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Coronary Artery Calcium Improves Risk Classification in Younger Populations

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ABSTRACT

OBJECTIVES This study sought to assess the effect of coronary artery calcium (CAC) on coronary heart disease (CHD) risk prediction in a younger population.

BACKGROUND CAC measured by computed tomography improves CHD risk classification in older adults, but the effectiveness of CAC in younger populations has not been fully assessed.

METHODS In the DHS (Dallas Heart Study), a multiethnic probability-based population sample, traditional CHD risk factors and CAC were measured in participants without baseline cardiovascular disease or diabetes. Incident CHD—defined as CHD death, myocardial infarction, or coronary revascularization—was assessed over a median follow-up of 9.2 years. Predicted CHD risk was assessed with a Weibull model inclusive of traditional risk factors before and after the addition of CAC as ln(CAC + 1). Participants were divided into 3 10-year risk categories, <6%, 6% to <20%, and ≥20%, and the net reclassification improvement (NRI) was calculated. We also performed a random-effects meta-analysis of NRI from previous studies inclusive of older individuals.

RESULTS The analysis comprised 2,084 participants; mean age was 44.4 ± 9.0 years. CAC was independently associated with incident CHD (hazard ratio per SD: 1.90, 95% confidence interval [CI] 1.51 to 2.38; $p < 0.001$). The addition of CAC to the traditional risk factor model resulted in significant improvement in the C-statistic (delta = 0.03; $p = 0.003$). Among participants with CHD events, the addition of CAC resulted in net correct upward reclassification of 21%, and among those without CHD, a net correct downward reclassification of 0.5% (NRI: 0.216, $p = 0.012$). Results remained significant when the outcome was restricted to CHD death and myocardial infarction and when individuals with diabetes were included. The NRI observed in this study was similar to the pooled estimate from previous studies (0.200, 95% CI: 0.140 to 0.258) and the addition of our study to the meta-analysis did not result in significant heterogeneity ($I^2 = 0\%$).

CONCLUSIONS CAC scoring also improves CHD risk classification in younger adults. (J Am Coll Cardiol Img 2015;8:1285–93) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CAC = coronary artery calcium

CHD = coronary heart disease

CI = confidence interval

HR = hazard ratio

MI = myocardial infarction

NRI = net reclassification improvement

Coronary artery calcium (CAC) measured by computed tomography has emerged as a powerful predictor of coronary heart disease (CHD) (1). Compared with most other novel risk markers, CAC has a greater impact on clinical metrics of discrimination (i.e., C-statistics) and risk classification (i.e., net reclassification improvement [NRI]) (2,3). In the most recent cardiovascular risk assessment guidelines, CAC scanning received a Class IIb recommendation (i.e., may be considered) for individuals ages 40 through 79 years in whom a risk-based treatment decision is uncertain (4).

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Three population-based studies have assessed the effects of CAC on CHD risk classification, with each study showing significant improvement in C-statistics and NRI when CAC was added to a traditional CHD risk factor model (5-7). Because the mean age in those cohorts ranged from 59 to 70 years, the effect of CAC on risk reclassification at the lower end of the age group targeted in recent guidelines has not been fully assessed.

We sought to determine the effects of CAC on CHD risk prediction in a young, multiethnic, probability-based population cohort and to compare our findings with data from older cohorts.

METHODS

STUDY SAMPLE. The DHS (Dallas Heart Study) is a multiethnic, probability-based population cohort of Dallas County adults, with deliberate oversampling of African Americans. Detailed methods of DHS have been described previously (8). All participants provided written informed consent, and the study protocol was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center. Briefly, between 2000 and 2002, 2,969 participants, ages 30 to 65 years, completed a detailed in-home survey, laboratory testing, and multiple imaging studies. Of these 2,969 individuals, 226 did not have an interpretable CAC scan; 74 reported previous cardiovascular disease defined as myocardial infarction (MI), stroke, or coronary revascularization; 6 had end-stage renal disease; 88 had missing data on traditional risk factor(s); and 191 had incomplete follow-up for nonfatal events (Online Figure 1). Because participants with diabetes (n = 300) are thought to have high cardiovascular risk, they were not included in the primary analysis (9,10). The final study population comprised 2,084 subjects free of diabetes and cardiovascular disease who were followed for fatal and nonfatal CHD events.

DEFINITIONS AND MEASUREMENTS. Race/ethnicity, history of cardiovascular diseases, individual medication usage, and smoking status were self-reported. Blood pressure, plasma glucose, and lipids were measured using standard methods (8). Diabetes was defined as fasting glucose ≥126 mg/dl, or nonfasting glucose ≥200 mg/dl, or reported diagnosis of diabetes coupled with the use of glucose-lowering medication. The study definitions of hypertension, metabolic syndrome, and family history of premature CHD used in the DHS have been previously published (11).

Electron-beam computed tomography measurements of CAC were performed in duplicate 1 to 2 min apart on an Imatron 150 XP scanner (Imatron Inc., San Bruno, California). Sufficient 3-mm slices were acquired (n = ~40) to span the heart during a single inspiratory breath-hold (12). The 2 CAC scores were determined using the Agatston method and then averaged.

CLINICAL OUTCOMES. DHS participants were prospectively followed for fatal and nonfatal cardiovascular outcomes, and events were ascertained through December 31, 2010 (13). Fatal events were tracked using the National Death Index (14). Participants were contacted annually and assessed for interval nonfatal cardiovascular events. In addition, participants were tracked for hospital admissions using the Dallas Fort Worth Hospital Council Data Initiative database (DFWHC ERF Information Quality Services Center Regional Data [2000 to 2011]; Dallas-Fort Worth Hospital Council Education and Research Foundation, Information and Quality Services Center, Irving, Texas). This includes hospital admission data for 70 of 72 hospitals in the Dallas Fort Worth metroplex. Using these data sources, >90% of participants were followed for nonfatal events. Primary records were requested for all suspected cardiovascular events, and these events were separately adjudicated by 2 cardiologists blinded to CAC assessment and all study variables (13).

The outcome for the primary analysis was defined as the time-to-first event of the composite of CHD-related death, nonfatal MI, or percutaneous or surgical coronary revascularization. All revascularization events (coronary artery bypass graft surgery and percutaneous revascularization) occurring within the first 3 months following CAC scanning were excluded from the analyses to minimize the possibility that the CAC test result influenced the revascularization event. Secondary analyses were performed for the composite outcome of hard CHD (CHD-related death and MI).

STATISTICAL ANALYSIS. Baseline demographic and clinical variables were compared between individuals