What is the relationship between visceral adiposity index (VAI) and total and free sex hormones in aging polish women?

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ABSTRACT

The visceral adiposity index (VAI) is a novel and very sensitive cardiometabolic predictor. The number of cardiovascular diseases in women increases with climacteric transformation. In 505 women aged over 65 years, randomly selected from the whole of Poland, we investigated whether VAI score was associated with sex hormones. We split the women into two groups on the basis of a VAI cut-off score of 2.0. In the group with normal VAI scores, we found significantly higher serum testosterone levels and a lower free estradiol index vs the group with abnormal VAI scores. VAI correlated positively with fasting glucose and insulin levels and with homeostatic model assessment of insulin resistance (HOMA-IR). Our data suggest a cardiometabolic protective role of testosterone in aging women.

KEYWORDS

Visceral adiposity index, cardiometabolic risk.

Introduction

Cardiovascular diseases are the most frequent cause of mortality in aging women. The term "cardiometabolic risk" was coined by the American Diabetes Association and American Heart Association to describe the overall risk of developing type 2 diabetes and cardiovascular diseases [1].

Today, waist circumference (WC) is the measure most commonly used to identify visceral obesity [2]. Yet we are still looking for a more precise cardiometabolic risk predictor [3]. Amato et al. proposed the visceral adiposity index (VAI) — a mathematical model based on simple parameters, both anthropometric (body mass index – BMI, WC) and functional (serum triglycerides – TG and high-density lipoprotein cholesterol – HDL-C) — as a marker of insulin resistance [4]. It has been demonstrated that an elevated VAI is associated with cardiometabolic risk predictors.

It must be also considered that total and free sex hormones as well as sex hormone-binding globulin (SHBG) play an important role in fat mass and fat distribution in women [5, 6]. This is best exemplified by fat redistribution during the climacteric transition, when visceral fat deposition increases and gynoid fat deposition decreases [7, 8]. As a consequence of the association of visceral obesity with insulin resistance, the majority of postmenopausal women presented increased cardiometabolic risk predictors and cardiovascular disease [9]. In contrast to the reproductive years and menopause, periods in a woman's life in which sex hormones are known to play a cardioprotective role, the associations between sex hormones and cardiometabolic risk predictors in aging women are not clear [6, 10].

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The goal of our study was to examine how VAI score was associated with serum levels of SHBG, estradiol (E2) and testosterone (T) and with the free estrogen index (FEI) and free androgen index (FAI) in aging women.

Material and methods

The research sample comprised 505 women aged 65-103 years recruited from the whole of Poland. The recruitment procedure has been described in a previously published paper [11]. We measured BMI and WC in all the women according to World Health Organization recommendations [12]. Blood samples were drawn from the cubic vein in the morning after an overnight fast and immediately centrifuged and stored at -20°C.

The biochemical and hormonal parameters investigated included: serum fasting glucose (FG), total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C) and TG, measured by an enzymatic method using Architect Plus 4100 by Abbott Diagnostica, Illinois, USA.

Fasting insulin (FI), T, E2, and SHBG levels in serum were estimated by a chemiluminescent method using Immulite 2000 by Siemens Healthcare, Erlangen, Germany. The FAI was cal-

culated by the formula: 100 x testosterone [nmol/l] / SHBG [nmol/l]. To convert testosterone to nanomolar values, the nanogram per mililiter value is multiplied by 3.47. Likewise, the FEI was calculated using the following formula: 100 x estradiol [nmol/ml] / SHBG [nmol/l]. To convert E2 to nanomolar values, the picogram per milliliter value is multiplied by 0.00367 [13, 14]. The VAI score was calculated as described elsewhere [15] using following formula: Female VAI = [WC/ 36.58 + (1.89 x BMI)] x (TG/0.81) x (1.52/HDL-C). The homeostatic model assessment – insulin resistance (HOMA-IR) value was calculated from the formula: (FG [nmol/l] x FI [mUI/l])/22.5 [16]. We divided the whole group into two subgroups on the basis of a VAI cut-off score of 2.0, which was suggested by Amato et al. for women over 65 years of age [4]. VAI scores above 2.0 were present in 151 (30%) women, while 354 (70%) had scores below 2.0. In both groups, we compared the mean values of serum E2, FEI, T, FAI, SHBG, FG, FI and HOMA-IR. Also, correlations between VAI score and sex hormones as well as carbohydrate metabolism parameters were estimated.

Ethical approval

Ethics Committee approval was obtained. The PolSenior project was approved by the Bioethics Commission of the Medical University of Silesia in Katowice, Poland. This study was performed after the patients, who had been informed in detail about the study, had signed an informed consent form, prepared according to the principles of the Helsinki Declaration [17].

Statistical analysis

The Statistical Packages for Social Sciences SPSS version 17 and MedCalc version 11.3 were used for data analysis. Baseline characteristics were presented as mean ± standard deviation (SD) for continuous variables. Normality of distribution for quantitative data was assessed by the Kolmogorov-Smirnov test. Differences between groups in univariate analysis were detected by the unpaired Student's t-test. Spearman's rank correlation test was used to estimate the associations between sex hormones and cardiovascular risk predictors.

Results

The mean values ± SD of BMI, WC, biochemical parameters (TC, HDL-C, LDL-C, TG, FG, FI, HOMA-IR) and hormonal parameters (E2, FEI, T, FAI) in a group of aging women are presented in table 1. The mean values ± SD of serum T, E2, SHBG and FG, FI as well as the FAI, FEI and HOMA-IR values calculated in a group of aging women with VAI scores > or < 2.0 are presented in table 2. Women with VAI scores above 2.0 presented statistically significantly lower serum T levels and FAI scores, and higher FEI scores. Also, serum SHBG levels were significantly lower in the group with VAI > 2.0. With regard to carbohydrate metabolism, women with VAI > 2.0 showed significantly higher serum FG, FI and HOMA-IR values.

Table 1

	Mean±SD
Age (years)	75.57±11.47
BMI (kg/m^2)	27.55±4.42
WC (cm)	92.27±1.44
TC (mg/dl)	210.52±43.63
HDL-C (mg/dl)	59.39±13.25
LDL-C (mg/dl)	126.86±37.69
TG (mg/dl)	116.29±48.45
FG (mg/dl)	91.96±11.38
FI (IU/ml)	6.30±4.1
HOMA-IR	1.47±1.04
E_2 (pg/ml)	6.51±2.56
FEI	0.04±0.02
T (ng/ml)	0.3±0.18
FAI	1.24±1.28
SHBG (nmol/l)	69.00±32.52

- To convert E2 to nanomolar, the picogram per milliliter value is multiplied by 0.00367.
- To convert T to nanomolar, the nanogram per mililiter value is multiplied by 3.47.
- To convert FG to mmol/l, the milligram per deciliter value is multiplied by 0.056.
- To convert TC, HDL-C, LDL-C to mmol/l, the milligram per deciliter value is multiplied by 0.011.
- To convert TG to mmo/l, the milligram per deciliter value is multiplied by 0.026.

Table 2

	VAI > 2.0 (n=131)	VAI < 2.0 (n=354)	Statistical significance
T (ng/ml)	0.15±0.09	0.22±0.20	p=0.0001
E_2 (pg/ml)	6.46±2.45	6.53±2.63	NS
SHBG	59.72±27.55	72.90±33.93	p=0.00001
FG	95.52±10.35	90.44±11.56	p=0.00001
FI	7.16±4.46	5.96± 3.90	p=0.002
FAI	1.11±0.09	1.30±1.24	p=0.04
FEI	0.05±0.03	0.04±0.02	p=0.00001
HOMA-IR	1.73±1.12	1.37±0.99	p=0.0003

We also estimated correlations between VAI score and sex hormones, as well as between VAI score and serum FG, FI and HOMA IR. We did not find any statistically significant correlation between VAI score and serum T, E2, FAI and FEI values in aging women. In contrast, VAI score was significantly correlated with FG (r=0.17; p=0.04), FI (r=0.24; p=0.04) and HOMA-IR (r=0.24; p=0.003) in aging women.

Discussion

It has been shown that VAI can be a useful tool for early detection of a condition of cardiometabolic risk, before it develops into an overt metabolic syndrome. It has also been observed that VAI correlates independently with insulin resistance in various endocrine diseases, such as acromegaly, poly-

cystic ovary syndrome (PCOS), type 2 diabetes, non-alcoholic fatty liver disease, viral hepatitis C and prolactinoma [15, 18, 19, 20].

The VAI is a useful indicator for evaluation of cardiometabolic risk with higher sensitivity and specificity than classical parameters such as WC, BMI and lipids, which are routinely used in order to evaluate visceral adipose function [21, 22, 23].

In the whole group of aging women investigated in this study, 30% presented elevated VAI scores, which were associated with lower serum T and SHBG levels compared with those recorded in the group with VAI scores < 2.0. It can be suggested that serum T may play a cardiometabolic protective role in aging woman.

However, normoglycemic women with PCOS and hyperandrogenism have been shown to present comparable VAI scores vs women with pre-diabetes [22]. Also, in another paper, it was shown that VAI scores in women with PCOS and in healthy controls were comparable. However VAI scores in obese vs non-obese women were significantly higher in the obese group [20, 24].

We also found higher serum FG, FI and HOMA-IR values in aging women with VAI scores > 2.0. Our results seem to be supported by data which show significantly higher HOMA-IR values in women with PCOS and elevated VAI scores [21, 22]. In contrast to Amato et al. data, we did not find correlations between biological age and VAI score [4]. However, this was a different ethnic population.

Investigating VAI score associations with serum T and E2, as well as FAI, FEI and SHBG, we did not find any correlations. Only in one study was FAI score found to correlate positively with VAI in women with PCOS, but it did not correlate with sex hormones, as it does in our study [22]. So, the association of VAI score with sex hormones in aging women needs further study. Similarly to other investigators, we found statistically significant correlations between VAI score and HOMA-IR [21, 22].

In conclusion, our original data show that the use of a VAI cut-off score of 2.0 for aging women can be a simple and useful method for identifying women with cardiometabolic risk. Also, it must be considered that serum T levels play a cardiometabolic protective role in aging women, in contrast to FEI, and this is an aspect that needs further study.

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