



Original / Ancianos

# Discriminatory power of indicators predictors of visceral adiposity evaluated by computed tomography in adults and elderly individuals

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## Abstract

**Introduction:** Identifying anthropometric methods of abdominal adiposity, predictors of excess area of visceral adipose tissue (VAT) allows rapid and low cost evaluation for the risk of cardiovascular diseases in the elderly.

**Objective:** To evaluate the discriminatory power of anthropometric indicators for detection of excess of the area of VAT.

**Methods:** Cross-sectional study comprising 194 adults and elderly individuals for comparison of both sexes and age groups. Anthropometric variables: waist-to-height Ratio (WHtR), waist-to-thigh Ratio (WTR), Abdominal Diameter Index (ADI) and Sagittal Abdominal Diameter Height Index (SAD/Height). The VAT area was identified by computed tomography (CT). Analysis with the ROC curve.

**Results:** There was a high correlation between the VAT area and most of the anthropometric indicators ( $p \leq 0.001$ ). Among elderly men, WHtR showed areas under the ROC curve over 0.90 and cutoff of 0.55 (sens: 85.7%; spec: 82.4%, PPV: 99.9%). For older women, the WHtR cutoff was 0.58 (sens: 81.0%; spec: 78.6%). For the SAD/Height, the areas under the ROC curve were  $\geq 0.83$  ( $p \leq 0.01$ ), with cutoffs of 0.12 for men and 0.13 for women.

**Conclusion:** There was a strong discriminatory power of the anthropometric indicators abdominal visceral obesity. The WHtR and SAD/Height showed better performance to predict the VAT area of risk in elderly, without the need of measuring it by computed tomography.

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Key words: Anthropometry. Visceral adipose tissue. Computerized tomography. Cardiovascular disease. Elderly.

## PODER DISCRIMINATORIO DE LOS INDICADORES PREDICTORES DE ADIPOSIDAD VISCERAL EVALUADOS MEDIANTE TOMOGRAFÍA EN LOS ADULTOS Y LAS PERSONAS DE EDAD AVANZADA

### Resumen

**Introducción:** La identificación de métodos antropométricos de adiposidad abdominal, los predictores de exceso del tejido adiposo visceral (TAV) permiten una evaluación rápida y de bajo costo del riesgo de enfermedades cardiovasculares en ancianos.

**Objetivo:** Evaluar el poder discriminatorio de los indicadores antropométricos para la detección de exceso del tejido adiposo visceral.

**Métodos:** Estudio transversal compuesto por 194 adultos y ancianos para la comparación entre ambos sexos y por grupos de edad. Las variables antropométricas: Razón cintura/estatura (RCE), Razón cintura/muslo (RCM), el Índice Diámetro Abdominal (SAD/muslo) e el Índice diámetro abdominal altura (SAD/estatura). El área TAV fue identificado por tomografía computarizada. Análisis con la curva ROC.

**Resultados:** Se observó una alta correlación entre el área del tejido adiposo visceral y la mayoría de los indicadores antropométricos ( $p \leq 0,001$ ). Entre los hombres de edad avanzada, la razón cintura/estatura mostró áreas bajo la curva ROC por encima de 0,90 y puntos de corte de 0,55 (sens: 85,7%, espec: 82,4%, VPP: 99,9%). Para las mujeres de edad avanzada, el corte fue de 0,58 (sens: 81,0%, espec: 78,6%). Para SAD/estatura, las áreas bajo la curva ROC fueron  $\geq 0,83$  ( $p \leq 0,01$ ), con puntos de corte de 0,12 para hombres y 0,13 para las mujeres.

**Conclusión:** Había se ha observado un fuerte poder discriminatorio de los indicadores antropométricos de obesidad abdominal visceral. La Razón cintura/altura y el diámetro abdominal estatura mostraron un mejor desempeño para predecir la área de TAV de riesgo en los ancianos, sin la necesidad de medirla por tomografía computarizada.

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Palabras clave: Antropometría. Tejido adiposo visceral. Tomografía computarizada. Enfermedad cardiovascular. Anciano.

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## Abbreviations

ADI: Abdominal Diameter Index.  
CT: Computerized Tomography.  
NPV: Negative predictive values.  
PPV: Positive predictive values.  
ROC: Receiver Operating Characteristic.  
SAD: Sagittal Abdominal Diameter.  
SAD/Height: Sagittal Abdominal Diameter Height Index.  
Sens: Sensitivity.  
Spec.: Specificity.  
ThC: Thigh Circumference.  
VAT: Visceral Adipose Tissue.  
WC: Waist Circumference.  
WHtR: Waist-to- Height Ratio.  
WTR: Waist-to-Thigh Ratio.

## Introduction

Androgenic obesity is closely associated with insulin resistance, hypertension and dyslipidemia, and high risk for type 2 diabetes, cardiovascular disease and mortality, threatening to reduce world's life expectancy<sup>1-3</sup>. These outcomes incidence are high in elderly individuals and the risk of developing or to worsen them must be identified accurately, and early.

The evaluation of abdominal visceral adiposity in the elderly is considered fundamental, but complex due to the influence of several factors, which need to be investigated and represent an important tool in geriatric clinic practice, established by the strong association between this fat and the damages arising from obesity<sup>4,5</sup>.

Among the imaging methods that guarantee accurate quantification of abdominal visceral fat compartments, computed tomography (CT) is considered as the "golden standard". However, its practical utilization is limited by the need of high cost technology and hard operation<sup>6</sup>. Studies show anthropometric indicators as alternative methods used to estimate the visceral fat excess and, consequently, of risk for cardiovascular events<sup>7,8</sup> and death<sup>9-11</sup>, however there are few studies that compare the VAT area using CT with anthropometrics indexes which include measurements of height and thigh circumference, especially in the elderly, as this study aims to do.

Anthropometric indicators of visceral adiposity are considered superior to general adiposity ones by being able to better predict the risk of cardiovascular diseases<sup>12,13</sup> besides using simple measures, fast, reproducible, that require portable and low cost instruments that can be applied as substitutes of CT in the visceral fat estimative, targeting early identification of risk for these outcomes, expanding its applicability in clinical practice and research.

This study aims to evaluate the discriminatory power of anthropometric indicators for the detection of

excess in the area of visceral adipose tissue (VAT) among the elderly in both sexes.

## Methods

### *Study design and data collection*

Cross-sectional study conducted at the University Hospital and School of Nutrition at Federal University of Bahia, at the city of Salvador, Brazil. Individuals adults (between 20-59 years old) and elderly (above 60 years old) took part in the research, and were randomized by convenience for equitable inclusion, by sex, age and body mass, determined by Body Mass Index = kg/m<sup>2</sup> specific for each age group<sup>14,15</sup>.

Exclusion criteria: individuals under the age of 20 years old, body mass index > 40 kg/m<sup>2</sup>, carriers of malnutrition and severe disorders (neural sequelae, dystrophy), pregnant and lactating women, individuals who had recently undergone abdominal surgery or who had tumors, hepatomegaly, splenomegaly or ascites or with any problem that compromised the recommended technique for anthropometric measurements and visceral fat by computed tomography.

Anthropometric and imaging by computed tomography (CT) evaluations, to estimate the visceral adipose tissue area, were held in the same day to avoid weight changes, in the composition and distribution of body fat in the individual.

### *Anthropometry*

Data collection was conducted by the Center of Research and Intervention on the Aging Area of UFBA's School of Nutrition. Anthropometric evaluation was performed by a properly trained and standardized staff and consisted of measurements of weight, height and waist circumference (WC) obtained according to the techniques proposed by Lohman et al<sup>16</sup>. Portable, digital scale (Filizola, São Paulo, Brazil) with capacity up to 150 kg and precision of 100 g was used to measure the weight with the individuals wearing light clothes and no shoes. Height was measured with a portable stadiometer (Seca, TBW Importing *Ltda.*). Circumferences were measured with a measuring tape made of inelastic synthetic material with 1 mm of precision. Waist circumference was measured at the midpoint between the lower costal margin and the iliac crest. The thigh circumference (ThC) was measured on the right side of the body, at the midpoint between the inguinal crease and the proximal border of the patella. The individual remained standing and with the right knee slightly bent.

The Sagittal Abdominal Diameter (SAD) was measured with the individual in supine position, between the iliac crests with the aid of abdominal caliper mobile shank technique (Holtain Kahn Abdomi-

nal Caliper®) proposed by Kahn<sup>17</sup>. Anthropometric data showed correlation coefficients intra and inter evaluator higher than 0.90 confirming the reliability of the measurements collection.

Anthropometric measurements evaluated were: Waist-to-Height Ratio (WHtR), Waist-to-Thigh Ratio (WTR); Abdominal Diameter Index (ADI = SAD/ThC) and Sagittal Abdominal Diameter Height index (SAD/Height).

#### Quantification of Visceral Adipose Tissue Area (VAT)

The visceral adipose tissue area was measured by computed tomography with the help of the Spirit Siemens tomograph of the Radiology Service in the University Hospital and was analyzed by the same technician. The examination was conducted in complete fasting of 4 hours with the patient in dorsal decubitus, arms extended above the head and exposure time of three seconds.

The examination was obtained by a single tomographic cut at the level of L4-L5 vertebrae, with a cut thickness of 10 mm. It was used the technique described by Seidell et al<sup>18</sup>. The tomography program was used with radiographic parameters of 140 kV and 45 mA, being employed the density of -50 and -150 Hounsfield Units to identify the adipose tissue. No barium or organic iodinated contrast agent was administered. The value  $\geq 130 \text{ cm}^2$  was considered as excess area of visceral adipose tissue and of risk for developing cardiovascular diseases<sup>19</sup>.

#### Statistical analysis

For data analysis descriptive statistics was used (measurements of central and dispersion tendencies) of continuous variables. The normality of the variables

was analyzed by the Kolmogorov-Smirnov test, and according to variables linearity we used Pearson correlation coefficient to determine the correlation between anthropometric indicators and VAT area, comparing adults and elderly, in both sexes. Analysis of ROC curves (Receiver Operating Characteristic) were used to evaluate and compare the indicators capacity to identify the excess of VAT area. Then, sensibility, specificity, positive predictive value (PPV) and negative predictive value (NPV), and their respective cutoffs with a more appropriate balance between them were examined.

Sensitivity was defined as the proportion of individuals with excessive VAT area correctly identified and specificity as the proportion of individuals without excessive VAT area correctly identified. Also identified were their respective cutoffs of best sensibility and specificity combination with superior predictive capacity of VAT area excess for each sex and age group. The significance level was set at  $p \leq 0.05$ . For analyses the statistical program SPSS was used (version 16.0, SPSS Inc., Chicago, IL, USA).

#### Ethical aspects

This study was approved by the Ethics Committee in Research of the Nutrition School of Federal University of Bahia, opinion n° 01/09. All subjects signed an informed consent term and they received their results for monitoring and / or clinical treatment, in addition to receiving professional nutrition care of the Nutritional ambulatory of the University Hospital.

#### Results

The general characteristics of the 194 evaluated patients are presented in table I. In the descriptive

**Table I**  
Descriptive analysis of the anthropometric variables and visceral adipose tissue area, and the mean comparison of these variables, by sex and age group

	Mean			Women		
	Adults (n = 51)	Elderly (n =45)	p	Adults (n = 49)	Elderly (n = 49)	p
BMI(kg/m <sup>2</sup> )	25.10 (3.50)	26.38 (4.32)	0.120	26.30 (4.94)	26.92 (3.90)	0.499
WC (cm)	88.30 (9.7)	93.90 (12.1)	0.016	84.70(11.5)	89.60 (9.9)	0.029
ThC (cm)	52.30 (5.1)	48.30 (5.4)	0.000	54.10 (7.4)	50.40 (5.9)	0.008
SAD(cm)	19.70 (2.7)	21.20 (3.8)	0.031	19.40 (3.1)	20.20 (3.0)	0.217
WHtR	0.51 (0.07)	0.57 (0.06)	0.000	0.53 (0.07)	0.59 (0.06)	0.000
WTR	1.69 (0.16)	1.94 (0.18)	0.000	1.57 (0.16)	1.79 (0.19)	0.000
SAD/Height	0.11 (0.02)	0.13 (0.02)	0.001	0.12 (0.02)	0.13 (0.02)	0.011
ADI	0.38 (0.05)	0.44 (0.06)	0.000	0.36 (0.04)	0.40 (0.05)	0.000
VAT (cm <sup>2</sup> )	96.50 (58.7)	157.80 (86.1)	0.000	71.84 (43.5)	122.50 (48.9)	0.000

Data presented as mean (standard deviation).

BMI: Body Mass Index; WC: Waist Circumference; SAD: Sagittal Abdominal Diameter; ThC:Thigh Circumference; WHtR: Waist-to- Height Ratio; WTR: Waist-to-Thigh Ratio; SAD/Height: Sagittal Abdominal Diameter Height Index; ADI: Abdominal Diameter Index (SAD/WThC); VAT: Visceral Adipose Tissue (area).

analysis, variables were compared for each sex and their respective age group, showing that most of the averages of abdominal adiposity anthropometric indicators, as well as the VAT area, were higher among the elderly in both sexes. For men the percentage of excess in VAT area was 26.5% in adults and 62.2% in the elderly. For women the percentage was 12.5% and 42.9%, respectively.

Among men it was found that most of the anthropometric indicators showed high correlations with the VAT area and this occurred regardless the age group, with the highest correlations of WHtR ( $r = 0.79$ ,  $p \leq 0.01$ , in both adults and elderly) and SAD/Height ( $r = 0.78$ ,  $p \leq 0.01$ , adults;  $r = 0.79$ ,  $p \leq 0.01$ , elderly) (table II).

For women, the anthropometric indicators showed positive and statistically significant correlations with

the VAT area. The WHtR and SAD/Height showed correlation of 0.73 ( $p \leq 0.01$ ) and 0.64 ( $p \leq 0.01$ ) respectively in adults and elderly. It was noted that in the group of elderly women the correlations between these indicators were not as strong when compared to the group of adult women (table II).

The lowest correlation was observed between thigh circumference and VAT area, in both sexes, statistical significance was observed among elderly men and adult women.

The table III shows the areas under the ROC curve of anthropometric indexes for detecting the excess in the area of visceral adipose tissue, their respective cutoffs points, sensibility and specificity values with better balance between themselves and their predictive positive and negative values. In general, it was observed

**Table II**  
Correlation coefficient between the anthropometric indicators and the visceral adipose tissue area, in both sexes

	Visceral Adipose Tissue Area			
	Men		Women	
	Adults	Elderly	Adults	Elderly
WC	0.76**	0.74**	0.75**	0.60**
ThC	0.19	0.34*	0.36*	0.24
SAD	0.70**	0.76**	0.75**	0.62**
WHtR	0.79**	0.79**	0.73**	0.64**
WTR	0.64**	0.62**	0.53**	0.35*
SAD/Height	0.78**	0.79**	0.73**	0.64**
ADI	0.60**	0.66**	0.67**	0.48**

WC: Waist Circumference; SAD: Sagittal Abdominal Diameter; ThC:Thigh Circumference; WHtR: Waist-to- Height Ratio; WTR: Waist-to-Thigh Ratio; SAD/Height: Sagittal Abdominal Diameter Height Index; ADI: Abdominal Diameter Index (SAD/WThC).

\* $p < 0.05$ ; \*\* $p < 0.01$ .

**Table III**  
Cutoffs, sensitivity and specificity of the anthropometrics indexes that correspond to a VAT area of  $\geq 130 \text{ cm}^2$  and the areas below the ROC Curve for men and women

	Visceral Adipose Tissue Area							
	Adults				Elderly			
	ROC Area (95% CI)	Cut-off	Sens. (PPV)	Spec. (NPV)	Roc Area (95% CI)	Cut-off	Sens. (PPV)	Spec. (NPV)
<b>Men</b>								
WHtR	0.91 ** (0.818- 1.008)	0.54	86.7 (66.9)	86.1 (95.2)	0.90 ** (0.882- 0.991)	0.55	85.7 (88.9)	82.4 (77.8)
WTR	0.90 ** (0.809 - 0.987)	1.77	93.3 (68.5)	86.1 (97.5)	0.87 ** (0.771- 0.973)	1.90	82.1 (85.2)	76.5 (72.2)
SAD/Height	0.84 ** (0.710- 0.964)	0.12	86.7 (50.3)	72.2 (94.4)	0.90 ** (0.791- 0.986)	0.12	82.1 (85.2)	76.5 (72.2)
ADI	0.83 ** (0.727- 0.943)	0.38	86.7 (50.3)	72.2 (94.4)	0.91 ** (0.828 - 0.991)	0.42	82.1 (88.5)	82.4 (73.7)
<b>Women</b>								
WHtR	0.87 ** (0.736- 1.008)	0.59	83.3 (42.2)	83.7 (97.2)	0.81 ** (0.678- 0.939)	0.58	81.0 (74.0)	78.6 (84.6)
WTR	0.80 * (0.637- 0.968)	1.57	83.3 (24.2)	62.8 (96.3)	0.63 (0.466- 0.789)	1.81	57.1 (50.0)	57.1 (63.9)
SAD/Height	0.88 ** (0.750- 1.002)	0.13	83.3 (39.0)	81.4 (97.2)	0.84 ** (0.716- 0.975)	0.13	81.0 (77.3)	82.1 (85.2)
ADI	0.84 ** (0.714 - 0.968)	0.38	83.3 (31.7)	74.4 (96.9)	0.73 ** (0.589 - 0.877)	0.41	71.4 (65.2)	71.4 (76.9)

ROC: Receiver Operating Characteristic, AUC: Areas under the ROC curves, WHtR: Waist-to-Height Ratio; WTR: Waist-to-Thigh Ratio; SAD/Height: Sagittal Abdominal Diameter Height Index; ADI: Abdominal Diameter Index (SAD/WThC); Sens.: Sensitivity; Spec.: Specificity; PPV: positive predictive value; NPV: negative predictive value; CI: Confidence interval (95%).

\* $p < 0.05$ ; \*\* $p < 0.01$ .

that most of the anthropometric obesity indicators showed areas of high discriminatory power, being statistically significant.

Among men, the WHtR had the highest predictive power for a VAT area > 130 cm<sup>2</sup>, with an area under the ROC curve above 0.90 and positive predictive values (PPV) with the highest probability of detecting a man with excess visceral fat when WHtR is higher than the cutoff 0.54 (sens.: 86.7%; spec.: 86.1%) in adults and higher than 0.55 (sens.: 85.7%; spec.: 82.4%) among the elderly, with a PPV of 88.9% (table III).

It is noteworthy that among elderly men the cutoff points were higher than those of adults, except for the SAD/Height, in which the values were similar. Overall, among elderly men, the indicators that had better predictive values were WHtR, SAD/Height and ADI (table III).

For women, the SAD/Height and WHtR were the ones that had the best predictive power, with area under the ROC curve above 0.80, in elderly women, and above 0.86 in the adults. The cutoff of the WHtR to identify excess abdominal visceral fat for elderly women was 0.58 (sens.: 81.0%; spec.: 78.6%). Similar to men, most of the cutoffs in the group of elderly women was higher than of adults (table III).

The WHtR and SAD/Height were the indicators with higher PPV, which had a higher probability of detecting an elderly woman with excess VAT area when its cutoff point was greater than 0.58 and 0.13, respectively, this probability being higher than 74%. On the other hand, the negative predictive values (NPV) found no excess in the VAT area in 97.2% of cases among adult women when the WHtR and SAD/Height were below their cutoff. For elderly women, the indicator with the highest NPV was SAD/Height, which found women without excess VAT area when SAD/Height was lower than 0.13 in 85.2% (table III).

The WTR and ADI showed areas under the ROC curve greater than 0.80 ( $p \leq 0.01$ ), in all age groups, except in elderly women (table III).

## Discussion

The present study shows that anthropometric indicators of abdominal obesity performed well in estimating visceral fat measured by CT, in particular the WHtR and SAD/Height in the elderly, on both sexes. In fact, abdominal obesity is one of the characteristics of global cardiometabolic risk and represents the general risk of developing cardiovascular diseases and Diabetes Mellitus type 2<sup>1</sup> and early identification becomes essential, especially when considering the body changes and fat distribution that occur with aging. Thus, these would be alternative methods and replace the computed tomography for estimating visceral fat.

In this study, the highest averages of anthropometric indicators of abdominal obesity and area of VAT were

presented by elderly men and women. The physiological changes that occur with aging consist also in higher fat concentration in the abdominal area, mainly visceral, and when this accumulation becomes excessive, there are greater chances for disorders already mentioned<sup>20-22</sup> because this fat is metabolically active and influences normal and pathological processes. Visceral fat increase can occur independently of total or central adiposity changes and represents a clinically relevant phenotype<sup>23-25</sup>.

There are studies<sup>7,8</sup> that suggest strong correlations between WC, the SAD and the VAT area measured by computed tomography, however, indexes derived from these anthropometrics indicators, such as WHtR and SAD/Height, have shown similar correlations with visceral fat, when compared with their isolated measurements, this was also found in the present study. However, Ashwell and Hsieh<sup>26</sup> showed that the WHtR is more sensitive to assess health risk than the WC in different populations, possibly by encompassing the adjustment for different heights. The elderly show a decrease in height that must be considered, and thus obtaining a more individualized evaluation of WC.

From this point of view, WHtR has been considered superior to several anthropometrics indicators for indicating high cardiovascular<sup>13,27</sup> and coronary risk<sup>28</sup>. The WHtR is also known as abdominal obesity index, its analysis suggests that waist circumference of an individual should not exceed half the value of its height<sup>26,29</sup>. The WHtR has the effect of neutralizing the differences between heights allowing to individualize the interpretation of fat concentration for different ages since height influences the value of WC.

To identify the discriminatory power of the main indicators studied here in predicting the excess of visceral fat, areas under the ROC curve were created. The WHtR and SAD/Height were the best discriminators of risk for the elderly in both sexes. In this study, WHtR showed high values of these areas as well as in other studies<sup>27,30,31</sup> translating into greater discriminatory power of the WHtR to identify androgenic obesity.

Of particular interest are the cutoffs those indicators for the elderly, that have not been previously identified, however the results presented here were from a specific group, and cannot be generalized. These cutoffs allow the detection of individuals at risk, being a practical, simple and widely applicable resource. It is important to consider the existence of body changes with the aging process, which could generate different WHtR cutoffs between age groups. In this study, the WHtR cutoffs (> 0.54 for men and > 0.58 for women) were slightly higher than those observed by other studies related to coronary disease risk, for hypertension and metabolic syndrome<sup>32-34</sup>. In general, the sensitivity and specificity of visceral obesity indicators were greater than 71.4% for most of the analyzes in this study.

There are indicators not yet explored such as WTR and ADI that were suggested as substitutes for the waist/hip ratio, able to estimate visceral fat and their risks<sup>17,35,36</sup>. In

the present study, results similar to the literature were found, revealing that these indicators also have good discriminatory power to predict excess visceral fat, especially in men. However, both WTR as ADI do not take in consideration the proportionality with respect to height, and may remain unchanged, if there is an increase, or decrease, in the measures WC or SAD and ThC. This reinforces the importance of using WHtR and SAD/Height that only change if there is a change in their central measurements, the WC and SAD, respectively.

In this study, there was the limitation of not considering the race because of the difficulty in classifying due to the large miscegenation of the local population. Moreover, being a cross-sectional study, it is impossible to establish causal relationships.

The discrepancies found between studies may be related to methodological differences, varied ethnic characteristics and the age factor, where the elderly are generally included in the same group of adults for analysis, disregarding the peculiarities of aging. In this study, the careful selection of the sample provided a greater representation of equitable groups in respect to the amount of visceral fat. Many studies used different anthropometric techniques, especially for WC and SAD, and/or used another image method and not CT, the golden standard for visceral fat quantification. In the present study the most recommended anatomical location for anthropometric techniques was used<sup>17,37</sup>.

This study complements the investigation published<sup>7</sup> where a strong correlation and accuracy of WC and SAD to identify the excess of the VAT area in adults and elderly was observed. Thus, it was proposed to evaluate if the indexes with WC and SAD measures, including the height and/or the ThC, would have better results in this prediction. It has been verified that the correlations were similar and the areas under the ROC curve were larger.

The WHtR and SAD/Height were good in predicting the VAT area of risk in elderly, without the need of measuring it by computed tomography. From the clinical point of view, those results have potential for practical application, since an investigation by CT to evaluate visceral fat becomes more elaborate, costly and emits radiation. On the other hand, indicators of abdominal obesity, presented here, especially WHtR, use body measurements obtained by traditional and simple techniques, non-invasive, of rapid acquisition and interpretation, reproducible and inexpensive, reinforcing its superiority in detecting fat-related changes associated with obesity.

In this regard, it is recommended to periodically measure these anthropometric indexes, expanding their clinical use and in epidemiological studies, as well as in screening for monitoring elderly, essential in subsidizing preventive strategies in individuals and populations.

### Potential Conflict of Interest

No potential conflict of interest relevant.

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### Study Association

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