Neck circumference is associated with carotid intimal-media thickness but not with coronary artery calcium: Results from The ELSA-Brasil

C.P. Baena [a,b], P.A. Lotufo [a,c], I.S. Santos [a,c], A.C. Goulart [a], M.S. Bittencourt [a], B.B. Duncan [d], S. Liu [e], I.M. Benseñor [a,c,*]

[a] Center for Clinical and Epidemiologic Research, Hospital Universitario, São Paulo, Brazil
[b] School of Medicine, Pontifícia Universidade Católica do Paraná, Curitiba, Brazil
[c] School of Medicine, University of São Paulo, São Paulo, Brazil
[d] Postgraduate Studies Program in Epidemiology, School of Medicine, Federal University of Rio Grande do Sul, Porto Alegre, Brazil
[e] School of Public Health, Brown University, Providence, RD, USA

Abstract *Background and aims:* It is uncertain whether neck circumference can be a risk indicator for subclinical atherosclerosis. We aimed to investigate their relationships measured by coronary artery calcium (CAC) and common carotid intima-media thickness (cc-IMT) with neck circumference in ELSA-Brasil.
Methods and results: In cross-sectional and sex-specific analyses of 2266 women (50.6 ± 8.4 yrs) and 1886 men (50.7 ± 9.0 yrs) with both cc-IMT and CAC, free from previous cardiovascular disease at baseline, we built logistic models using diverse cut-off points for CAC score (0 vs >0, <100 vs ≥100, <400 vs ≥400 Agatston units) and cc-IMT (<75th percentile vs ≥75th; <90th percentile vs ≥90th) as dependent variables, after which adjustments for age and traditional cardiovascular risk factors were made. Mean neck circumference was 33.6 (± 2.4 cm) for women and 38.8 (± 2.6 cm) for men. In fully adjusted models including sociodemographic, cardiovascular risk factors and body-mass index and waist circumference, for each 1 standard deviation increase in neck circumference we found an odds ratio (OR, 95% CI) for IMT above the 75th percentile of (1.52, 1.16; 1.99) for women and (1.66, 1.28; 2.14) for men, and above the 90th cc-IMT percentile [1.66 (1.19; 2.32) for men but not for women [1.21 (0.80; 1.82)]. We found no association between neck circumference and CAC using different cut-off points ($p > 0.05$ for all).
Conclusion: Neck circumference was significantly and independently associated with cc-IMT but not with CAC in women and men, indicating a possible effect of perivascular fat tissue on atherosclerosis.
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Introduction

Obesity is a global epidemic of our time with increased mortality and morbidity [1]. Despite its tight connection with other cardiovascular risk factors and metabolic syndrome, it is now clear that different patterns of fat distribution confer heterogeneous additional cardiovascular risk beyond body-mass index (BMI) itself [2—5]. Body fat

* Corresponding author. Center for Clinical and Epidemiological Research, Hospital Universitário, Av. Lineu Prestes 2565 3° andar, CEP 05508-000, São Paulo, SP, Brazil. Tel./fax: +55 11 30919300.

distribution is a matter of interest for more than 50 years now [6,7], yet only recently the study of specific fat depots effects on cardiovascular risk has gained attention [8–11]. Neck circumference can be described as a marker of upper body subcutaneous fat deposit, which has been independently associated with several cardiometabolic risk factors such as total cholesterol [9,10], HDL-cholesterol [9,10], LDL-cholesterol [8,10], triglycerides [8,10,11], systolic and diastolic blood pressure levels [8–10] and fasting glucose [8,10]. These associations were reported in observational studies of diverse populations as significant even after multivariate adjustment including BMI and waist circumference. Changes in neck circumference were also correlated with changes in cardiovascular risk profile [12]. Some studies have also associated neck circumference with measures of metabolic syndrome and insulin resistance, as well [4,8,13].

Common carotid intima-media thickness (cc-IMT) is a noninvasive measure that has been used as a surrogate outcome for atherosclerotic disease [14] in population-based [15] and clinical studies [16]. More recently, it has been proposed as a potential predictor of individual cardiovascular risk in clinical practice [17]. As another noninvasive measure of subclinical atherosclerosis, coronary artery calcification (CAC) have also been used for risk prediction of cardiovascular events. The presence and extent of CAC is a well-known predictor of future risk for cardiovascular disease (CVD) and also for all-cause mortality in individuals with no previous history of CVD [18,19].

The association between neck circumference and both these measurements of subclinical atherosclerosis has been studied in the Framingham Heart Study offspring, where the neck circumference was correlated to internal carotid intima-media thickness (IMT), a marker of subclinical atherosclerosis. In multivariable models, a 1−SD increase in neck circumference was associated with a 0.071 mm increase in internal carotid IMT and with a 0.025 mm increase in common carotid IMT. Both associations remained significant after multivariable adjustment including BMI [20]. Pokharel et al., evaluated cross-sectionally the relationship between neck circumference and subclinical atherosclerosis measured by CAC and carotid plaques in a middle-aged population of retired national football league players. Although they found a high prevalence of CAC and carotid plaques, they did not find any association of these subclinical atherosclerosis indexes with neck circumference [21].

The Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) is an ongoing prospective cohort study of civil servants with relatively high prevalence of overweight and obesity. Thus, we decided to investigate neck circumference as a potential marker of subclinical atherosclerosis indexes through its association with both cc-IMT and CAC in the ELSA-Brasil São Paulo site.

Methods

ELSA-Brasil is a multicenter prospective cohort, which enrolled 15,105 civil servants aged 35−74 years (54% women) from 6 Brazilian cities (Belo Horizonte, Porto Alegre, Rio de Janeiro, Salvador, São Paulo and Vitória [22−24]). The study aims to investigate factors associated with the development and progression of CVD, diabetes, and other chronic conditions. Baseline assessment consisted of an evaluation lasting approximately 7 h, which included in-person interviews conducted by trained personnel [25]. These standardized interviews were focused on sociodemographic characteristics, health, and medical history, use of medication, as well as, clinical and laboratory measurements [26]. Approvals were obtained from the institutional review boards of all the centers, and all the subjects signed an informed consent form.

Design and population study

Of the 15,105 participants in ELSA-Brasil, CAC was done in a subsample of 4412 at the research center of Sao Paulo. We included in this analysis all individuals with complete data on cc-IMT, CAC and neck circumference measurement at baseline. We excluded 260 participants with known previous CVD (coronary heart disease, myocardial revascularization, heart failure and stroke), leaving 4152 participants that were included for this analysis.

Common carotid intima-media thickness

The technique for cc-IMT measurement has been previously applied in other population-based studies [27,28], and it has been published in the ELSA-Brasil [29]. The protocol was performed using a Toshiba (Aplio XG™) with a 7.5 MHz linear transducer. IMT was measured in the outer wall of a pre-defined carotid segment of 1 cm in length from 1 cm below carotid bifurcation, during three cardiac cycles. The carotid images during three cardiac cycles were obtained and sent to the centralized reading center in São Paulo. We used MIA™ software to standardize the reading and interpretation of carotid scans as previously described. IMT measurements are presented as the maximum values for the thickness of the right and left arteries measured at the far wall.

Coronary artery calcium score

All participants underwent a CAC examination performed with a 64-detector computed tomography scanner (Brilliance 64, Philips Healthcare, Best, Netherlands). After the scout images, each patient underwent an ECG-gated prospective calcium score examination with a tube potential of 120 kV and a tube current adjusted to body habitus. Images were reconstructed in 2.5 mm slice thickness using standard filtered back projection. The CAC was expressed as Agatston units 20, and the percentile was evaluated in a blinded fashion by an experienced cardiologist using semiautomatic software (Calcium Scoring, Philips Workstation). CAC severity was further categorized as 0 or >0, <100 or ≥100, and <400 or ≥400.