

Relation of Thoracic Aortic and Coronary Artery Calcium to Cardiovascular Risk Factors (from The Brazilian Longitudinal Study of Adult Health [ELSA-Brazil])



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Thoracic aortic calcium (TAC) and coronary artery calcium (CAC) are associated with an increased risk of cardiovascular disease (CVD) and death. However, risk factors associated with arterial calcium may vary across vascular beds. We verified whether TAC is associated with the same risk factors as is CAC in adults without established CVD. Cross-sectional analysis including 2,433 participants (aged 38 to 78 years) of ELSA-Brazil cohort in Minas Gerais, Brazil. Nonenhanced ECG-gated multislice computed tomography were performed to detect calcium in the thoracic aorta and the coronaries (2015 to 2016). Multivariate logistic regression evaluated the associations of both TAC and CAC with CVD risk factors (smoking, body mass index, physical activity, alcohol intake, family history of CVD, low-density lipoprotein- and high-density lipoprotein-cholesterol, HbA1c, blood pressure, antidiabetic, antihypertensive, and lipid lowering medications). Overall prevalence of TAC and CAC were 69% and 43%, respectively. CAC prevalence was lower among women (31%) than men (56%) (Adjusted odds ratio [OR] 0.30; 0.24 to 0.38). After adjustments, black individuals were less likely to have any CAC as compared with whites (OR 0.63; 0.47 to 0.86). Neither sex, nor race/skin color were statistically associated with TAC. Use of antidiabetic medications remained associated with CAC (OR 1.80; 1.23 to 2.631.01), but not with TAC. All other risk factors, except education, alcohol, physical activity and HbA1c, persisted statistically associated with both TAC and CAC in the final analysis, with small differences in the magnitudes of the ORs. In conclusion, the only disagreements seen in the risk factors associated with CAC and TAC were sex, race/skin color, and use of antidiabetic medications. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;124:1655–1661)

Many studies have demonstrated that the presence of either coronary artery calcium (CAC) or thoracic aortic calcium (TAC), detected by computed tomography (CT), are

markers of subclinical atherosclerosis and are associated with an increased risk of cardiovascular events.^{1,2} Allison et al (2012) followed up 4,544 individuals who underwent whole body CT to ascertain, and found after about 7.8 years, that the calcium in thoracic aorta, carotids, and iliac arteries were associated with total mortality, whereas the presence of CAC was associated with cardiovascular disease (CVD) mortality.³ Knowledge on the association of particular cardiovascular risk factors to the presence of calcium in thoracic aorta and/or coronary arteries may contribute to understand the different mechanisms of atherosclerosis. We performed a cross-sectional study to assess the prevalence of TAC and CAC and verify if TAC is associated with the same cardiovascular risk factors as is CAC in participants from Minas Gerais Investigation Center of ELSA-Brazil Study without overt CVD.

Methods

The study is embedded in the ELSA-Brazil Study, a multicenter cohort designed to investigate the determinants of CVD and diabetes.⁴ The study started in 2008 and included 15,105 civil servants. Eligibility criteria included active and retired employees of 6 institutions, aged 35 to 74 year.⁵ The present study was conducted in the Minas Gerais

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Grant Support: The study was funded by the Brazilian Ministry of Health (Science and Technology Department) and the Brazilian Ministry of Science, Technology and Innovation (FINEP and CNPq). Grant numbers: 01 06 0010-00 and 01-10-0643-03 (RS); 01 06 0212-00 and 01-10-0742-00 (BA); 01 06 0300-00 and 01-12-0284-00 (ES); 01 06 0278-00 and 01 10 0746 00 (MG); 01 06 0115-00 and 01-10-0773-00 (SP); and 01 06 0071-00 and 01-11-0093-01 (RJ). This study also received support from the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES). S.M.B and A.L.P.R. are recipients of an unrestricted award for established researchers from CNPq and are also supported by a research grant (Pesquisador Mineiro) from FAPEMIG, the research agency of the State of Minas Gerais, Brazil. See page 1660 for disclosure information.

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Investigation Center. Multislice Computed Tomography (MSCT) was performed in 2015 to 2016 after the second visit (2012 to 2014), which enrolled 2,923 participants. Exclusion criteria for MSCT scan was pregnancy, postpartum, breast-feeding (until 6 months post childbirth), exposure to radiation at work, any piece of metal in the chest (e.g., pacemaker and coronary stent), current radiotherapy, nonparticipation in second visit to Investigation Center and refusal to perform MSCT scan. A total of 2,638 participants were scanned. Of these, 63 reported a history of CVD at second visit and were excluded from this analysis. History of CVD was defined as medical history of myocardial infarction ($n = 15$), congestive heart failure ($n = 21$), stroke ($n = 24$) or cardiac surgery ($n = 13$). Additionally, in 142 participants measurements of both CAC and TAC were not available due to use of different scan protocol, in which the aortic arch was not included. Thus, 2,433 participants were included in the present study.

Written informed consent was obtained from each participant included in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and our protocol has been priorly approved by the Universidade Federal de Minas Gerais's ethics committee on research in humans.

Sociodemographic, behavioral, and medical history factors were obtained by face-to-face questionnaires. Race/skin color were self-reported and participants could choose from a fixed set of categories based on Brazilian Census classification: white; brown or "pardo"; black and others (Indigenous and Asian were grouped in the same category because its smaller participants number).⁵ Educational level was categorized into university degree, complete secondary school, complete elementary school, and incomplete elementary school. Smoking was assessed by the following questions: "Are you or have you ever been a smoker, that is, have you smoked at least 100 cigarettes (5 cigarette packs) throughout your life?" and "Do you currently smoke cigarettes?" (never smoker, former smoker, and current smoker).⁶ Never smoker were the reference group. Physical activity was assessed by the short version of the International Physical Activity Questionnaire and participants were classified as insufficient (<600 metabolic equivalent-min/week), moderate (600 to 3000), and vigorous (≥ 3000).⁷ Excessive use of alcohol was defined as ≥ 210 g of ethanol per week for men and ≥ 140 g for women.⁵ Family history of premature CVD was defined as "positive" if the participant reported a case of acute myocardial infarction, myocardial revascularization or sudden death in first-degree relative (men aged ≤ 55 and women ≤ 65 years old).⁴

Body mass index (BMI) was calculated by dividing the participant's weight in kilograms by height in meters squared. Blood pressure was measured 3 times in the seated position after 5 minutes of rest, automatically (Omron 765CP; Omron, Kyoto, Japan) in the left arm, 2 cm above the cubital fossa, and the average of the second and third measurements was considered to obtain systolic and diastolic blood pressure as continuous variables in mm Hg.⁸ Blood samples were collected in after 12-hours overnight fast to measure hemoglobin A1c (HbA1c), high-density lipoprotein (HDL)-cholesterol and low-density lipoprotein (LDL)-cholesterol.⁴ The use of antidiabetic, antihypertensive, and lipid

lowering medications was self-reported. All participants were asked about the use of continuous medication in the previous 2 weeks and were instructed to bring prescriptions and/or drugs used to the study clinic.⁹

Imaging was performed with a 64-slice MSCT scanner (*Lightspeed*, General Electric). The scanogram encompassed all thoracic aorta, and the heart, from 1 cm above the top of the aortic arch to the heart apex as is shown in [Figure 1](#). The scan consisted of 56 to 88 images. Before performing the scan, the participants exercised breath holding. Within a single breath hold consecutive nonoverlapping 2.5 mm thick slices were acquired with 20×0.62 mm collimation, 120 kVp, 100 mAs and prospective electrocardiogram triggering at 70% of the cardiac cycle. The media of effective dose calculated was 1.75 mSv.

Calcium was identified and scored by only one experienced radiologist, using semiautomatic software (*Smart Score 4.0*). Correlation study was performed with a second experienced radiologist. A random sample of 50 participants was scored twice by the observer and once by the other radiologist, who has only participated in this correlation study. Intraclass correlation coefficients for all arteries scored were higher than 0.99 for intraobserver and interobserver analysis.

The software highlighted in green all calcium based on a threshold of 130 Hounsfield Unit (HU).¹⁰ Then, the observer went over every axial image and clicked on the green lesions to turn them another codified color as is shown in [Figure 1](#). CAC presence consisted of any calcified lesions identified within left main, left anterior descending, left circumflex, and right coronary artery. The presence of TAC was defined as any calcium on the aortic arch, ascending, and descending aorta wall, from the sinutubular junction until the last image of heart apex. Calcium from Valsalva sinus and aortic valve was not included.

Descriptive statistics was based on mean and standard deviation for continuous variables and frequency distribution for categorical variables. Continuous variables were compared with Student *t* test and categorical variable with Pearson's chi-square test. TAC and CAC were dichotomized as present (Agatston score >0) or absent ($=0$). The independent association of sociodemographic, lifestyle, laboratory, and clinical risk factors with TAC and CAC were assessed using multivariate logistic regression analyses. The analysis consisted of 4 stages for TAC and CAC separately: model zero (univariate analysis); Model 1 was adjusted for sociodemographic factors (age, gender, race/skin color, and education); Model 2 added lifestyle factors (smoking, physical activity, and alcohol intake), BMI, and family history of CVD; Model 3 included the remaining risk factors (LDL- and HDL-cholesterol, HbA1c, blood pressure, antidiabetic, antihypertensive, and lipid lowering medications). All associated covariables with $p < 0.20$ in the univariate analysis were considered in the multivariate models, but only the variables that remained statistically associated at the level of $p < 0.05$ remained in the final analysis (Model 3) of TAC or CAC. The confidence interval corresponded to 95%. Statistical analyses were performed with Stata/MP 14.0 for MAC (StataCorp LP, College Station, Texas).

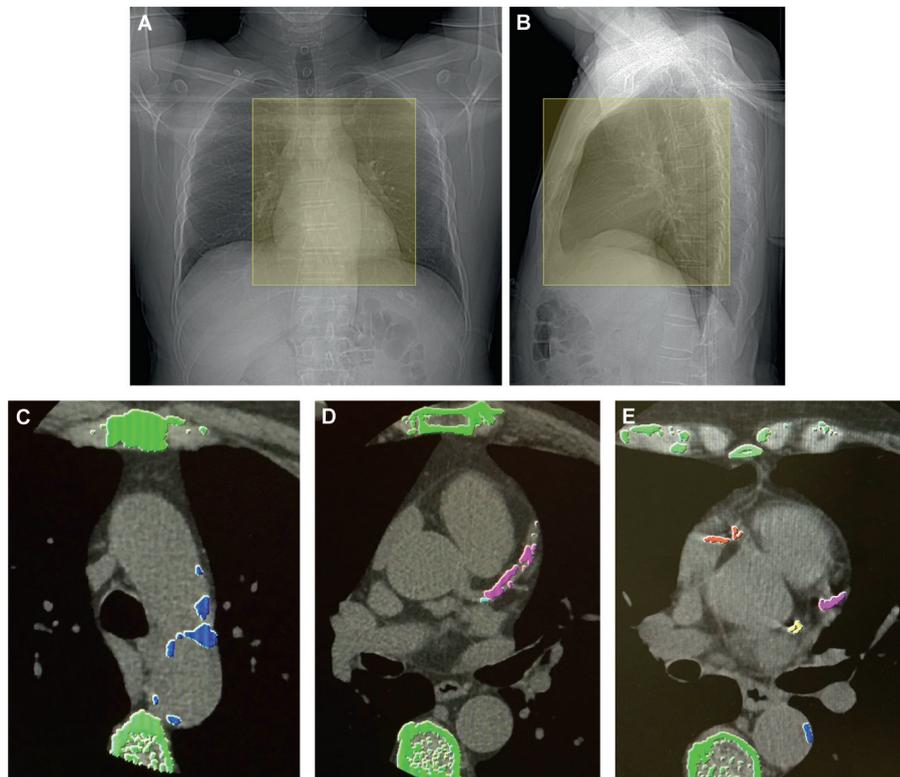


Figure 1. (A and B) Scanogram: frontal and lateral views. Yellow rectangles represent the tomographic acquisition area. (C, D and E) Screens obtained by "Smart Score" software showing any calcium area highlighted in green. Calcium in different vascular beds are shown according to codified colors: blue, aortic arch (C and E); pink, anterior descending artery (D and E); light blue, left main coronary artery (D); red, right coronary artery and yellow, circumflex artery (E).

Results

The overall prevalences of TAC and CAC were 69% and 43%, respectively. Figure 2 shows a Venn diagram with the intersection of all study participants according to the presence or absence of CAC and/or TAC. About 24% of participants were free from both TAC and CAC, while 37% had

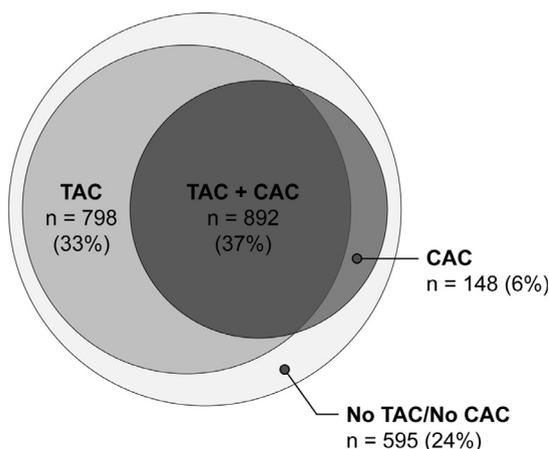


Figure 2. Venn diagram showing the intersection of individuals according to presence or absence of coronary artery calcium (CAC) and thoracic aortic calcium (TAC). Percentages refer to the overall population (n = 2,433). ELSA-Brasil, 2015-2016.

TAC and CAC, simultaneously. Almost all participants with CAC also had TAC (94%).

Figure 3 shows the prevalences of TAC and CAC according to gender and age category. The prevalence of CAC was significantly lower in women than in men at all age groups, whereas the prevalence of TAC was quite similar between genders throughout age groups.

Table 1 shows the distribution of the study population characteristics in total and according to presence or absence of TAC and CAC. Overall, the mean age was 55.6 ± 8.7 years; 54% women; nearly half were whites (49%); about 67% had university degree. Thirty-eight percent were either current or former smoker; and 33% had a family history of CVD. In all the factors included in Table 1, only gender, race/skin color, physical activity, excessive use of alcohol, and HDL-cholesterol were not statistically associated with the presence of TAC at the level of $p < 0.05$. Whereas only physical activity and LDL-cholesterol had nonsignificant association with CAC in the univariate analysis. The results of the multivariate analysis for cardiovascular risk factors associated with the presence of TAC and CAC are shown in Tables 2 and 3, respectively. Increasing age, current smoking, family history of CVD, higher BMI, LDL-cholesterol and systolic blood pressure, lower HDL-cholesterol and use of lipid and blood pressure lowering medications, all remained associated with greater odds ratio (OR) for TAC and CAC, with small differences in the magnitude of the associations. The chance of having CAC was lower in women than men,

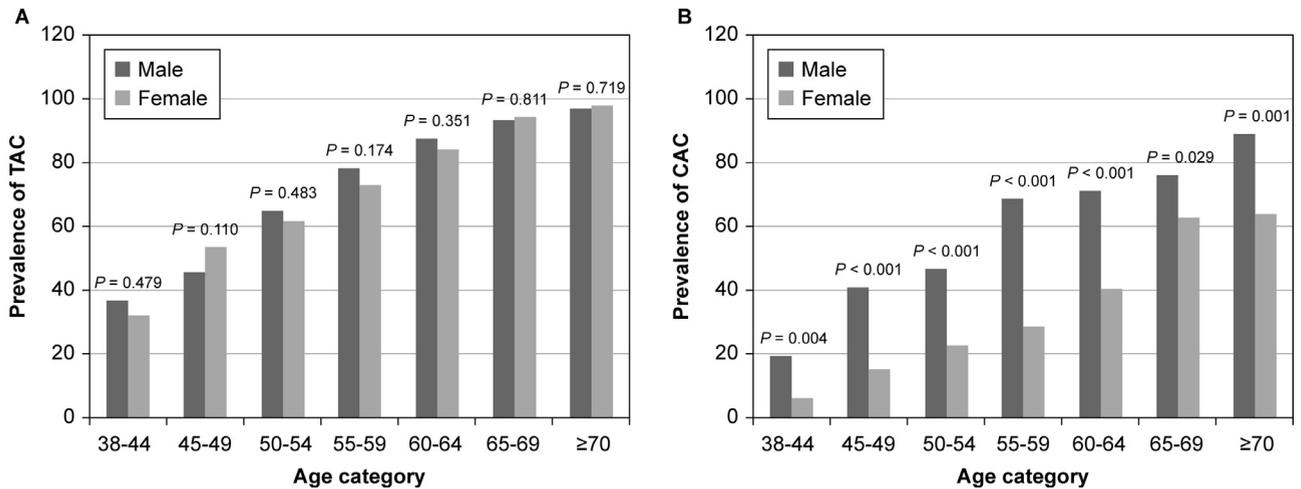


Figure 3. (A and B) Prevalences of thoracic aortic calcium (TAC) and coronary artery calcium (CAC) according to gender and age category, respectively. ELSA-Brasil, 2015-2016.

Table 1

Characteristics of all population and according to presence or absence of thoracic aortic calcium (TAC) and coronary artery calcium (CAC). ELSA-Brasil, 2015-2016

| Variables | Population N = 2,433 (100%) | TAC = 0 N = 743 (30.5%) | TAC >0 N = 1,690 (69.5%) | p Values | CAC = 0 N = 1,393 (57.3%) | CAC >0 N = 1,040 (42.7%) | p Values |
|--------------------------------------------|-----------------------------------|-------------------------------|--------------------------------|------------------|---------------------------------|--------------------------------|------------------|
| Age (years) | 55.6 ± 8.7 | 50.2 ± 6.8 | 58.0 ± 8.4 | <0.001 | 52.9 ± 8.0 | 59.2 ± 8.3 | <0.001 |
| Women | 1,314 (54.0%) | 400 (53.8%) | 914 (54.1%) | 0.910 | 903 (64.8%) | 411 (39.5%) | <0.001 |
| Race/skin color | | | | 0.378 | | | <0.001 |
| White | 1,169 (48.6%) | 337 (46.2%) | 832 (49.7%) | | 625 (45.4%) | 544 (53.1%) | |
| Brown | 850 (35.4%) | 276 (37.8%) | 574 (34.3%) | | 501 (36.4%) | 349 (34.0%) | |
| Black | 319 (13.3%) | 97 (13.3%) | 222 (13.3%) | | 208 (15.1%) | 111 (10.8%) | |
| Others (Asian, Indigenous) | 65 (2.7%) | 20 (2.7%) | 45 (2.7%) | | 44 (3.2%) | 21 (2.1%) | |
| Educational level | | | | <0.001 | | | <0.001 |
| University degree | 1,627 (66.9%) | 540 (72.8%) | 1,087 (64.4%) | | 958 (68.8%) | 669 (64.4%) | |
| Complete secondary school | 616 (25.3%) | 174 (23.4%) | 442 (26.2%) | | 354 (25.5%) | 262 (25.2%) | |
| Complete elementary school | 102 (4.2%) | 17 (2.3%) | 85 (5.0%) | | 42 (3.0%) | 60 (5.8%) | |
| Incomplete elementary school | 86 (3.5%) | 11 (1.5%) | 75 (4.4%) | | 38 (2.7%) | 48 (4.6%) | |
| Smoker | | | | <0.001 | | | <0.001 |
| Never | 1,494 (61.5%) | 539 (72.6%) | 955 (56.5%) | | 961 (69.1%) | 533 (51.3%) | |
| Past | 705 (29.0%) | 161 (21.7%) | 544 (32.2%) | | 318 (22.8%) | 387 (37.3%) | |
| Current | 232 (9.5%) | 42 (5.7%) | 190 (11.3%) | | 113 (8.1%) | 119 (11.4%) | |
| Physical activity | | | | 0.078 | | | 0.064 |
| Insufficient | 1,732 (71.2%) | 543 (73.2%) | 1,189 (70.4%) | | 1,016 (73.0%) | 716 (68.9%) | |
| Moderate | 498 (20.5%) | 132 (17.8%) | 366 (21.7%) | | 263 (18.9%) | 235 (22.6%) | |
| Vigorous | 201 (8.3%) | 67 (9.0%) | 134 (7.9%) | | 113 (8.1%) | 88 (8.5%) | |
| Excessive use of alcohol | 254 (10.4%) | 69 (9.3%) | 185 (10.9%) | 0.220 | 109 (7.8%) | 145 (14.0%) | <0.001 |
| Family history of CVD | 807 (33.2%) | 202 (27.2%) | 605 (35.8%) | <0.001 | 409 (29.4%) | 398 (38.3%) | <0.001 |
| Body mass index (kg/m ²) | 27.0 ± 4.7 | 26.1 ± 4.4 | 27.4 ± 4.8 | <0.001 | 26.6 ± 4.6 | 27.5 ± 4.8 | <0.001 |
| LDL-cholesterol (mg/dl) | 115.0 ± 30.3 | 112.2 ± 28.7 | 116.3 ± 30.9 | 0.002 | 115.0 ± 29.3 | 115.1 ± 31.6 | 0.926 |
| HDL-cholesterol (mg/dl) | 53.6 ± 13.4 | 54.3 ± 13.7 | 53.3 ± 13.3 | 0.113 | 55.2 ± 13.3 | 51.4 ± 13.4 | <0.001 |
| Hemoglobin A1c (%) | 5.5 ± 0.9 | 5.3 ± 0.7 | 5.5 ± 1.0 | <0.001 | 5.3 ± 0.7 | 5.6 ± 1.1 | <0.001 |
| Systolic blood pressure (mm Hg) | 120.5 ± 15.5 | 116.2 ± 13.4 | 122.4 ± 15.9 | <0.001 | 117.6 ± 14.6 | 124.4 ± 15.8 | <0.001 |
| Diastolic blood pressure (mm Hg) | 77.6 ± 9.7 | 76.4 ± 9.1 | 78.1 ± 9.9 | <0.001 | 76.7 ± 9.5 | 78.8 ± 9.8 | <0.001 |
| Use of lipid lowering medications | 525 (21.7%) | 87 (11.8%) | 438 (26.1%) | <0.001 | 194 (14.0%) | 331 (32.0%) | <0.001 |
| Use of antidiabetic medications | 191 (7.9%) | 26 (3.5%) | 165 (9.8%) | <0.001 | 56 (4.0%) | 135 (13.0%) | <0.001 |
| Use of blood pressure lowering medications | 861 (35.4%) | 145 (19.5%) | 716 (42.4%) | <0.001 | 374 (26.9%) | 487 (46.9%) | <0.001 |

Data were presented as mean ± standard deviation, or n (%). CVD = cardiovascular disease; HDL = high density lipoprotein; LDL = low density lipoprotein.

Table 2

Variables associated with thoracic aortic calcium (TAC) in the univariate and multivariate analysis. ELSA-BRASIL, 2015-2016. (N = 2,419)

| Variables | MODEL 0 (Univariate) | MODEL 1 | MODEL 2 | MODEL 3 (Final) |
|--------------------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| Age (years) | 1.14 (1.12-1.15)*** | 1.14 (1.12-1.15)*** | 1.14 (1.12-1.15)*** | 1.12 (1.11-1.14)*** |
| Women | 1.01 (0.85-1.20) | 0.93 (0.77-1.13) | 0.92 (0.75-1.12) | 1.10 (0.88-1.39) |
| Smoker | | | | |
| Never | 1.00 | | 1.00 | 1.00 |
| Past | 1.91 (1.55-2.34)*** | | 1.19 (0.94-1.49) | 1.21 (0.95-1.53) |
| Current | 2.55 (1.80-3.62)*** | | 2.19 (1.51-3.18)*** | 2.16 (1.48-3.14)*** |
| Body mass index (kg/m ²) | 1.06 (1.04-1.08)*** | | 1.07 (1.05-1.09)*** | 1.04 (1.02-1.07)*** |
| Family history of CVD | 1.49 (1.24-1.81)*** | | 1.29 (1.04-1.59)* | 1.25 (1.01-1.55)* |
| LDL-cholesterol (mg/dl) | 1.00 (1.00-1.01)** | | | 1.01 (1.00-1.01)*** |
| HDL-cholesterol (mg/dl) | 0.99 (0.99-1.00) | | | 0.99 (0.98-0.99)* |
| Systolic blood pressure (mm Hg) | 1.03 (1.02-1.04)*** | | | 1.01 (1.00-1.02)** |
| Use of blood pressure lowering medications | 3.03 (2.47-3.72)*** | | | 1.67 (1.31-2.12)*** |
| Use of lipid lowering medications | 2.64 (2.06-3.39)*** | | | 1.37 (1.03-1.82)* |

Data were presented as odds ratio (95% confidence interval). CVD = cardiovascular disease; HDL = high density lipoprotein; LDL = low density lipoprotein.
* p ≤ 0.05; ** p ≤ 0.01; *** p ≤ 0.001

Table 3

Variables associated with coronary artery calcium (CAC) in the univariate and multivariate analysis. ELSA-Brasil, 2015-2016. (N = 2,388)

| Variables | MODEL 0 (Univariate) | MODEL 1 | MODEL 2 | MODEL 3 (Final) |
|--------------------------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| Age (years) | 1.10 (1.08-1.11)*** | 1.11 (1.09-1.12)*** | 1.10 (1.09-1.12)*** | 1.09 (1.07-1.10)*** |
| Women | 0.35 (0.30-0.42)*** | 0.28 (0.23-0.34)*** | 0.27 (0.23-0.33)*** | 0.30 (0.24-0.38)*** |
| Race/skin color | | | | |
| White | 1.00 | 1.00 | 1.00 | 1.00 |
| Brown | 0.80 (0.67-0.96)** | 0.97 (0.79-1.18) | 0.94 (0.77-1.15) | 0.87 (0.70-1.07) |
| Black | 0.61 (0.47-0.79)*** | 0.77 (0.58-1.03) | 0.70 (0.53-0.94)* | 0.63 (0.47-0.86)** |
| Others (Asian, Indigenous) | 0.55 (0.32-0.93)* | 0.69 (0.39-1.24) | 0.75 (0.42-1.34) | 0.69 (0.38-1.26) |
| Smoker | | | | |
| Never | 1.00 | | 1.00 | 1.00 |
| Past | 2.19 (1.83-2.63)*** | | 1.39 (1.13-1.71)** | 1.41 (1.14-1.75)** |
| Current | 1.90 (1.44-2.51)*** | | 1.74 (1.28-2.37)*** | 1.67 (1.22-2.30)*** |
| Body mass index (kg/m ²) | 1.04 (1.02-1.06)*** | | 1.06 (1.04-1.08)*** | 1.03 (1.01-1.05)** |
| Family history of CVD | 1.49 (1.26-1.77)*** | | 1.43 (1.18-1.74)*** | 1.35 (1.10-1.64)** |
| HDL-cholesterol (mg/dl) | 0.98 (0.97-0.98)*** | | | 0.99 (0.98-0.99)* |
| LDL-cholesterol (mg/dl) | 1.00 (1.00-1.00) | | | 1.01 (1.00-1.01)*** |
| Systolic blood pressure (mm Hg) | 1.03 (1.02-1.04)*** | | | 1.01 (1.00-1.02)** |
| Use of antidiabetic medications | 3.57 (2.58-4.93)*** | | | 1.80 (1.23-2.63)** |
| Use of blood pressure lowering medications | 2.40 (2.03-2.85)* | | | 1.47 (1.19-1.82)*** |
| Use of lipid lowering medications | 2.89 (2.37-3.53)* | | | 2.01 (1.58-2.56)*** |

Data were presented as odds ratio (95% confidence interval). CVD = cardiovascular disease; HDL = high density lipoprotein; LDL = low density lipoprotein.
* p ≤ 0.05; ** p ≤ 0.01; *** p ≤ 0.001

but there was no statistical differences between genders regarding TAC. Race/skin color differences were also observed only for CAC, with blacks being less likely to have any CAC compared with whites. Similarly, the use of antidiabetic drugs remained associated only with CAC in the final Model.

Discussion

The present study showed a much higher prevalence of TAC compared with CAC. After full adjustments, the chances of CAC were higher in men and lower in black individuals as compared with white ones. However, there were no differences in TAC chances regarding gender and race/skin color. All other cardiovascular risk factors but the use of

antidiabetic medication, were statistically associated with both TAC and CAC with subtle differences in the OR.

Considering the few studies that compared the overall prevalences of TAC and CAC and that have also included the aortic arch in TAC analysis, our results contrast with those of Craiem et al as they found similar prevalences of TAC (64%) and CAC (62%) in a sample of 970 adults (77% men), aged 57 ± 9 years.¹¹ In contrast, our results agree with Jacobs et al findings concerning the greater prevalence of TAC (97%) than CAC (75%), even though their prevalences were much higher than ours, possibly because they studied a high-risk population of heavy smokers, 83% men.¹²

Even though extensive evidences exist that men are more likely to have CAC,¹²⁻¹⁵ the absence of gender differences in the chances of having TAC remains controversial.

Some studies found greater prevalence of TAC in men and others in women. Nasir et al studied 8,549 individuals (69% men, mean age: 52 ± 9 years) and demonstrated slightly higher prevalence of TAC in women,¹⁶ while the Heinz Nixdorf Study analyzed 4,025 participants (47% men, mean age: 59 ± 9 years) and showed higher TAC prevalence in men.¹³ However, the CT scan protocols of these latter studies did not include the aortic arch and, hence their prevalences cannot be directly compared with ours as this may impact gender differences in the prevalence of TAC. Reports including the aortic arch are scarce, but some show that women concentrate more calcium in this segment than men,^{11,17,18} even though the inclusion of the aortic arch in the analysis will increase the prevalence of TAC in both genders. Craiem et al investigated a population of asymptomatic subjects at increased cardiovascular risk, and showed that TAC prevalence doubled from 31% to 64% after using the scan method covering the aortic arch.¹¹

Our study found an absence of race/skin color difference in the prevalence of TAC, whereas CAC was 40% lower in black individuals as compared with white ones, and this difference was not explained by cardiovascular risk factors. Our results on CAC are in accordance with the MESA study, as they also found lower chance of CAC (OR 0.78; 95% confidence interval 0.74 to 0.82) in blacks as compared with whites.¹⁹ However, they disagree with MESA concerning the prevalence of TAC, as they reported lower prevalence of TAC in African Americans (27%) than in whites (42%).²⁰ Such differences might be related to the inclusion of the aortic arch in our study, as there appear to be race differences concerning the distribution of calcium along the aorta. In the MESA cohort, blacks had higher prevalence of calcium in the ascending portion of the aorta than whites, whereas they showed lower calcium in the descending aorta segment.²¹ Unfortunately, studies comparing TAC prevalence in different race/skin color are scarce, indicating an important gap to be pursued in future research, and do not know whether race differences also exist regarding the aortic arch that could account for the absence of race/skin color difference in TAC prevalence that we found. Finally, race/skin color findings in the Brazilian population must be interpreted considering 2 important facts (1) self-referred race/skin color does not equate biological ancestry information²²; (2) different from other multiethnic populations, the Brazilian population has not only intrapopulation ethnic diversity, but also intraindividual ancestry variety.²³

The finding of no statistical association between variables related to diabetes and TAC in the present study may reflect a true weaker association of diabetes and calcification in the aortic territory, when compared with coronary arteries. Indeed, in the MESA Study insulin resistance, evaluated by the homeostasis model assessment index, was associated with the presence of CAC, but not TAC in individuals without diabetes, even though significant associations were seen between insulin resistance and TAC in individuals in the 3rd tertile of subcutaneous and visceral fat areas.²⁴ In contrast, a recent study showed that higher HbA1c and the presence of diabetes were associated with thoracic aorta calcium after adjustment for several risk factors.²⁵ However, we cannot discard that our finding of no

association reflect differences in diabetes contribution to the pathophysiologic pathways of atherosclerosis in distinct arterial territories.

The race/skin color and gender differences in TAC and CAC prevalences found here may also express different underlying pathophysiologic processes relevant to different diseases. There are 2 mechanisms of vascular calcium: intimal (atherosclerotic) and medial (arteriosclerotic).²⁶ Whereas CAC is mostly intimal, medial calcium is common in the aorta and uncommonly reported in the coronary arteries.²⁷ Abramowitz et al posit that TAC can be the result of both atherosclerotic and nonatherosclerotic processes, with the former occurring in the tunica intima of the vessel wall and the latter occurring in the tunica media.²⁸ Thomas et al suggested that medial calcium may reflect biological aging.²⁹

The present study has limitations. It is cross-sectional analysis and the temporality of the associations cannot be established. The prevalences found cannot be extrapolated to the Brazilian population, given that ELSA-Brasil is a cohort of civil servants in urban areas, and in this study they come from just one Brazilian state.⁴ To counterbalance these limitations, the strengths of our study include a large multiethnic well-characterized sample; measurements of calcium from aortic arch, ascending, and descending thoracic aorta segments for which there is very limited literature; the comparison with CAC, and simultaneous adjustments for most risk factors for CVD.

In conclusion, we found differences between TAC and CAC prevalences in genders and race/skin color that might be related to the mechanisms of calcium formation across different vascular beds. Further studies using similar protocols, including aortic arch and the analysis of each segment of the aorta separately, might shed some light in the potential contribution of TAC in the classification of cardiovascular risk and whether it varies by gender, race/skin color or diabetes status.

Disclosures

The authors have no conflicts of interest to disclose. The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit for publication.

Acknowledgment

The authors would like to thank all participants from Minas Gerais Investigation Center of ELSA-Brasil and the Centro de Imagem e Medicina Molecular, UFMG, Brazil, where the CT scans were performed.

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