Relationship between common carotid intima-media thickness and thoracic aortic calcification: The Multi-Ethnic Study of Atherosclerosis

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ARTICLE INFO

ABSTRACT

Background: Mean maximum carotid intima-media thickness (CIMT) is associated with both coronary artery disease and cerebral thromboembolism. Thoracic aortic calcification (TAC) detected by computed tomography (CT) is also highly associated with vascular disease and cardiovascular risk. No previous study has examined the relationship between CIMT and TAC in a large patient cohort. We performed a cross-sectional study to determine whether, at baseline, there is a relationship between CIMT and CT-determined TAC score.

Methods: In the Multi-Ethnic Study of Atherosclerosis, the study cohort included a population based sample of four ethnic groups (Chinese, White, Hispanic and African-American) of 6814 women and men ages 45–84 years. After exclusion of 198 persons due to incomplete information, we compared results of 6616 participants with both CIMT and TAC. TAC was measured from the lower edge of the pulmonary artery bifurcation to the cardiac apex. CIMT at the common carotid artery site was represented as the mean maximal CIMT of the right and left near and far walls, respectively. Multivariable relative risk regression analysis was used to evaluate relationships between TAC and CIMT.

Results: The prevalence of TAC was 28% ($n = 1846$) and the mean maximum ($+SD$) CIMT was 0.87 ± 0.19 mm. A higher prevalence of TAC was noted across increasing CIMT quartiles (1st: 12%, 2nd: 21%, 3rd: 30%, 4th: 49%, $p < 0.0001$). One standard deviation increase in CIMT was associated with a 16% higher likelihood for presence of TAC after adjusting for demographics and cardiovascular disease (CVD) risk factors (95% CI: 1.12–1.26). In addition, individuals with CIMT in the highest quartile, as compared to those with CIMT in the first quartile, had a 76% higher likelihood for presence of TAC (prevalence ratio [PR]: 1.76, 95% CI: 1.37–2.26). In race-ethnic stratified analyses, similar associations were seen in all groups. Among those with TAC > 0, a higher CIMT was significantly associated with continuous TAC scores (log transformed) in the overall population as well as among all ethnic-racial groups.

Conclusions: Our study demonstrates that TAC is associated with increasing severity of carotid atherosclerotic burden as measured by CIMT. The combined utility of these two noninvasive measures of subclinical atherosclerosis for CVD risk assessment needs to be determined in future studies.

1. Introduction

Numerous studies have reported on the correlations between atherosclerosis in the coronary and extra-coronary vascular beds [1,2]. However, no previous study has examined the relationship between extra-coronary calcification and carotid intima-media thickness (CIMT) as measured by B-mode ultrasonography which has been widely used to evaluate cardiovascular risk, and many studies have shown a close relationship between carotid atherosclerosis and coronary artery calcification (CAC) [3–8]. Calcific aortic disease in the thoracic aorta is common in the elderly, and population based prospective studies have shown that patients with thoracic aortic calcification (TAC) have significantly higher cardiovascular disease (CVD) events and stroke [9–12]. Allison et

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al in a moderate-sized cohort using whole-body electron beam tomography (EBT) showed that the incidence and progression of calcification in various vascular beds differed [13]. Aortic involvement rapidly increased by age 60 [6,14] while carotid involvement showed the slowest increases among the various arterial beds. Moreover, studies evaluating coronary artery calcium (CAC) and CIMT are only moderately correlated, with a stronger relationship of CVD events using CAC [15–17]. Kallikazaros et al., using a small cohort of patients without a history of atherosclerotic CVD, demonstrated that these individuals had a high prevalence of both aortic and carotid plaques [18]. In the current study, we compared carotid atheroma and aortic calcification using CIMT and TAC, respectively, in a multi-ethnic population.

2. Methods

The Multi-Ethnic Study of Atherosclerosis (MESA) was initiated in July 2000 to investigate the prevalence, correlates and progression of subclinical cardiovascular disease in individuals without known CVD [19]. This prospective cohort study includes 6814 women and men ages 45–84 years old recruited from six U.S. communities (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; Northern Manhattan, NY; and St. Paul, MN). There are 38% White ($N = 2624$), 28% African American ($N = 1895$), 22% Hispanic ($N = 1492$), and 12% Chinese ($N = 803$) individuals. All participants underwent both non-enhanced cardiac CT for evaluation of CAC and carotid ultrasound. All participants provided written informed consent. An ancillary study, supported by the National Institutes of Health, was performed to measure aortic and valvular calcification on the CAC scans obtained for the MESA study. The study was approved by the Institutional Review Board of all participating institutions. Of 6814 participants, 198 were excluded due to incomplete CIMT ($N = 197$) or TAC ($N = 1$) data.

Baseline medical history, anthropometric measurements, and laboratory data for the present study were taken from the first examination of the MESA cohort (July 2000 to August 2002). These self-administered questionnaires were available in English, Spanish, and Chinese. Information about age, gender, ethnicity, and medical history were obtained by questionnaires. Resting blood pressure was measured three times in the seated position, and the average of the 2nd and 3rd readings was recorded. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or use of baseline blood pressure lowering medication. Use of antihypertensive and other medications were based on clinic staff entry of prescribed medications. Body mass index was calculated from the equation weight (kg)/height (m^2). Total and high density lipoprotein (HDL-C) were measured from blood samples obtained after a 12-h fast. Low density lipoprotein (LDL-C) was estimated by the Friedewald equation with triglycerides measured in fasting state [18]. Current smoking was defined as having smoked a cigarette in the last 30 days. Diabetes mellitus was defined as a fasting glucose ≥ 126 mg/dl or use of hypoglycemic medications. C reactive protein (CRP) was measured using the BNII nephelometer (N High Sensitivity CRP; Dade Behring Inc., Deerfield, IL) at the Laboratory for Clinical Biochemistry Research (University of Vermont, Burlington, VT). Analytical intra-assay CVs ranged from 2.3 to 4.4% and inter-assay CVs ranged from 2.1 to 5.7%.

3. Thoracic aortic calcification assessment

All participants underwent two consecutive CT scans at baseline. Three sites used an Imatron C-150XL CT scanner (GE-Imatron, San Francisco, CA), and three sites used a multidetector CT scanner (four slice). The method has been reported previously [20]. Image slices were obtained with the participant supine, with no couch angu-

lation. A minimum of 35 contiguous images with a 2.5- or 3-mm slice thickness was obtained, starting above the left main coronary artery to the bottom of both ventricles. Each scan was obtained in a single breath hold. Section thickness of 3 mm, field of view of 35 cm, and matrix of 512×512 were used to reconstruct raw image data. The nominal section thickness was 3.0 mm for electron beam CT and 2.5 mm for four-detector row CT. Spatial resolution can be described by the smallest volume element, or voxel, for the protocol for each system: 1.15 mm^3 for four-detector row CT (0.68 mm × 0.68 mm × 2.50 mm) and 1.38 mm^3 for electron beam CT (0.68 mm × 0.68 mm × 3.00 mm). Thoracic aortic wall calcification in the segment of the ascending and/or descending thoracic aorta adjacent to the heart (imaged on every study of coronary calcium) was scored by using the same lesion definition. The sum of all TAC was reported for each study. This region of the thoracic aorta was included on the images of every study of coronary calcium and was quantified by using the same lesion definition (threshold and minimum lesion size) as used for coronary calcification [21]. The absence of TAC was assigned a score of 0.

4. Carotid intima-media thickness assessment

In concordance with the consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force, we used CIMT of the common carotid artery [22]. Trained technicians in each field center performed B-mode ultrasonography of the right and left near and far walls of the common carotid artery. They used the Logiq 700 ultrasound device (General Electric Medical Systems, Waukesha, WI) to record images. An ultrasound reading center (Department of Radiology, Tufts-New England Medical Center, Boston, MA) measured maximal CIMT of the common carotid site as the mean of the maximum CIMT of the near and far walls of the right and left sides.

5. Statistical methods

CIMT was categorized into quartiles for analyses. TAC was dichotomized as present (Agatston score > 0) or absent (Agatston score = 0). Distributions of demographics and cardiovascular risk factors were compared across these groups. A simple approach to separate the qualitative difference between absence and presence of TAC from the quantitative effect of TAC was used. TAC was modeled as a dichotomous variable (TAC = 0 versus TAC > 0) and as a continuous variable (ln(TAC)) among those with detectable TAC. Because the prevalence of TAC in our cohort is greater than 10%, odds ratios (ORs) overestimate the prevalence ratio (PR). Therefore, PR estimates are presented from the regression model
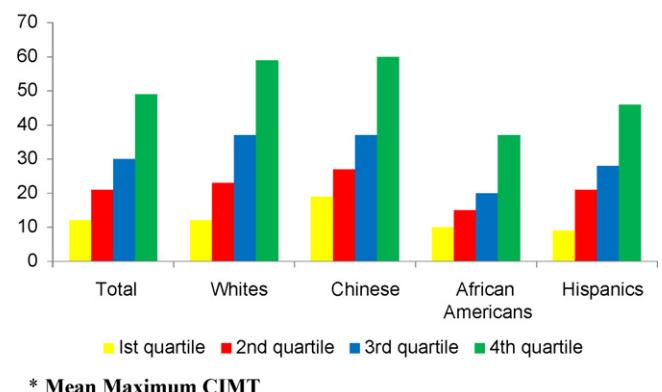

* Mean Maximum CIMT

Fig. 1. Prevalence of TAC according to common CIMT quartiles.