellitus and 10-year risk for Coronary Heart Disease (CHD), in subjects from general population in southern Brazil.

Methods

This cross-sectional study enrolled 99 subjects, aged 30 to 80 years without cardiovascular disease or other relevant chronic diseases (i.e. cancer and AIDS) were selected from primary health care centers in the city of Esteio, Rio Grande do Sul. The Ethics Committee of the Institute of Cardiology of Rio Grande do Sul approved the protocol, which was in accordance with the

Declaration of Helsinki and all patients signed a consent term to participate in the study.

Demographic data (age, sex and self-reported skin color), information regarding education (years at school), lifestyle characteristics [smoking, abusive alcohol consumption (≥ 30 g for men and ≥ 15 g for women) and physical activity] were collected using a standardized questionnaire. Measurements of blood pressure (BP) were made using an aneroid sphygmomanometer according to current guidelines [17] and the known previous medical diagnoses were used to detect patients with hypertension, type-2 diabetes mellitus and dyslipidemia. Framingham Risk Score (FSR) was calculated and categorized as low ($< 10\%$), intermediate ($10- < 20\%$) and high risk ($\geq 20\%$) for CHD in 10 years [18].

Weight (kg) was measured with patients in light clothes, barefoot, in a 100g scale (Filizola®, model 31, IN Filizola - SA, Sao Paulo, Brazil) and height was obtained with a Tonelli® stadiometer with a 0.1cm scale, model E120 A (IN Tonelli - SA, Santa Catarina, Brazil) [19]. BMI was calculated by the weight (kg)/height (m^2). WC was obtained with a plastic, flexible, inelastic measuring tape in the middle point between the lower costal rib and the iliac crest in a perpendicular plane, with the patient standing in both feet and with both arms hanging freely.

Serum lipids (total cholesterol, HDL-cholesterol and triglycerides) were measured by colorimetric enzymatic method, at the certified laboratory by the Public Health System of Esteio. DAAT, in cm^2 , was calculated according to formula: $-382.9 + [1.09 \times \text{weight} - (\text{kg})] + [6.04 \times \text{WC} - (\text{cm})] + [-2.29 \times \text{BMI}]$ for men and $-278 + [-0.86 \times \text{weight} - (\text{kg})] + [5.19 \times \text{WC} - (\text{cm})]$ for women [6]; LAP Index, in $cm.mmol/l$, was calculated for men $[(\text{WC} (\text{cm}) - 65) \times \text{TG} (\text{mmol})]$ and women $[(\text{WC} (\text{cm}) - 58) \times \text{TG} (\text{mmol})]$ [10]; and VAI was calculated according to $[\text{WC}/(39.68 + 1.88 \times \text{BMI})] \times [\text{TG}/1.03] \times [1.31/\text{HDL-C}]$ for men and $[\text{WC}/(36.58 + 1.89 \times \text{BMI})] \times [\text{TG}/0.81] \times [1.52/\text{HDL-C}]$ for women [12].

Statistical analyses were performed using SPSS (Statistical Package for the Social Sciences, version 17.0, IL, USA). Mean (SD) and percentage were compared using Analysis of Variance (ANOVA) or Pearson's chi-square test. We tested the potential relationship of diabetes, FSR and indices of visceral adiposity (DAAT, LAP and VAI) using Analysis of Covariance Models (ANCOVA), with the adjustment for age, gender, BMI, physical activity and diagnosis of dyslipidemia. The statistical significance level was set at a two-tailed type I error of 0.05.

Results

A total of 14 men's and 85 women's with an average years of 57.4 ± 11.9 were enrolled in this study. Among that 77.8% are whites and 36.4% are smokers (Ex- or current). Prevalence of type-2 DM, hypertension and dyslipidemia were respectively, 33.3%, 62.6% and 62.6%, 6.1% had abusive alcohol consumption, and 83.8% practiced some physical activity. According to FSR, 24.2% of the subjects were classified as low risk, 53.5% intermediate risk and 22.2% high risk for CHD in 10 years.

Regarding traditional anthropometric indices, men had lower

values of BMI and WC when compared to women (27.9 ± 5.1 vs. 31.7 ± 6.1 , $p=0.03$ for BMI; 96.1 ± 12.9 vs. 99.9 ± 13.1 , $p = 0.3$ for WC). Men also showed lower values of VAI and LAP (log transformed), but higher values of DAAT (6.9 ± 3.3 vs. 8.9 ± 3.9 , $p = 0.07$ for VAI; 3.9 ± 0.9 vs. 4.3 ± 0.5 , $p = 0.2$ for LAP and 217.5 ± 83.8 vs. 175.2 ± 56.8 , $p = 0.09$ for DAAT). However, we assessed data on a small number of men in our study and despite statistical significance about some data, it is hard to make meaningful conclusion compared to women.

Table 1 shows that participants with type-2 diabetes were older, had higher VAI, DAAT, LAP and diastolic blood pressure. BMI was similar among type-2 diabetes groups and there was no statistical difference between values of WC. Regarding risk for cardiovascular disease (Table 2), subjects with $\text{FSR} \geq 20\%$ were also older and had higher VAI, LAP, systolic and diastolic blood pressure. DAAT, BMI and WC were similar among all age groups.

After adjustment for confounding factors, type-2 diabetes was associated with DAAT ($p = 0.03$) and a trend for LAP ($p = 0.05$). On the other hand, VAI index was significantly higher among subjects with higher risk for CHD ($p = 0.01$) (Table 3).

Table 1: Characteristic of participants according to type-2 diabetes mellitus [mean \pm SD, n (%)].

| | No type-2 diabetes N = 68 | Type-2 diabetes N = 31 | P-value |
|--|------------------------------|---------------------------|---------|
| Age (years) | 56.7 \pm 12.4 | 58.9 \pm 11.1 | 0.4 |
| Gender | | | 0.1 |
| Men | 7 (50) | 7 (50) | |
| Women | 61 (71.8) | 24 (28.2) | |
| Years of school | 6.8 \pm 3.3 | 6.9 \pm 3.3 | 1.0 |
| Smoking | | | 0.2 |
| Current or ex-smoker | 22 (61.1) | 14 (38.9) | |
| Never | 46 (73) | 17 (27) | |
| Alcoholic abusive consumption | | | 0.4 |
| Yes | 11 (78.6) | 3 (21.4) | |
| No | 277 (66.6) | 139 (33.4) | |
| Physical activity | | | 0.4 |
| Yes | 55 (63.3) | 28 (37.7) | |
| No | 13 (81.3) | 3 (18.8) | |
| Body Mass Index (BMI, kg/m^2) | 31.1 \pm 6.3 | 31.2 \pm 5.8 | 0.9 |
| Waist circumference (cm) | 98.1 \pm 13.7 | 102.1 \pm 11.5 | 0.2 |
| Visceral Adiposity Index | 8.1 \pm 3.6 | 9.6 \pm 4.3 | 0.07 |
| Deep-abdominal-adipose-tissue (DAAT, cm^2) | 172.2 \pm 63.9 | 200.9 \pm 55.5 | 0.03 |
| Lipid Accumulation Product (LAP Index, $cm.mmol/l$) | 4.2 \pm 0.7 | 4.5 \pm 0.4 | 0.02 |
| Systolic Blood Pressure (mmHg) | 128.4 \pm 16.1 | 132.6 \pm 17.3 | 0.2 |
| Diastolic Blood Pressure (mmHg) | 79.7 \pm 9.8 | 83.9 \pm 11.2 | 0.06 |

Table 2: Characteristic of participants according to Framingham Score Risk [mean ± SD, n (%)].

| | LCR N = 24 | ICR N = 53 | HCR N = 22 | P-value |
|--|---------------|---------------|---------------|---------|
| Age (years) | 43.4 ± 5.6 | 59.2 ± 8.4 | 68.4 ± 10.1 | < 0.001 |
| Gender | | | | 0.09 |
| Men | 4 (28.6) | 10 (71.4) | 0 (0) | |
| Women | 20 (23.5) | 43 (50.6) | 22 (25.9) | |
| Years of school | 7.8 ± 3.5 | 6.7 ± 3.1 | 6.1 ± 3.3 | 0.2 |
| Smoking | | | | 0.1 |
| Current or ex-smoker | 5 (13.9) | 20 (55.6) | 11 (30.6) | |
| Never | 19 (30.2) | 33 (52.4) | 11 (17.5) | |
| Alcoholic abusive consumption | | | | 0.4 |
| Yes | 2 (33.3) | 4 (66.7) | 0 (0) | |
| No | 22 (23.7) | 49 (52.7) | 22 (23.7) | |
| Physical activity | | | | 0.1 |
| Yes | 17 (20.5) | 46 (55.4) | 20 (24.1) | |
| No | 7 (43.8) | 7 (43.8) | 2 (12.4) | |
| Body Mass Index (kg/m ²) | 31.6 ± 7.8 | 31.2 ± 5.5 | 30.7 ± 5.8 | 0.9 |
| Waist circumference (cm) | 99.5 ± 15.8 | 98.6 ± 12.8 | 101.0 ± 10.8 | 0.8 |
| Visceral Adiposity Index | 6.2 ± 2.8 | 8.6 ± 3.6 | 11.2 ± 3.9 | < 0.001 |
| Deep-abdominal-adipose-tissue (DAAT, cm ²) | 182.6 ± 74.1 | 179.2 ± 63.5 | 184.6 ± 47.7 | 0.9 |
| Lipid Accumulation Product (LAP Index, cm.mmol/l) | 3.9 ± 0.7 | 4.3 ± 0.6 | 4.5 ± 0.4 | 0.01 |
| Systolic Blood Pressure (mmHg) | 117.9 ± 11.4 | 130.4 ± 16.5 | 140.9 ± 12.7 | <0.001 |
| Diastolic Blood Pressure (mmHg) | 77.1 ± 9.9 | 81.7 ± 10.9 | 83.6 ± 8.5 | 0.08 |

LCR: Low Cardiovascular Risk; ICR: Intermediate Cardiovascular Risk; HCR: High Cardiovascular Risk

Table 3: Anthropometric indexes adjusted-means* according to type-2 diabetes and Framingham Score Risk [mean ± SD, (CI 95%)].

| | DAAT | LAP | VAI |
|---|-------------------------------|-------------------------|--------------------------|
| Type-2 Diabetes mellitus | | | |
| Without type-2 diabetes mellitus | 175.6 ± 37.4 (166.6-184.6) | 4.2 ± 0.5 (4.1-4.3) | 8.2 ± 3.6 (7.4-9.1) |
| With type-2 diabetes mellitus | 193.5 ± 37.9 (179.9-206.9) | 4.4 ± 0.50 (4.3-4.6) | 9.4 ± 3.7 (8.1-10.7) |
| P-value | 0.03 | 0.05 | 0.1 |
| Framingham Score Risk | | | |
| Low Risk for CHD (< 10%) | 190.5 ± 52.2 (169.3-211.7) | 4.1 ± 0.7 (3.8-4.4) | 6.5 ± 4.9 (4.5-8.4) |
| Intermediated Risk for CHD (10 - < 20%) | 173.4 ± 38.4 (162.9-183.9) | 4.3 ± 0.5 (4.2-4.4) | 8.5 ± 3.6 (7.5-9.5) |
| High Risk for CHD (≥ 20%) | 189.9 ± 45.8 (170.5-209.3) | 4.7 ± 0.6 (4.2-4.7) | 11.2 ± 4.3 (9.4-12.9) |
| P-value | 0.1 | 0.3 | 0.01 |

*Adjusted for age, gender, BMI, physical activity and diagnosis of dyslipidemia. DAAT: Deep-Abdominal-Adipose-Tissue; LAP: Lipid Accumulation Product Index; VAI: Visceral Adiposity Index

Conclusions

To our knowledge, this is the first study comparing three different simple measurements to estimate visceral adiposity (DAAT, VAI and LAP) among southern Brazilian men and women, and also the first one that evaluated a possible relationship between DAAT, type-2 diabetes mellitus and risk for cardiovascular disease. Besides, we found an association of DAAT and LAP with type-2 diabetes and of VAI with 10-year risk for CHD, after controlling for overall adiposity and other factors. Our population had higher levels of abdominal and overall

obesity detected by different indices, but as expected, most of the anthropometric indicators were increased among those who had type-2 diabetes and high cardiovascular risk.

Women have naturally more subcutaneous fat when compared with men, while higher deposits of visceral fat are found among men [20]. Our data shows that men had higher levels of DAAT but lower levels of LAP and VAI. DAAT is calculated only with anthropometric measurements while LAP and VAI are calculated with WC, BMI and biochemical data. None of men were classified with higher risk for CHD in our study, suggesting that

women had a worse metabolic profile and it could reflect on their values of LAP and VAI. Besides, studies had failed to demonstrate positive associations of VAI and LAP with incident CVD and type-2 diabetes in men [13,15]. Even lower visceral adipose tissue compartments acts more negatively to the metabolic profile in women than in men [21]. We reinforce, however, that in our study only a small number of men were assessed and these data may limit the interpretation and extrapolation among other populations.

Surrogates of traditional indices of adiposity may perform better in predicting type-2 diabetes and CVD risk in specific populations, depending on sex, age, ethnicity and clinical condition [22]. In our study, we were able to find different associations according to visceral index assessed. As expected, values of DAAT, LAP and VAI were higher among subjects with diabetes, but DAAT and LAP were not associated with the 10-year risk for CHD. A possible explanation regarding the HDL-cholesterol values, are also used to calculate VAI and FSC, characterizing a possible interaction between both variables. Besides, mechanisms of CHD are complex and could not be explained and detected just by FSC, which has some limitations [23,24].

Some limitations of this exploratory study are the sample size (which might have contributed due to the lack of association among some variables), for which there is a lack of an imaging method to confirm a true correlation between VAI, LAP, DAAT and visceral adipose tissue. A small number of men's were included in the study and their cross-sectional design is different from a longitudinal study that, does not detect the real risk between these measurements of visceral obesity, incidence of type-2 diabetes and CHD. Besides, no data were available about cholesterol lowering drugs. We emphasize, however, that our data are very informative and could be a good guide for upcoming studies using imaging techniques as a diagnostic tool.

In conclusion, we found a positive relation of DAAT and LAP with type-2 diabetes and VAI with a 10-year risk of cardiovascular disease, independent of overall obesity. Our data need to be confirmed in other populations, but these simple tools for assessment of visceral fat tissue should be considered in the clinical practice.

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