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The applicability of the Visceral Adiposity Index (VAI) for predicting visceral fat

Aplicabilidade do Índice de Adiposidade Visceral (IAV) como preditor de gordura visceral

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Abstract – As obesity has reached epidemic proportions and given the current recognition of central adiposity as an important cardiometabolic risk factor, several researchers have focused on developing and validating predictive indexes and equations to evaluate Visceral Adipose Tissue (VAT). This study evaluates the applicability of the Visceral Adiposity Index (VAI) for predicting cardiometabolic risk in individuals treated in a hospital In the northeast region of Brazil. The VAT was evaluated by computed tomography (CT) and the VAI was calculated through specific equations for each gender. The sample involved adult and elderly patients of both genders followed up in a cardiology outpatient clinic. The following cardiometabolic parameters were collected: fasting glycemia, glycated hemoglobin, lipid profile, C-reactive protein (CRP) and uric acid. The simple linear regression was used to evaluate the explanatory power of the VAI in relation to the volume of VAT determined by CT. The predictive capacity of VAI in relation to the volume of VAT determined by CT was 25.8% (p=0.004) for males and 19.9% (p<0.001) for females. VAI correlated strongly with the triglyceride (TG) (p<0.001) and TG/high-density lipoprotein (HDL) ratio (p<0.001) and inversely correlated with HDL (p<0.001). Moreover, VAI showed low correlation with the following variables: abdominal circumference, total cholesterol, low density lipoprotein, fasting glycemia, and glycated hemoglobin (p<0.05). VAI was associated with variables considered as cardiometabolic risk factors, but exhibited a low predictive capacity regarding the volume of VAT determined by CT. Thus, caution is recommended in its use in Brazilian individuals.

Keywords: Abdominal obesity; Cardiovascular abnormalities; Metabolic syndrome.

Resumo – *Em razão de a obesidade ter alcançado proporções epidêmicas e dado ao atual reconhecimento da adiposidade central como um importante fator de risco cardiometabólico, diversos pesquisadores têm se dedicado em desenvolver e validar índices e equações preditivas para avaliar o Tecido Adiposo Visceral (TAV). Este estudo avaliou a aplicabilidade do Índice de Adiposidade Visceral (IAV) como preditor de risco cardiometabólico em indivíduos atendidos em um hospital no nordeste brasileiro. O TAV foi avaliado por tomografia computadorizada (TC) e o IAV foi calculado através de equações específicas para cada sexo. A amostra envolveu pacientes adultos e idosos de ambos os sexos acompanhados no ambulatório de cardiologia. Os seguintes parâmetros cardiometabólicos foram coletados: glicemia de jejum, hemoglobina glicada, perfil lipídico, proteína C-reativa e ácido úrico. Regressão linear simples foi empregada para avaliar o poder explicativo do IAV em relação ao volume de TAV determinado por TC. A capacidade preditiva do IAV em relação ao volume de TAV determinado pela TC foi de 25,8% (p=0,004) para o sexo masculino e 19,9% (p<0,001) para o sexo feminino. O IAV se correlacionou fortemente com as variáveis TG (r=0,916, p< 0,001) e TG/HDL (r=0,952, p<0,001) e inversamente com o HDL (r=-0,441, p<0,001), além disso, apresentou baixa correlação com as variáveis: circunferência abdominal, colesterol total, lipoproteína de baixa densidade, glicemia de jejum e hemoglobina glicada (p<0,05). O IAV associou-se com variáveis consideradas fatores de risco cardiometabólico, porém exibiu baixa capacidade preditiva em relação ao volume de TAV determinado pela TC, sendo recomendada cautela em sua utilização em indivíduos brasileiros.*

Palavras-chaves: *Obesidade abdominal; Anormalidades cardiovasculares; Síndrome metabólica.*

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INTRODUCTION

Central adiposity, which is considered as an important cardiometabolic risk factor[1], represents fat accumulation in the abdominal region and is characterized by the two following distinct fat compartments: subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT)[2]. These compartments present different metabolic and functional behaviors[3], with the second being metabolically more active and deleterious on cardiometabolic parameters[1].

Computed tomography (CT) is considered the other standard method for VAT quantification[4]. Notwithstanding, it has some disadvantages, such as high cost and complexity, low accessibility, long execution time, and risk of exposure to ionizing radiation[5]. Anthropometric measures are also considered as tools of evaluation of corporal and abdominal adiposity. However, they are not able to differentiate subcutaneous and visceral fat, which are considered as predictive methods[6].

Studies demonstrated that the use of anthropometric parameters in association increase the accuracy in VAT estimation and help reducing the limitations of each isolated variable[7]. In this context, several researchers have focused on developing and validating predictive indexes and equations to evaluate VAT[8], which consist of mathematical models based on the combination of simple, accessible, less invasive, and lower cost parameters, such as anthropometry, that can offer a highly significant evaluation of abdominal fat accumulation while exempting the disadvantages of reference methods, such as imaging tests[7,8].

The Visceral Adiposity Index (VAI) consists of a mathematical model that uses anthropometric indicators (body mass index (BMI) and abdominal circumference (AC)) and biochemical parameters such as triglycerides (TG) and high-density lipoprotein (HDL), being widely used as a predictor of VAT and in the screening of cardiometabolic risk[9,10].

Amato et al.[9] created and validated the VAI in 1.498 primary health care patients in Italy with a BMI between 20 and 30 kg/m^2, obtaining a strong correlation with the VAT, which was identified by magnetic resonance imaging and expressed an inverse correlation with insulin sensitivity, being indicated as a useful marker for the screening of cardiometabolic risk associated with visceral obesity.

Although several studies confirm the usefulness of using VAI in populations of different races and ethnicities, it is necessary that previous validation occurs in population groups different from the one in which it was validated[11], since fat distribution varies between genders, age, and race[1]. In Brazil, some studies have used VAI as a cardiometabolic risk marker[12,13], but few evaluated its applicability compared to a reference method in the Brazilian population. In this context, the objective of this study is to evaluate the applicability of VAI in a Brazilian sample.

METHOD

The validation study was developed at an outpatient nutrition clinic of a public university hospital that is reference in cardiology in the Brazilian Northeast, with data collection being carried out from 2013 to 2015 and involving 115 adult and elderly individuals of both genders and aged ≥20 years.

The sample size was calculated considering an α error of 5%, a β error of 20%, an estimated mean correlation between VAI and VAT of 0.5 (p) obtained in a pilot study, and a variability of 0.15 (d^2). Using the formula $n= [(Z_{\alpha/2}+Z_{\beta/2})^2 x (p x (1-p)]/d^2$, the minimum sample size of 88 individuals was obtained. To correct any losses, the sample was increased by 30%, resulting in 115 sample units.

The sample was constructed based on voluntary adherence and patients were selected on a first visit. Individuals with physical limitations that prevent them to perform the anthropometric evaluation; patients with edema, ascites, anasarca, hepato and/or splenomegaly; individuals in recent postoperative recovery of abdominal surgery and/or who underwent surgical treatment for weight loss; pregnant women and women who had children up to 6 months before the survey was screened; individuals on medication that can cause lipodystrophy or under medication for weight loss; patients with consumptive diseases; and individuals with claustrophobia were excluded from the study.

The protocol of this study was based on the ethical norms for research involving human beings contained in Resolution 466/12 of the National Health Council, being submitted to the evaluation of the Research Ethics Committee on Human Beings of the University of Pernambuco (UPE) and approved under the protocol number 271.400/2013. The individuals were previously informed of the research objectives, as well as of the methods adopted and, through their agreement, signed a free and informed consent form.

The VAT was evaluated by Computed Tomography (CT), using a Philips Brilliance CT-10 slice tomograph (*VMI Indústria e Comércio Ltda, Lagoa Santa, MG*, Brazil). The test was performed after a four-hour fasting with the patient in the supine position. The tomographic section was obtained with the radiographic parameters of 140 kV and 45 mA at the L4 level, having a thickness of 10 mm. The total abdominal fat area and the visceral fat area were manually delineated with a free cursor by circumventing each region. All skin surfaces were excluded from the marking area. The VAT area was determined by taking the inner borders of the rectus abdominis and the internal oblique and lumbar quadrants, by excluding the vertebral body, and by including the retroperitoneal, mesenteric, and omental fat, being described in cm^2. To identify the adipose tissue, the density values of -50 and -250 Hounsfield were used[14].

The VAI was calculated according to the following gender-specific equations (Equations 1 and 2) developed by Amato et al.[9], where the body mass index (BMI) is expressed in kg/m^2, the abdominal circumference (AC) is expressed in cm, and biochemical parameters such as triglycerides (TG) and high density lipoprotein (HDL) are expressed in mmol/L.

Male:

$$\text{VAI} = \left(\frac{AC}{39.68 + (1.88 x IMC}\right) x \left(\frac{TG}{1.03}\right) x \left(\frac{1.31}{HDL}\right) \quad (1)$$

Female:

$$\text{VAI} = \left(\frac{AC}{36.58 + (1.89 x IMC}\right) x \left(\frac{TG}{0.81}\right) x \left(\frac{1.52}{HDL}\right) \quad (2)$$

Among anthropometric measures, the body mass index (BMI) was evaluated according to the equation recommended by the World Health Organization[15], and the abdominal circumference (AC) was measured at the midpoint between the last rib and the iliac crest[16].

The following biochemical parameters were evaluated: fasting glycemia, glycated hemoglobin (HbA1C), lipid profile (triglycerides (TG), total cholesterol (TC) and fractions, non-HDL cholesterol, and the TG/HDL-c ratio), C-reactive protein (CRP), and uric acid. A fasting period from 9 to 12 hours was required to collect the samples, considering a preparation protocol for the institution's

exams[17]. Glycemia, lipid profile, and uric acid were analyzed by the enzymatic method, and HbA1c and CRP were analyzed by turbidimetry. Biochemical analyzes were performed using an integrated Cobas 400® analyzer (Roche Diagnostics) at the Clinical Analysis Laboratory in service. The TG/HDL-c ratio was used as the atherogenicity index by reflecting the particle size of LDL-c[18]. Data on anthropometric, biochemical and CT were collected on the same day.

Data on age, gender, and race were collected among the demographic variables. The race was self-defined by the interviewee, considering white, brown, and black[19], being later dichotomized in white and non-white individuals. Regarding clinical variables, the presence of comorbidities such as systemic arterial hypertension (SAH), diabetes mellitus (DM), and metabolic syndrome (MS) were evaluated. SAH and DM were considered when the patient reported their previous diagnosis issued by the physician, the use of antihypertensive or hypoglycemic drugs, and/or the registry in his/her medical record. MS was determined according to the criteria described by the National Cholesterol Education Program[20].

The data were analyzed using the Statistical Package for Social Sciences - SPSS version 13.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were tested for normality of distribution by the Kolmogorov Smirnov test and were described as mean and standard deviation when presenting normal distribution. The Student-t test for independent samples was used to compare the means of anthropometric, biochemical, and visceral fat parameters between genders. The proportions were compared by Pearson's Chi-square test.

The Pearson or Spearman coefficients were used to evaluate the relationship between VAT and VAI with the anthropometric and metabolic parameters. The simple linear regression was used to evaluate the explanatory power of the VAI in relation to the volume of VAT determined by CT. Statistical significance was considered when the p value <0.05.

RESULTS

A total of 115 individuals with mean age of 55.7 (±11.8) years were included, who were predominantly female (72.2%) and presenting a higher proportion of non-white individuals (72.2%). The prevalence of SAH, DM, and MS prevalences were 66.1%, 27.8%, and 53.9%, respectively.

Table 1 describes the sample characteristics by gender. There was no statistically significant difference for age, BMI, lipid profile, fasting glycemia levels, HbA1C, CRP, and prevalence of SAH, DM, and MS between genders (p>0.05). Although all of these characteristics were similar, males presented higher values of AC (p=0.047), higher levels of uric acid (p<0,001), and higher concentration of VAT by the reference method.

The predictive capacity of the VAI (r^2) in relation to the VAT volume determined by the CT was 25.8% (p=0.004) for males and 19.9% (p<0.001) for females, as can be observed in Figures 1 and 2, respectively.

VAT presented a moderate correlation with the variables BMI, AC, TG, TG/HDL, and uric acid (r>0.400, p<0.001) and inverse correlation with HDL (r= -0.329, p<0.001).

VAI correlated strongly with TG (r= 0.916, p<0.001) and TG/HDL (r= 0.952, p<0.001) and correlated inversely with HDL (r= -0.441, p<0.001). The index also presented a low correlation with the following variables: AC, CT, LDL, fasting glycemia, and HbA1c (p<0.05) (Table 2).

Table 1. Characteristics of the sample, stratified by gender (n=115).

Variable	Male (n=32)	Female (n=83)	**p-value***
Age, years (average/SD)	56.5 (±11.3)	55.4 (±12.0)	0.636
BMI, kg/m2 (average/ SD)	29.5 (±5.6)	30.0 (±5.6)	0.720
AC, cm (average/SD)	103.3 (±14.0)	97.7 (±13.3)	0.047
TC, mg/dl (average/SD)	204.0 (±54.5)	203.1 (±53.7)	0.931
HDL, mg/dl (average/SD)	45.0 (±12.1)	52.9 (±21.3)	0.052
LDL, mg/dl (average/SD)	129.0 (±45.4)	121.8 (±46.4)	0.454
TG mg/dl (average/SD)	162.1 (±115.7)	149.1 (±85.0)	0.509
Fasting glycemia, mg/dl (average/SD)	111.0 (±26.5)	115.5 (±46.0)	0.601
HbA1C, mg/dl (median/IQ)	6.4 (6.1-6.9)	6.5 (6.1-7.2)	0.671
Uric Acid, mg/dl (average/SD)	5.9 (±1.6)	4.7 (±1.2)	<0.001
CRP, mg/dl (average/SD)	3.1 (±5.5)	5.1 (±5.3)	0.150
VAI (average/SD)	2.5 (±2.1)	2.9 (±2.3)	0.403
VAT, cm2 (average/SD)	339.0 (±124.6)	252.7 (±76.0)	<0.001
Arterial hypertension Sistemic (n, %)	23 (71.9)	53 (63.9)	0.522
Diabetes Mellitus (n, %)	7 (21.9)	25 (30.1)	0.514
Metabolic Syndrome (n, %)	15(46.9)	47 (56.6)	0.465

*Student's t-test for comparison of average, Mann Whitney's U-test for comparison of medians and Chi-square of Pearson for comparison of proportions. SD: Standard Deviation; BMI: Body Mass Index; AC: Abnominal circumference; TC: total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; TG: triglycerides; HbA1C: glycated hemoglobin; CRP: C-reactive protein; VAI: visceral adiposity index; VAT: Visceral Adipose Tissue.

Table 2. Correlation between VAT and VAI with cardiometabolic parameters and inflammatory status in both genders (n=115).

Variable	VAT r	VAT p-value	VAI r	VAI p-value
Age	0.143	0.127	0.069	0.477 [1]
BMI	0.424	<0.001	0.163	0.088 [1]
AC	0.616	<0.001	0.279	0.003 [1]
TC	0.134	0.156	0.281	0.003 [1]
LDL	0.129	0.171	0.207	0.030 [1]
HDL	-0.329	<0.001	-0.441	<0.001 [1]
TG	0.438	<0.001	0.916	<0.001 [1]
TG/HDL	0.463	<0.001	0.952	<0.001 [1]
Fasting glycemia	-0.004	0.963	0.224	0.020 [1]
HbA1C	0.187	0.053*	0.226	0.022 [2]
CRP	0.126	0.252	-0.037	0.747 [1]
Uric Acid	0.455	<0.001	0.169	0.102 [1]

[1]Pearson's correlation; [2]Spearman's correlation. VAT: Visceral Adipose Tissue; VAI: visceral adiposity index; BMI: Body Mass Index; AC: Abdominal circumference abdominal; TC: Total cholesterol; LDL: low density lipoprotein; HDL: High density lipoprotein; TG: triglycerides; HbA1C: glycated hemoglobin; CRP: C-reactive protein.

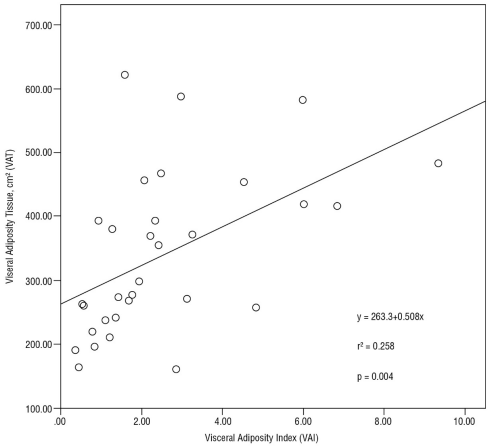

Figure 1. Simple linear regression between the Visceral Adiposity Index (VAI) and the Visceral Adipose Tissue (VAT) obtained by computed tomography in males.

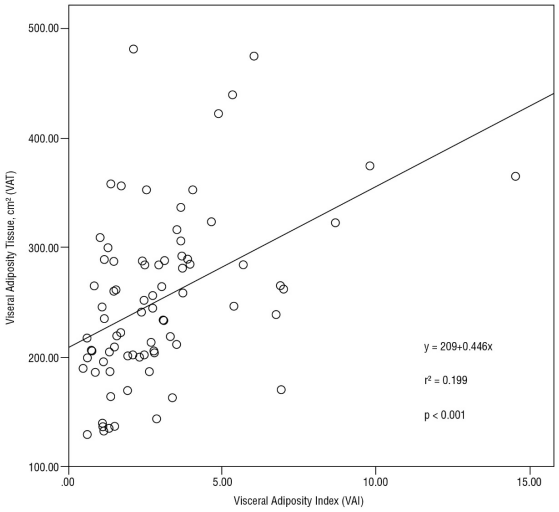

Figure 2. Simple linear regression between the Visceral Adiposity Index (VAI) and the Visceral Adipose Tissue (VAT) obtained by computed tomography in females.

DISCUSSION

The results showed better correlations of The VAI with variables considered as cardiometabolic risk factors, such as TG, TG/HDL, and HDL, with the latter of which being inverse. It is important to highlight that the predictive capacity of the VAI in relation to the volume of VAT determined by the reference method was low.

The utility of predictive measures and VAT volumes depends on their degree of association with reference methods that perform an accurate quantification of visceral fat, differentiating it from subcutaneous fat. In this study, the predictive capacity of VAI in relation to the VAT volume determined by CT was low, which contrasts with the results obtained by Amato et al.[9], who observed a strong association of VAI with VAT measured by magnetic resonance. Another study, conducted by Borruel et al.[21] evaluating Caucasian young adults reported a moderate association of VAI with VAT obtained by ultrasonography, although stronger correlations were obtained for AC and BMI.

These divergences can be attributed to the heterogeneity of sample characteristics, with differences in race, ethnicity, age, and gender among the populations studied[1]. Differences in the predictive value of indicators of obesity according to ethnicity were also reported in other investigations[22, 23].

It is important to emphasize that the authors who validated the index, in later clarifications[10,24], did not recommend its application in individuals with MS, with TG above 279 mg/dL, and with BMI ≥40 kg/m^2. In our study, although few individuals had TGs above this cut (10.4%) and only 5.5% had BMI ≥40 kg/m^2, we obtained a high prevalence of MS (53.9%). In addition, when comparing the characteristics of our sample with those of the group recruited for index formulation and validation in the original study by Amato et al.[9], we verified some differences. While our study found a mean age of 55.7 (±11.8) years, a female prevalence of 72.2%, and a BMI range from 18.9 to 44.5 kg/m^2, Amato et al.[9] reported a mean age of 43.46 (±14.3) years, female prevalence of 62.8%, and BMI from 20 to 30 kg/m^2.

Similar to the data found in the present study, Knowles et al.[25] and Schuster et al.[26] reported that the VAI showed a strong correlation with TG concentrations and an

inverse correlation with HDL. However, it is important to note that both biochemical parameters comprise the VAI equation, which may support the association found.[26]

The VAI also showed a strong correlation with the variable TG/HDL ratio in our findings. Du et al.[27], who evaluated the association between indicators of visceral adiposity and risk of diabetes, also found a correlation between VAI and the TG/HDL ratio. Other authors[28], when comparing the performance of VAI and the TG/HDL in the identification of individuals with an adverse cardiometabolic profile, have described that VAI seemed to offer no clinical benefit compared to the determination using the TG/HDL ratio. However, Peng et al.[24] attributed the result found by such authors to the racial difference of the study population.

Several authors reported an association of VAI with all the parameters of SM[25,27], which is a result also found in the present study. However, it is important to consider that three of the variables that make up the VAI (AC, TG, and HDL) are expressed in the SM criteria, thus being an indicator that reinforces the limitation of the use of VAI in patients diagnosed with SM[10].

When comparing the performance of the VAI with the VAT obtained by CT, we verified that the VAI correlated with a greater number of parameters, suggesting a better performance for tracking cardiometabolic risk. This finding should be interpreted with caution, considering the low explanatory power of the VAI in relation to the VAT. In addition, it should be considered that the parameters associated with VAI, which were not correlated with VAT (fasting glycemia, HB1AC, LDL-c, and CT), had a low correlation with the index.

Some limitations need to be considered in interpreting the presented results. This study did not present a random sample and the study participants were drawn from a reference hospital in cardiology. In addition, the prevalence of MS was greater than 50%. Since only outpatients were included and knowing the high prevalence of MS in the study population, the extrapolation of the data to the general population should be performed with due caution.

CONCLUSION

The present study showed association of VAI with several variables considered as cardiometabolic risk factors. However, when analyzing the predictive capacity of VAI in relation to the volume of VAT determined by the reference method (TC), a low explanatory power was found, recommending caution in its use in Brazilian individuals.

The results of this study evidenced the need for further research to evaluate the ability of VAI to predict VAT and to detect cardiometabolic abnormalities in population groups with a health profile and body fat distribution pattern different from the one that was evaluated in this study.

COMPLIANCE WITH ETHICAL STANDARDS

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Ethical approval

This study is affiliated to Emergency Cardiovascular University of Pernambuco and was approved by the ethics committee of the Ethics and Research Committee on Human Beings of the University of Pernambuco (UPE), being approved under protocol number 271.400/2013. It was was written in accordance with the standards set by the Declaration of Helsinki.

Conflict of interest statement

The authors have no conflict of interests to declare.

Author Contributions

Conception and design of the experiment: CPSP, ASD, IKGA. Realization of the experiments: CPSP, IGR, APDL. Data analysis: NFS, CPSP. Contribution with reagents/research materials/analysis tools: ASD, IKGA, APDL, IGR. Article writing: NFS, CPSP. All authors read and approved the final version of the manuscript.

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