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Adiposity phenotypes are associated with type-2 diabetes: LAP index, body adiposity index, and neck circumference

Aline Marcadenti [a, b], Flavio D. Fuchs [a, c], Leila B. Moreira [a], Miguel Gus [a, c], Sandra C. Fuchs [a, d, *]

[a] Postgraduate Studies Program in Cardiology, School of Medicine, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil
[b] Department of Nutrition, Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, RS, Brazil
[c] Division of Cardiology, Hospital de Clínicas de Porto Alegre, Porto Alegre, RS, Brazil
[d] Postgraduate Studies Program in Epidemiology, School of Medicine, Universidade Federal do Rio Grande do Sul, R. Ramiro Barcelos 2600, CEP 90035-003, Porto Alegre, RS, Brazil

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ABSTRACT

Background and aims: Adiposity phenotypes can be detected by anthropometric indexes associated with type-2 diabetes mellitus (T2DM). Besides body mass index (BMI) and waist circumference (WC), new indices seem to be able to identify T2DM. This study aimed to evaluate independent associations of T2DM with lipid accumulation product (LAP index), neck circumference (NC) and body adiposity index (BAI) in patients with hypertension.
Methods: A cross-sectional study was carried out among 430 patients with hypertension. The T2DM diagnosed was standardized. WC and NC (cm) were measured and BMI was calculated. LAP index was calculated separately for men [(WC-65) × TG] and women [(WC-58) × TG]; BAI was evaluated in percentiles according to hip (cm)/[height (m)$^{1.5}$]-18.
Results: Participants were aged 58.3 ± 11.7 years, had systolic blood pressure (SBP) 154.2 ± 24.9 mmHg, diastolic blood pressure (DBP) 89.0 ± 14.7 mmHg, and BMI 30.1 ± 6.0 kg/m^2. There was 145 men and 285 women, and 142 participants had T2DM. Analyses carried out separately by gender showed that among men, BAI at the 75th percentile increased about 60% the risk of T2DM, while among women, those in the upper quartile of LAP and NC had increased risk of T2DM (prevalence ratio (PR): 2.93; 95%CI: 1.62–5.28 and 3.30; 95%IC: 1.78–6.14, respectively), after adjustment for potential confounders.
Conclusions: Adiposity phenotypes such as LAP index and neck circumference were independently associated with T2DM in hypertensive women, and BAI was associated with T2DM in men.

1. Introduction

The dysfunction of the adipose tissue is one of the mechanisms responsible for systemic metabolic complications, such as low-grade inflammation, insulin resistance, and dyslipidemia [1]. The detection of differences in the morphology and secretory function of adipose tissue deposits showed that they have distinct inflammatory profiles as well as associations with insulin resistance and metabolic syndrome [2]. In patients with severe obesity, systemic insulin resistance was linked to inflammation in both subcutaneous and visceral adiposity depots. The findings suggest that examination of subcutaneous regions easily accessible by transcutaneous biopsy may be useful in clinical studies designed to investigate disease-associated adiposity phenotypes [3]. On the other hand, anthropometric indices have been used to establish adiposity phenotypes and their associations with diseases.

The accumulated fat in the abdominal region, which includes fat from the subcutaneous and the visceral adipose tissue (VAT), is a risk factor for type-2 diabetes (T2DM) [4] and hypertension [5,6]. However, fat from abdominal cavity organs is more strongly associated with hypertension [7,8], T2DM [8,9], cardiovascular disease [10,11], and mortality [12] than subcutaneous adiposity tissue (SAT). In addition, although waist circumference (WC) does not distinguish VAT from SAT compartments in the abdomen [13], it is a better predictor of hypertension and T2DM [4,6] than body mass

* Corresponding author. Centro de Pesquisa Clínica, 5º Andar, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul, Ramiro Barcellos, 2350. 90.035-903, Porto Alegre, RS, Brazil
E-mail addresses: scfuchs@terra.com.br, sfuchs@hcpa.edu.br (S.C. Fuchs).

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index (BMI) [5]. In the attempt to identify an anthropometric index able to assess visceral obesity independently of total adiposity, some non-traditional anthropometric indicators have been investigated.

Lipid accumulation product index (LAP) [14] has been used to detect impaired glucose tolerance and insulin resistance among individuals with higher risk for cardiovascular disease [15,16] and T2DM [17,18] in the general population. Body adiposity index (BAI) [19] is an option to BMI in determining the percentage of body fat, which is correlated with insulin sensitivity in obese women [20], T2DM in Caucasians [12] and emerging cardiovascular risk factors among young people [21]. However, in a middle-age adult population, variation of BAI was positively associated with changes in systolic and diastolic blood pressure, urinary excretion of albumin, but not with left ventricular mass [22]. Neck circumference (NC) has been characterized as a pathogenic fat depot correlated with VAT, detected by imaging methods, and with other adiposity indicators as WC [23]. NC has been associated with increased levels of fasting plasma glucose [24,25] and insulin resistance in the general population [26]. Among these several anthropometric indicators, LAP index and NC seem to be potentially able to discriminate the visceral compartment as a predictor of cardiovascular risk [14,24]. Therefore, the aim of this study was to evaluate adiposity phenotypes associated with type-2 diabetes: LAP index, BAI, and NC in patients with hypertension.

2. Patients and methods

2.1. Study population

This cross-sectional study enrolled men and women, aged 18–80 years, with hypertension, selected from primary health care centers, outpatient hypertension clinic of a reference center (Hospital de Clinicas de Porto Alegre, HCPA), or from the general population, for evaluation and management of hypertension. Participants were mostly from low and middle-income families, of Porto Alegre, in southern Brazil.

This analysis included 430 patients with hypertension with no diagnosis of heart failure, myocardial infarction, or stroke in the six months prior to the enrollment, or other relevant chronic diseases. Pregnant women were excluded. The study protocol was approved by the Ethics Committee of the Hospital de Clínicas de Porto Alegre (GPPG number 04–465), which is accredited by the Office of Human Research Protections as an Institutional Review Board. A written informed consent was obtained from all participants, which was in accordance with the Declaration of Helsinki.

Demographic data (age, sex and self-reported skin color) and information regarding education (years at school) and lifestyle characteristics (smoking, abusive alcohol consumption, physical activity) were collected using a standardized questionnaire by trained interviewers. Alcohol consumption was detected by type, frequency, and quantity of each beverage. Men and women who had consumed at least 30 or 15 g of ethanol per day, respectively, were classified as having abusive consumption. Current or ex-smokers were those participants who had smoked 100 or more cigarettes during lifetime *vs.* never smokers. The International Physical Activity Questionnaire (IPAQ) was used to evaluate physical activity, which was categorized as low to moderate *vs.* high [27].

Trained medical students, under the supervision of an attending physician, performed standardized measurements of anthropometric indexes and blood pressure (BP). BP was determined using an aneroid sphygmomanometer with an adequate sized cuff to the arm circumference. Hypertension was diagnosed by systolic BP $\geq$ 140 or diastolic BP $\geq$ 90 mmHg (average of six measurements obtained in three visits) or use of antihypertensive lowering agents [28]. Fasting blood glucose $\geq$126 mg/dl, glycated hemoglobin $\geq$6.5% or previous medical diagnosis were used to detect patients with T2DM [29].

Weight (kg) was measured with patient using light clothes, barefoot, in a 100 g scale (Filizola®, model 31, IN Filizola - SA, Sao Paulo, Brazil). Height was obtained with patient barefoot in the standing position, and with both arms hanging freely at the side with palms facing thighs, using a Tonelli® stadiometer with 0.1 cm scale, model E120 A (IN Tonelli - SA, Santa Catarina, Brazil). BMI was calculated by 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 patient standing in both feet, approximately 20 cm apart, and with both arms hanging freely. The cut-off points for abdominal obesity were defined according to World Health Organization criteria ($\geq$88 cm, for women, $\geq$ 102 cm, in men). NC was measured with the head straight and eyes staring forward, horizontally, one inch above the laryngeal prominence. Hip circumference was measured at the level of the widest circumference over the buttocks with the research assistant kneeling at the side of the participant, so that the level of maximum extension could be seen. The anthropometric measurements were carried out in duplicate, one week apart, by certified interviewers independently and periodically reassessed. BAI was calculated using the formula: hip (cm)/[height (m)$^{1.5}$]-18 [19].

Serum triglycerides were measured by calorimetric enzymatic method, at the certified laboratory of the Hospital. LAP index was calculated from WC, in centimeters, plus serum triglycerides, in mmol, for men [(WC-65) × TG] and women [(WC-58) × TG] [14].

2.2. Sample size and statistical analysis

A minimum sample from 368 patients would be necessary to detect a prevalence ratio of at least 1.9, with 80% power and a 95% confidence interval (CI), with a prevalence of T2DM estimated in 28% in obese and 15% in non-obese patients [14], and with a 3:1 exposed to non-exposed ratio. Data were expressed as mean ± standard deviation (SD) or frequency (%). T-test (with Welch correction) and Pearson's chi-square test were used in the Statistical Package for the Social Science (SPSS), version 17.0, IL, USA. Pearson's Correlation was used to detect correlation among anthropometric indicators. The assumptions of normal distribution of data and homogeneity in variances were tested using the Shapiro-Wilks test (for normal distribution) and Levene's test (for homogeneity of variances).

LAP index and NC were presented in quartiles and BAI was categorized at the 75th percentile, separated for men and women ($\geq$31.6%, in men; $\geq$41.5%, in women). The associations between anthropometric indexes and T2DM were analyzed by Modified Poisson Regression and expressed as prevalence ratio (PR) and 95% CI, after the control for confounding factors. In addition, based on C-statistic, areas under the receiver operating characteristic curves (ROC-AUC) were calculated. The ROC-AUC of the five anthropometric indicators were compared using a nonparametrical test [30]. Besides the cut-off at the 75th percentile, BAI was also tested at the 12th percentile, separated for men and women ($\geq$25.7%, in men; $\geq$31.0%, in women). Sensitivity, Specificity, positive and negative probability post-test (PPPT and NPPT) were calculated. Finally, the net reclassification improvement (NRI), as a category-based NRI, of the new indicators was compared with standard obesity indicators [31,32].

3. Results

A total of 145 men and 285 women were assessed, with an