

## Body fat distribution and its risk for cardiovascular events in 10 years: *Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)*

A distribuição de gordura corporal está relacionada ao risco de eventos cardiovasculares em 10 anos: *Estudo Longitudinal de Saúde do Adulto (ELSA-Brasil)*

La distribución de la grasa corporal está relacionada con el riesgo de eventos cardiovasculares en 10 años: *Estudio Longitudinal de Salud en Adultos (ELSA-Brasil)*

Bárbara Bruna Rodrigues de Oliveira <sup>1</sup>

Carolina Gomes Coelho <sup>2</sup>

Sandhi Maria Barreto <sup>2</sup>

Luana Giatti <sup>2</sup>

Larissa Fortunato Araújo <sup>1</sup>

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### Abstract

Body fat distribution seems to have different effects in cardiovascular diseases (CVD). We aimed to estimate the associations between lower limbs and trunk fat ratio and the 10-year CVD risk, and isolated risk factors in men and women. A total of 10,917 participants from ELSA-Brasil were eligible for this cross-sectional study. Associations between lower limb/trunk fat ratio with the percentage of 10-year CVD risk – according to the Framingham Risk Score – and its risk factors (systolic blood pressure, total cholesterol and HDL-cholesterol, diabetes, and use of antihypertensive medication) were performed using generalized linear models, linear and logistic regressions. All analyses were stratified by gender and adjustments were made by age, self-reported skin color, educational attainment, alcohol consumption, leisure physical activity, hypolipidemic drug use and, for women, menopausal status. In this study, 55.91% were women, with a mean age of 52.68 (SD = 6.57) years. A higher lower limb/trunk fat ratio was related to lower 10-year CVD risk, as well as a reduction in systolic blood pressure, total cholesterol, and antihypertensive drug use, also an increasing HDL-cholesterol in both genders, but this relationship was stronger in women. Besides, a protective relationship to diabetes was observed in women. Higher fat accumulation in the lower body, when compared to the trunk, seems to have a lower risk of CVD and associated risk factors – even in the presence of fat in the abdominal region – with women presenting lower risks than men.

Body Composition; Body Fat Distribution; Cardiovascular Diseases

### Correspondence

S. M. Barreto

Faculdade de Medicina, Universidade Federal de Minas Gerais.  
Av. Alfredo Balena 110, Belo Horizonte, MG 30130-100, Brasil.  
Sandhi.barreto@gmail.com

<sup>1</sup> Programa de Pós-graduação em Saúde Pública, Universidade Federal do Ceará, Fortaleza, Brasil.

<sup>2</sup> Faculdade de Medicina, Universidade Federal de Minas Gerais, Belo Horizonte, Brasil.



## Background

Cardiovascular diseases (CVD) are the leading cause of death worldwide, corresponding to 32% (17.8 million) of deaths in 2017 <sup>1</sup>, and in all Brazilian regions <sup>2</sup>. The body composition and body fat location are strongly related to many risk factors for CVD <sup>3,4,5,6,7,8,9</sup>. The adipose tissue located in the abdominal area has been shown to be pathogenic and leading to metabolic disorders <sup>10,11</sup>. Otherwise, lower body fat – including glutes, legs and hips – is considered a “metabolic sink” due to its low rate of lipolysis, fatty acid absorption, and blood flow <sup>12</sup>. Also, lower body fat is the most insulin sensitive adipose tissue <sup>13</sup>. Thus, it is inversely associated with metabolic risk factors, including hyperinsulinemia, dyslipidemia, and hypertension, as well as directly associated with the reduction in the incidence of type 2 diabetes mellitus and the occurrence of CVD <sup>14,15</sup>.

Individual body composition is influenced by gonadal hormones <sup>16</sup>. Women usually accumulate fat at lower body, and men tend to accumulate it in the abdominal region. Besides, men generally have more risk factors for CVD, such as hypertension, smoking, alcohol consumption, and physical inactivity <sup>17,18</sup>. On the other hand, women have estrogens that protect them from CVD during child-bearing age. However, these sex hormones decline after menopause <sup>19</sup>.

Previous studies investigated the independent relationship of different body fat regions neglecting the combination among them and/or considering the presence of isolated risk factors for CVD <sup>5,10,13,20,21,22,23,24</sup>. However, the combination of lower limbs and trunk body fat measurements seems to be more accurate to assess and to classify individuals regarding cardiovascular and metabolic risk when compared to independent measurements. Since the locations of body fat are not independent, it is possible that their effects on health are also not independent. Furthermore, those studies that evaluated fat ratio between body regions did not distinguish men and women <sup>13,25,26</sup>, making it difficult to confirm whether there is gender effect modification. Thus, this study aims to investigate whether the higher fat ratio between lower limbs and trunk is associated with a lower risk for CVD in 10 years by the *Framingham Risk Score* (FRS) and its risk factors in adults and whether this relationship is stronger in women compared to men.

## Methods

### Study type and population

A cross-sectional study was conducted using data from the second wave of the *Brazilian Longitudinal Study of Adult Health* (ELSA-Brasil). ELSA-Brasil is a multicenter cohort of active and retired civil servants, aged from 35 to 74 years, from universities and research institutions located in municipalities from six Brazilian states: Belo Horizonte (Minas Gerais State), São Paulo, Rio de Janeiro, Vitória (Espírito Santo State), Salvador (Bahia State), and Porto Alegre (Rio Grande do Sul State). Its main objective is to investigate the incidence and progression of CVD and diabetes and their social, behavioral, biological, and environmental determinants. More detailed information about ELSA-Brasil can be found in previously published studies <sup>27,28</sup>.

Those who reported medical diagnosis for CVD ( $n = 877$ ), body mass index (BMI) below  $18.5 \text{ kg/m}^2$  ( $n = 95$ ) and age equal to or above 65 years ( $n = 2,125$ ) were excluded. The exclusion of low weight individuals and older adults is due to their specific body composition, differently affecting cardiovascular risk. Furthermore, participants with missing information – due to missing answers for any question or those who did not undergo the physical measurements – were excluded in the analysis, as follows: ratio between the amounts of fat in the lower limbs and trunk ( $n = 692$ ), self-reported skin color ( $n = 106$ ), educational attainment ( $n = 6$ ), alcohol consumption ( $n = 11$ ), physical activity ( $n = 1$ ), use of lipid-lowering medication ( $n = 37$ ), and total cholesterol ( $n = 17$ ). At the end, data from 10,047 participants were eligible for the study.

### **Response variable**

The response variable was the percentage of risk for CVD in 10 years, calculated using the FRS. The FRS is gender-specific and considers in its composition: age, total cholesterol, high-density level (HDL) cholesterol, systolic blood pressure, diabetes, smoking, and the use of antihypertensive drugs<sup>28</sup>. Variables were obtained by standardized face-to-face interviews and clinical and laboratory procedures. Participants were fasting and instructed to avoid drinking alcoholic beverages and caffeine, as well as to avoid exercising within 12 hours prior to examinations. Blood samples were collected after 10 to 14-hours fasting and stored using standardized protocol. These parameters were measured in ELSA-Brasil, as follows:

- (1) Age was measured at continuous age and categorized into:  $\leq 44$ ; 45 to 49; 50 to 54; 55 to 59; and 60 to 64 years;
- (2) Total cholesterol was analyzed by enzymatic colorimetric assay (ADVIA Chemistry; <https://www.siemens-healthineers.com/br>) using fasting blood samples<sup>27</sup> and grouped into the following ranges:  $< 160$ ; 160 to 199; 200 to 239; 240 to 279; and  $\geq 280$ mg/dL;
- (3) HDL-cholesterol was analyzed by the same method as total cholesterol and grouped into the following ranges:  $\geq 60$ ; 50 to 59; 45 to 49; 35 to 44;  $< 35$ mg/dL;
- (4) Diabetes was defined in the same way as the FRS: use of medication to treat diabetes (insulin or hypoglycemic drugs) or fasting blood glucose  $\geq 126$ mg/dL. Fasting blood glucose was determined by the enzymatic method (hexokinase) using the ADIVA 1200 device. The use of anti-diabetes drugs was obtained from self-report and verification of medical prescriptions and medication boxes. The drugs were classified according to Anatomical Therapeutic Chemical criteria;
- (5) Blood pressure was measured with the validated Omron HEM 705CPINT oscillometric device (Omron Co.; <https://www.omron.com>) after a 5-minute rest in sitting position in a controlled temperature room (20–24°C); the mean from the last two of the three measurements performed was used, with a one-minute interval between measurements, also obtained in the fasting period. The following cutoff points for systolic blood pressure were used:  $< 120$ ; 120 to 129; 130 to 139; 140 to 149; 150 to 159 and  $\geq 160$ mmHg;
- (6) The information about the use of antihypertensive drugs was obtained in the same method as for anti-diabetes drugs;
- (7) Participants who reported smoking at least 100-lifetime cigarettes and who reported currently smoking were categorized as “smokers”. Those who reported not currently smoking were classified as non-smokers. The following questions were used to define smoker status: “Are you or have you ever been a smoker, i.e., have you smoked at least 100 cigarettes (five packs of cigarettes) in your lifetime? Do you currently smoke cigarettes?”

The total point of FRS was used as continuous and categorical variables considering cutoff proposed by D’Agostino et al.<sup>29</sup>: 0 to  $< 6\%$  (low risk), 6 to 20% (medium risk) and  $> 20\%$  (high risk).

### **Explanatory variable of interest**

The fat of lower body and trunk – in kilograms (kg) – were determined by a vertical direct segmental multifrequency electrical impedance device (InBody 230; <https://inbody.com/en>). The equipment uses the multifrequency system (10 impedance measurements at 20 and 100kHz frequency) of tetrapolar electrodes with an eight-point tactile electrode. The volunteers were instructed to fast for at least 4 hours, previously empty the bladder, refrain from strenuous exercise and alcohol 24 hours prior to the test, and not use metallic fittings (e.g., watches, rings, earrings) during the test. During the evaluation, the participants remained in the study uniform to determine body weight in kilograms; and then placed their hands and feet on the instrument tactile electrodes for impedance measurement according to the manufacturer’s instructions. The results of the measurement by the impedance device provided the values of percentage of fat per body compartment in kilograms. Then, the amount of fat on the trunk and lower limbs was obtained. In this analysis, exposure was investigated by lower limbs/trunk fat ratio. Lower limbs region includes glutes, hips, and legs (right and left) and trunk region includes chest, abdomen, and back (and does not include arms, neck, and head fat).

Bioelectrical impedance analysis (BIA) measurements were performed once by trained professionals, who were certified before and throughout the study, using pre-established standard procedures, equipment, and techniques.

### **Covariables**

The following variables related to both exposure and outcome were considered as confounders for adjustment from the most relevant similar studies that investigated this association<sup>30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48</sup>: age as categories in descriptive analysis ( $\leq 44$ ; 45 to 49; 50 to 54; 55 to 59; and 60 to 64 years old) and as continuous in multivariate analysis – to remove residual confounding –; educational attainment [university degree or more ( $> 15$  years), high school (11-14 years), complete elementary school (8-10 years) and incomplete elementary school (0-7 years)]; self-reported skin color (white, brown-skinned or *pardo*, black, Asian descendant and Brazilian indigenous); leisure physical activity (light, moderate, and intense) assessed by the *International Physical Activity Questionnaire* (IPAQ) and; regarding alcohol consumption, the participants were categorized as: drinking moderately (men, consumption  $< 210$ g of alcohol and women, consumption  $< 140$ g of alcohol per week, nonuser, and drinking excessively (men, consumption  $\geq 210$ g of alcohol and women, consumption  $\geq 140$ g of alcohol per week).

### **Statistical analysis**

All analyses were stratified by gender. Pearson's chi-square test was performed for qualitative variables, analysis of variance (ANOVA) for quantitative variables with normal distribution, and Wilcoxon test for quantitative variables with asymmetric distribution. The mean (SD) fat amounts of lower body limbs, trunk and its ratio were compared by category of FRS using ANOVA.

Generalized linear model (GLM) with a logarithmic link and gamma distribution was used to measure the association of lower limb/trunk fat ratio with Framingham risk score for CVD. In a GLM, the exponentiation of the mean response represents the ratio of the arithmetic means (AMR) of the compared categories, which are in the same scale of the original response variable, i.e., percentage of FRS<sup>49</sup>.

Firstly, an unadjusted analysis of lower limb/trunk fat ratio and the FRS (Model 1) were performed. Then, sequential adjustments were made for age, self-reported skin color, educational attainment (Model 2), alcohol consumption, leisure physical activity and smoking (no/yes) for individuals FRS components models (Model 3), and finally for hypolipidemic medication use, and menopause status for women (Model 4). Subsequently, considering full adjustment, the association between lower limb/trunk fat ratio content with individual FRS components was measured using linear regression (systolic blood pressure, total cholesterol, and HDL-cholesterol) and logistic regression (diabetes and use of antihypertensive medication) according to the characteristics of each response variable. Analyses were performed using Stata 15.0 (<https://www.stata.com>).

### **Ethical aspects**

The project was approved by the Brazilian National Research Ethics Committee (CONEP) in compliance with *Resolution n. 196/1996* and other complementary resolutions. The research was approved by the Research Ethics Committees of the six institutions involved. All participants signed the informed consent form before conducting interviews and examinations.

## Results

Among 10,047 participants, men represented 44.09% of the total population. These men were younger, lower educated, mostly self-reported skin their color as brown-skinned or *pardo*; they presented excessive alcohol use, diabetes and intense leisure physical activity, higher levels of systolic blood pressure, total cholesterol, percentage of risk for CVD and lower levels of HDL-cholesterol compared to women (Table 1).

**Table 1**

Characteristics of the study population. *Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)*, 2012-2014.

Characteristics	Men n (%)	Women n (%)
Sex	4,430 (44.09)	5,617 (55.91)
Age (years) *		
≤ 44	611 (13.79)	691 (12.30)
45-49	980 (22.12)	1,164 (20.72)
50-54	1,114 (25.15)	1,447 (25.76)
55-59	965 (21.78)	1,277 (22.73)
60-64	760 (17.16)	1,038 (18.48)
Race/Skin color self-reported **		
White	2,267 (51.17)	2,886 (51.38)
Brown-skinned or <i>pardo</i>	1,401 (31.63)	1,522 (27.10)
Black	630 (14.22)	1,004 (17.87)
Asian descendant	76 (1.72)	161 (2.87)
Brazilian indigenous	56 (1.26)	44 (0.78)
Educational attainment **		
University degree or more	2,379 (53.70)	3,447 (61.37)
High school	1,476 (33.32)	1,833 (32.63)
Complete elementary school	306 (6.91)	221 (3.93)
Incomplete elementary school	269 (6.07)	116 (2.07)
Alcohol consumption **		
Moderate	2,643 (59.66)	3,172 (56.47)
Nonuser	1,196 (27.00)	2,201 (39.18)
Excessive	591 (13.34)	244 (4.34)
Physical activity **		
Light	3,137 (70.81)	4,395 (78.24)
Moderate	784 (17.70)	876 (15.60)
Intense	509 (11.49)	346 (6.16)
Use of hypolipidemic		
No	3,693 (83.36)	4,650 (82.78)
Yes	737 (16.64)	967 (17.22)
Menopause status		
No	-	1,889 (34.31)
Yes	-	3,616 (65.69)
Smoking		
No	3,896 (87.95)	4,999 (89.00)
Yes	534 (12.05)	618 (11.00)

(continues)

Table 1 (continued)

Characteristics	Men n (%)	Women n (%)
Systolic blood pressure (mg/dL) **		
< 120	1,977 (44.63)	3,620 (64.45)
120-129	1,185 (26.75)	1,117 (19.89)
130-139	674 (15.21)	507 (9.03)
140-149	336 (7.58)	229 (4.08)
150-159	146 (3.30)	89 (1.58)
≥ 160	112 (2.53)	55 (0.98)
Use of antihypertensive medication		
No	3,053 (68.92)	3,867 (68.84)
Yes	1,377 (31.08)	1,750 (31.16)
HDL-cholesterol (mg/dL) **		
≥ 60	573 (12.93)	2,332 (41.52)
50-59	1,071 (24.18)	1,763 (31.39)
45-49	848 (19.14)	764 (13.60)
35-44	1,639 (37.00)	685 (12.20)
< 35	299 (6.75)	73 (1.30)
Total cholesterol (mg/dL) **		
< 160	698 (15.76)	715 (12.73)
160-199	1,825 (41.20)	2,236 (39.81)
200-239	1,408 (31.78)	1,910 (34.00)
240-279	402 (9.07)	615 (10.95)
≥ 280	97 (2.19)	141 (2.51)
Diabetes **		
No	3,648 (82.35)	4,879 (86.86)
Yes	782 (17.65)	738 (13.14)
Framingham Risk Score [median (1st-3rd quartile)] **	10.82 (6.80-17.64)	4.30 (2.65-7.18)

Note: Pearson's chi-square test was performed for qualitative variables, ANOVA for quantitative variables with normal distribution, and Wilcoxon test for quantitative variables with asymmetric distribution.

\* p-value < 0.05;

\*\* p-value < 0.01.

In both genders, participants at high 10-year CVD risk had higher fat means (in kilograms) of lower body limbs and trunk compared to individuals at low and medium 10-year CVD risk (p-value < 0.01). Women had higher means of fat amounts of lower body limbs and trunk in all cardiovascular risk categories when compared to men. Also, those with a low risk of CVD in 10 years showed a higher difference in means between lower limbs fat and trunk fat (p-value < 0.01), and this relationship was higher in women compared to men (Table 2).

Table 3 shows the associations of lower limb/trunk fat ratio with risk for CVD. In unadjusted model (Model 1), the one-unit increase in the lower limb/trunk fat ratio reduces the risk for CVD by 38% in men (AMR: 0.62; 95%CI: 0.56; 0.68) and 82% in women (AMR: 0.18; 95%CI: 0.13; 0.22). After completed adjustment (Model 4) we observed small changes in association magnitudes (AMR for men: 0.69; 95%CI: 0.64; 0.74; AMR for women: 0.23; 95%CI: 0.18; 0.29). The associations were stronger in women compared to men.

Table 4 shows the association between the lower limb/trunk fat ratio with each individual component of FRS among men and women. The one-unit increasing in the difference between the fat locations was associated with a reduction in systolic blood pressure, total cholesterol, and antihypertensive drug use, also an increase in HDL-cholesterol in both genders, but this relationship was stronger in women. Moreover, women presented a protective relationship to diabetes.

**Table 2**

Description of fat amounts of lower body limbs and trunk according to categories of risk for cardiovascular disease in 10 years. *Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)*, 2012-2014.

FRS	Men Mean (SD)	Women Mean (SD)
Lower body limbs (kg) *		
Low	5.49 (1.91)	7.65 (2.53)
Medium	6.33 (2.16)	8.50 (2.69)
High	6.94 (2.19)	8.68 (2.85)
Trunk (kg) *		
Low	10.55 (4.38)	13.76 (4.71)
Medium	12.61 (4.71)	15.74 (4.72)
High	14.17 (4.64)	16.29 (4.98)
Lower limb/trunk fat ratio (kg) *		
Low	0.54 (0.09)	0.56 (0.06)
Medium	0.51 (0.12)	0.54 (0.06)
High	0.49 (0.07)	0.53 (0.07)

FRS: *Framingham Risk Score*; SD: standard deviation.

Note: ANOVA test.

\* All p-values were below 0.01.

**Table 3**

Associations of lower limb/trunk fat ratio with risk for cardiovascular disease in 10 years. *Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)*, 2012-2014.

Model	Men AMR (95%CI) *	Women AMR (95%CI) *
1	0.62 (0.56; 0.69)	0.17 (0.13; 0.22)
2	0.68 (0.63; 0.73)	0.22 (0.17; 0.27)
3	0.69 (0.64; 0.74)	0.23 (0.18; 0.29)
4	0.69 (0.64; 0.74)	0.23 (0.18; 0.29)

95%CI: 95% confidence interval; AMR: arithmetic mean ratio.

Note: performed generalized linear model with logarithmic link and gamma distribution. Model 1: unadjusted analysis; Model 2: Model 1 + adjustment for age, self-reported skin color and educational attainment; Model 3: Model 2 + alcohol consumption and leisure physical activity; and Model 4: Model 3 + hypolipidemic drug use and menopausal status (for women).

\* All p-values were below 0.01.

**Table 4**

Associations of lower limb/trunk fat ratio with cardiovascular risk factors. *Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)*, 2012-2014.

	Men Coefficient (95%CI)	Women Coefficient (95%CI)
Total cholesterol *	-39.83 (-49.78; -29.88) **	-53.35 (-67.12; -39.58) **
HDL-cholesterol *	18.61 (15.93; 21.28) **	31.04 (26.06; 36.02) **
Systolic blood pressure *	-12.78 (-16.62; -8.93) **	-15.16 (-20.57; -9.74) **
Antihypertensive medication ***	0.03 (0.01; 0.12) **	0.37 (0.14; 0.99) #
Diabetes ***	1.03 (0.37; 2.86)	0.04 (0.01; 0.19) **

95%CI: 95% confidence interval.

\* Performed linear regression;

\*\* p-value < 0.01;

\*\*\* Performed logistic regression. Adjusted for age, self-reported skin color and educational attainment; alcohol consumption, smoking and leisure physical activity; hypolipidemic drug use and menopausal status (for women).

# p-value < 0.05.

## Discussion

Our study showed that the higher amount of fat in the lower limbs in relation to the trunk was associated with a lower risk of CVD in 10 years. We also observed that the highest lower limb/trunk fat ratio was associated with a reduction in systolic blood pressure, total cholesterol, and use of antihypertensive drugs, in addition to an increase in HDL-cholesterol in both genders. All associations described were stronger in women. Furthermore, women presented the highest protective relationship against diabetes.

Previous studies reinforce the evidence that higher fat in the lower body limbs has a protective relationship for CVD <sup>21,26,50,51</sup>, while an elevated fat percentage located in the trunk increases its occurrence <sup>11,23,30,52,53</sup>. For example, in a longitudinal study using data from 15,686 individuals of *National Health and Nutrition Examination Survey* (NHANES) without history of CVD, the highest lower limb/trunk fat ratio was related to lower waist circumference, blood pressure, glucose levels, insulin resistance, LDL cholesterol and triglycerides, higher HDL-cholesterol levels and better glomerular filtration rate <sup>21</sup>.

In our study – although considering all 10-year cardiovascular risk categories – women presented a higher amount of fat in the lower limbs and trunk, also presenting a higher difference compared to men. In addition, after adjusting for all covariables, the protective relationship of lower limb fat remained statistically significant in both genders, with a stronger relationship for women. Similar results were also found in the *Characteristics and Course of Heart Failure Stages A-B and Determinants of Progression (STAAB) Cohort Study* conducted with 980 participants (aged 30-79 years), which used the SCORE algorithm to estimate cardiovascular risk at 10 years. Women had a higher prevalence of general obesity, but a lower risk of CVD in 10 years <sup>31</sup>. A higher magnitude of association was also found among women compared to men in a cross-sectional study of 4,256 Japanese (aged 20-79 years), in which the higher amount of fat in the lower limbs was associated with a lower risk of developing cardiovascular events <sup>32</sup>.

The same was observed in 4,950 participants (2,119 men and 2,831 women) aged 29 to 55 years at the Oxford Biobank, in which women presented higher amounts of fat in the lower limbs, while men in the trunk. An increase in lower limbs mass at any trunk fat level was generally associated with lower fasting glucose, triglycerides, HOMA-IR, and mean blood pressure, which had a protective relationship on cardiovascular risk and this relationship was somewhat stronger in women <sup>30</sup>. However, other studies have found significant associations only among men <sup>33,34,35</sup>. Such studies included adults and older people and the absence of statistical significance in women may be due to a large number of older women and/or a lack of adjustment for potential confounding variables.



Our results were not affected by these factors, since the analyses were adjusted for the presence of menopause, and people aged over 64 were excluded from our study, removing the possibility of confounding or effect modification by advanced ages. Even if women have some protection from CVD due to increased fat accumulation in the lower limbs, menopause leads to a decline in sex hormones (estrogen and progesterone), increasing fat in the trunk region and consequently increasing the CVD risk<sup>36,37</sup>. However, a favorable and low-risk profile on CVD in postmenopausal women using hormone replacement therapy was observed in previous studies<sup>38,39,40,41,42,43,44,45,46</sup>.

Nevertheless, in the Women's Health Initiative (WHI) cohort study of 2,683 postmenopausal U.S. women (aged 50-79 years), without CVD at baseline, with normal weight (BMI: 18.5 to 24.9 kg/m<sup>2</sup>) and using hormone replacement therapy, the higher amount of trunk fat mass compared to lower body limbs was associated higher blood pressure, insulin resistance, HOMA-IR, adipokines (leptin and adiponectin), inflammatory markers [leukocyte count, high sensitivity C-reactive protein (CRP) and interleukin-6], lipids (triglycerides and LDL cholesterol). Thus, postmenopausal women with a higher trunk fat and lower limbs fat had a three times higher risk of CVD compared to those with opposite values of higher fat amount on lower body limbs and lower trunk fat, even when considering adjustment for hormone replacement therapy<sup>47</sup>.

A systematic review study concluded that the sex chromosome might influence factors underlying metabolic disorders such as obesity, dyslipidemia, and inflammation. It is well known that gonadal hormones have substantial effects on fat storage and susceptibility to CVD and type 2 diabetes among men and women. Thus, essential differences between genders can be found regarding the distribution of adipose tissue in the body, with men accumulating higher amounts of visceral adipose tissue and women with higher fat accumulation in the subcutaneous (lower body limbs) deposits<sup>48</sup>.

Specific associations between body fat regions and risk factors for CVD are plausible, as the upper and lower body contains divergent fat deposits with profoundly distinct biological functions<sup>14,47</sup>. Several mechanisms potentially responsible for these adipose deposition-dependent associations have been proposed, including regional differences in the severity of adipose inflammation, lipid storage and renewal, adipokine release, and endocrine effects<sup>13,14,54</sup>. Even for similar types of fat, leg adipose tissue was less susceptible to the unregulated release of free fatty acids, resulting in lipotoxicity than abdominal subcutaneous adipose tissue, reinforcing the hypothesis that lower body deposits are the ideal site for fat storage<sup>35,47,55</sup>.

Some limitations need to be considered when interpreting our results. Firstly, since we performed a cross-sectional analysis, we have no temporality between body composition and FRS components and cannot claim causality. We did not evaluate the body composition through the dual-energy X-ray absorptiometry (DXA) method, which is the gold standard for this measurement – although it is not the most adequate method for large population epidemiological studies – in the use of practical clinical evaluations.

Moreover, we used bioelectrical impedance, a cheaper and less invasive method compared to DXA, because numerous studies have investigated the validity of BIA for measuring body composition, comparing its results with DXA, and these studies reported that BIA showed good overall agreement with DXA in healthy adults. All comparisons between measurements provided by BIA and DXA showed strong significant correlations between both methods, acceptable limits of agreement for body fat percentage and absence of significant biases between BIA and DXA<sup>56,57,58,59,60,61</sup>. Our study was conducted in a multicenter study population with a large sample size and geographical diversity, allowing us to include subjects with different cultural and racial characteristics. Furthermore, it was developed in a low- and middle-income country with a high and growing prevalence of overweight and obese people, which is a current public health problem – reinforcing the relevance of understanding the role of fat localization in the risk of CVD. We stratified the analysis by gender, allowing us to verify the differences between men and women in the pattern of fat accumulation that led to higher or lower risk for developing CVD. Furthermore, we removed effects from potential confounders of this relationship such as sociodemographic characteristics, health behaviors and conditions.

## Conclusion

Our results suggest that higher fat amount in the lower limbs in relation to the trunk exerts a lower risk of CVD in 10 years and this relationship is stronger in women compared to men. When a population is dealing with an epidemic of overweight and obesity it is essential to understand the patterns of body fat accumulation and the different ways it affects the development of CVD. This knowledge also supports the optimization of health spending, since it targets specific actions for at-risk populations and reduce morbidity and mortality.

## Contributors

B. B. R. Oliveira, L. F. Araújo, and C. G. Coelho contributed to the study conceptualization, methodology, data analysis, writing, and review. S. M. Barreto and L. Giatti contributed to the data analysis and review. All authors approved the final version of the manuscript.

## Additional informations

ORCID: Bárbara Bruna Rodrigues de Oliveira (0000-0001-6726-9176); Carolina Gomes Coelho (0000-0002-7294-3724); Sandhi Maria Barreto (0000-0001-7383-7811); Luana Giatti (0000-0001-5454-2460); Larissa Fortunato Araújo (0000-0001-6695-0365).

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## Resumo

A distribuição de gordura no corpo parece ter efeitos diferentes nas doenças cardiovasculares (DCV). Objetivou-se estimar as associações da razão de gordura entre membros inferiores e tronco com o risco de DCV em 10 anos e os fatores de risco independentes em homens e mulheres. Um total de 10.917 participantes do ELSA-Brasil eram elegíveis para este estudo transversal. As associações da razão de gordura entre os membros inferiores e tronco com o percentual de risco de DCV em 10 anos, de acordo com a Escala de Risco de Framingham, e os respectivos fatores de risco (pressão arterial sistólica, colesterol total e HDL colesterol, diabetes e uso de medicação anti-hipertensiva), foram avaliados com modelos lineares generalizados, lineares e de regressão logística. Todas as análises foram estratificadas por sexo, e os ajustes foram feitos por idade, raça/cor, escolaridade, consumo de álcool, atividade física, uso de medicação hipolipemiante e, para as mulheres, estado de menopausa. Na amostra do estudo atual, 55,91% eram mulheres, com média de idade de 52,68 anos (DP = 6,57). A maior diferença entre a gordura dos membros inferiores e tronco foi associada com menor risco de DCV em 10 anos e com redução na pressão arterial sistólica, colesterol total e uso de medicação anti-hipertensiva, assim como um aumento no HDL colesterol em ambos os sexos (mas essa correlação foi mais forte em mulheres). Além disso, foi observada uma relação protetora contra diabetes, apenas em mulheres. O acúmulo maior de gordura nos membros inferiores, comparado com o tronco, parece estar associado a um risco menor de DCV e aos fatores de risco, mesmo na presença de gordura na região abdominal, e esse efeito é mais forte nas mulheres que nos homens.

Composição Corporal; Distribuição da Gordura Corporal; Doenças Cardiovasculares

## Resumen

Las distribuciones de grasa corporal parecen tener diferentes efectos en las enfermedades cardiovasculares (ECV). Nuestro objetivo fue estimar las asociaciones entre extremidades inferiores/ratio de grasa troncal y el riesgo de ECV a los 10 años, y sus factores de riesgo aislados, en hombres y mujeres. Un total de 10.917 participantes de ELSA-Brasil fueron elegibles para este estudio transversal. Las asociaciones de la ratio de grasa entre la parte inferior del cuerpo y el tronco, con el porcentaje de riesgo de ECV a los 10 años, según la Escala de Riesgo de Framingham, y sus factores de riesgo (presión sanguínea sistólica, colesterol total y colesterol HDL, diabetes, y uso de medicación antihipertensiva), se realizaron usando modelos lineales generalizados, regresiones lineales y logísticas. Todos los análisis fueron estratificados por sexo y los ajustes se hicieron por edad, raza/color de piel autoinformado, nivel educativo, consumo de alcohol, actividad física durante el ocio, uso de medicamentos hipolipemiantes y, para mujeres, estatus menopáusico. En este estudio, un 55,91% fueron mujeres, con una media de edad de 52,68 (SD = 6,57) años. Una ratio de masa adiposa más alta entre las extremidades inferiores/tronco estuvo asociada a un riesgo menor de ECV en 10 años, también una reducción en la presión sistólica sanguínea, colesterol total, y el consumo de medicamentos antihipertensivos, también en un incremento del colesterol HDL en ambos sexos, pero esta relación fue más fuerte en mujeres. Asimismo, una relación protectora frente a la diabetes se observó solo en mujeres. Una acumulación más alta de grasa en las extremidades inferiores, comparada con la del tronco, parece tener un riesgo más bajo de ECV y sus factores de riesgo, incluso con la presencia de grasa en la región abdominal, además este efecto es más fuerte en mujeres comparadas con los hombres.

Composición Corporal; Distribución de la Grasa Corporal; Enfermedades Cardiovasculares

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