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Association of Coronary Artery Calcium and Coronary Heart Disease Events in Young and Elderly Participants in the Multi-Ethnic Study of Atherosclerosis: A Secondary Analysis of a Prospective, Population-Based Cohort

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Abstract

Objective: To evaluate the association of coronary artery calcium (CAC) and coronary heart disease (CHD) events among young and elderly individuals.

Participants and Methods: This is a secondary analysis of data from a prospective, multiethnic, population-based cohort study designed to study subclinical atherosclerosis. A total of 6809 persons 45 through 84 years old without known cardiovascular disease at baseline were enrolled from July 2000 through September 2002. All participants had CAC scoring performed and were followed up for a median of 8.5 years. The main outcome measures studied were CHD events, defined as myocardial infarction, definite angina or probable angina followed by revascularization, resuscitated cardiac arrest, or death attributable to CHD.

Results: Comparing individuals with a CAC score of 0 with those with a CAC score greater than 100, there was an increased incidence of CHD events from 1 to 21 per 1000 person-years and 2 to 23 per 1000 person-years in the 45- through 54-year-old and 75- through 84-year-old groups, respectively. Compared with a CAC score of 0, CAC scores of 1 through 100 and greater than 100 impart an increased multivariable-adjusted CHD event risk in the 45- through 54-year-old and 75- through 84-year-old groups (hazard ratio [HR], 2.3; 95% CI, 0.9-5.8; for those 45-54 years old with CAC scores of 1-100; HR, 12.4; 95% CI, 5.1-30.0; for those 45-54 years old with CAC scores >100: HR, 5.4; 95% CI, 1.2-23.8; for those 75-84 years old with CAC scores of 1-100; and HR, 12.1; 95% CI, 2.9-50.2; for those 75-84 years old with CAC scores >100).

Conclusion: Increased CAC imparts an increased CHD risk in younger and elderly individuals. CAC is highly predictive of CHD event risk across all age groups, suggesting that once CAC is known chronologic age has less importance. The utility of CAC scoring as a risk-stratification tool extends to both younger and elderly patients.

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The American Heart Association and the European Society of Cardiology guidelines ascribe a Class IIA recommendation for coronary artery calcium (CAC) testing in asymptomatic patients at intermediate risk for coronary heart disease (CHD).[1,2] Given the reliance of risk-scoring algorithms on chronologic age, this recommendation excludes many young and elderly patients who are typically classified as being at low and high risk, respectively. Less than 10% of young patients

and approximately 22% of elderly patients are considered to be at intermediate risk.[3,4] The utility of CAC testing in young and elderly patients has therefore not been well delineated.

A potential argument against the use of CAC scoring in elderly patients is that because the burden of calcified coronary atherosclerotic plaque increases with age,[5] most elderly patients will have some CAC, thus reducing the ability of CAC to refine risk stratification in elderly individuals. Although elderly individuals might be

expected to have an increased prevalence of CAC, few studies have specifically investigated the effect of increasing CAC on the incidence of CHD events in elderly individuals.[4,6-9]

In contrast, the utility of CAC scoring in young patients may be questioned because of the potential burden of noncalcified coronary plaque.[5] Therefore, CAC scoring may not fully capture the potential CHD risk associated with rupture-prone, noncalcified coronary plaque.[10] The utility of CAC scoring in young patients is even more obscure, given the concerns of radiation exposure and cost-effectiveness. Prior attempts to clarify the role of CAC testing in young individuals have been limited by a low incidence of CHD events[11] and referral bias.[6]

We hypothesized that CAC would be a similarly strong, independent predictor of absolute and relative risk of CHD events in patients 75 through 84 years old, as well as in young patients 45 through 54 years old. We also studied whether the CHD event risk would be lower in an elderly patient with a CAC score of 0 compared with a young individual with a high CAC score.

METHODS

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective, population-based cohort that comprises 4 prespecified ethnicities (white, African American, Hispanic, and Chinese) and 6 US communities (Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; New York, New York; and St Paul, Minnesota). The primary goal of MESA is to evaluate the characteristics and risk factors of subclinical cardiovascular disease. The study design has been previously described.[12]

A total of 6809 persons 45 through 84 years old without known cardiovascular disease at baseline were recruited from July 2000 through September 2002, and had CAC scoring performed. The institutional review boards of each site approved the study, and all participants gave written informed consent.

Risk Factor Measurement

A questionnaire was used to obtain demographic data, cardiovascular risk factors, and medical history. Resting blood pressure was measured 3 times with the study participant in a seated position using a Dinamap model Pro

100 automated oscillometric sphygmomanometer (Critikon). The mean of the last 2 measurements was used in analysis. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides, and plasma glucose levels were measured after a 12-hour fast.

Hypertension was defined as a blood pressure of 140/90 mm Hg or higher or the use of antihypertensive medications. Diabetes mellitus was defined as a fasting glucose level of 126 mg/dL or higher (to convert to mmol/L, multiply by 0.055) or the use of antihyperglycemic medications. A family history of CHD was defined as a first-degree relative with a history of CHD, coronary angioplasty, or coronary artery bypass surgery. Participants were classified as current, former, or never smokers.

CAC Measurement

The MESA CAC scanning protocol has been previously described.[13] Chest computed tomography (CT) was performed using either a cardiac-gated electron-beam CT scanner (Chicago, Los Angeles, and New York field centers; Imatron C-150, Imatron) or a prospective electrocardiogram-triggered multidetector CT scanner acquired at 50% of the R-R interval. Four 2.5-mm sections were acquired for each cardiac cycle in sequential or axial scan mode (the Baltimore, Forsyth County, and St Paul field centers; Lightspeed, General Electric Medical Systems, or Volume Zoom, Siemens).

Each participant underwent 2 CTs, and the mean of both Agatston CAC scores[14] was used in analysis. All CTs were read at a single center by 2 independent cardiologists (including M.J.B.). There was acceptable intraobserver and interobserver agreement (κ=0.93 and 0.90, respectively).

Definition of CHD Event

The primary end point was the incidence of all CHD events during the study period. A CHD event was defined as myocardial infarction, definite angina or probable angina followed by revascularization, resuscitated cardiac arrest, or CHD death, whereas a hard CHD event was defined as CHD death or nonfatal myocardial infarction. Angina was graded as absent, probable, or definite based on clinical judgment. Definite angina required documentation of symptoms distinct from myocardial infarction diagnoses. A classification of definite