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ORIGINAL INVESTIGATIONS

10-Year Coronary Heart Disease Risk Prediction Using Coronary Artery Calcium and Traditional Risk Factors

Derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) With Validation in the HNR (Heinz Nixdorf Recall) Study and the DHS (Dallas Heart Study)

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ABSTRACT

BACKGROUND Several studies have demonstrated the tremendous potential of using coronary artery calcium (CAC) in addition to traditional risk factors for coronary heart disease (CHD) risk prediction. However, to date, no risk score incorporating CAC has been developed.

OBJECTIVES The goal of this study was to derive and validate a novel risk score to estimate 10-year CHD risk using CAC and traditional risk factors.

METHODS Algorithm development was conducted in the MESA (Multi-Ethnic Study of Atherosclerosis), a prospective community-based cohort study of 6,814 participants age 45 to 84 years, who were free of clinical heart disease at baseline and followed for 10 years. MESA is sex balanced and included 39% non-Hispanic whites, 12% Chinese Americans, 28% African Americans, and 22% Hispanic Americans. External validation was conducted in the HNR (Heinz Nixdorf Recall Study) and the DHS (Dallas Heart Study).

RESULTS Inclusion of CAC in the MESA risk score offered significant improvements in risk prediction (C-statistic 0.80 vs. 0.75; $p < 0.0001$). External validation in both the HNR and DHS studies provided evidence of very good discrimination and calibration. Harrell's C-statistic was 0.779 in HNR and 0.816 in DHS. Additionally, the difference in estimated 10-year risk between events and nonevents was approximately 8% to 9%, indicating excellent discrimination. Mean calibration, or calibration-in-the-large, was excellent for both studies, with average predicted 10-year risk within one-half of a percent of the observed event rate.

CONCLUSIONS An accurate estimate of 10-year CHD risk can be obtained using traditional risk factors and CAC. The MESA risk score, which is available online on the MESA web site for easy use, can be used to aid clinicians when communicating risk to patients and when determining risk-based treatment strategies. (J Am Coll Cardiol 2015;66:1643–53)

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ABBREVIATIONS AND ACRONYMS

CAC = coronary artery calcium
CHD = coronary heart disease
ECG = electrocardiogram
MI = myocardial infarction

Coronary artery calcium (CAC) scores derived from routine cardiac-gated noncontrast computed tomography scans are a commonly used method for enhancing clinical cardiovascular risk prediction. Importantly, CAC scores are incremental but not redundant with traditional risk factors, and therefore, integration of both sets of information can enhance risk assessment. Indeed, the added value of CAC over and above traditional risk factors for prediction of cardiovascular events has been demonstrated in several studies (1–11). However, to date, no published risk scores are available to clinicians to incorporate CAC into routine 10-year risk prediction.

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The MESA (Multi-Ethnic Study of Atherosclerosis), due to its population-based, multiethnic composition and availability of 10 years of follow-up for incident CHD events, provides a unique opportunity to describe how CAC might be optimally combined with traditional risk factors in risk prediction. In this paper, we describe a novel MESA risk score that can be used to estimate 10-year CHD risk in patients with a CAC measurement. We also provide a score without inclusion of CAC for evaluation of the effect of including CAC in the novel risk score. We believe that the MESA risk score could be immediately used for communication of risk with patients after CAC scoring, to guide risk-based treatment decisions in clinical practice, as well as in designing future research studies that might use CAC to target high-risk subpopulations.

METHODS

STUDY PARTICIPANTS. MESA was designed to study the prevalence, risk factors, and progression of subclinical cardiovascular disease (CVD) in a multiethnic cohort. A detailed description of the study design and methods has been published previously (12). Briefly, 6,814 participants age 45 to 84 years who identified themselves as white, African-American, Hispanic, or Chinese were recruited from 6 U.S. communities from 2000 to 2002. All participants were free of clinically apparent CVD. The research was approved by the institutional review boards at all participating institutions, and all participants gave informed consent.

MEASUREMENT OF CAC. CAC was measured using electrocardiogram (ECG)-gated electron-beam computed tomography at 3 field centers and multidetector computed tomography at the other 3 field centers (12,13). Images were analyzed independently at a central reading center, and the amount of CAC was quantified using the Agatston scoring method (14). Rescan agreement was high using both electron-beam and multidetector computed tomography scanners (15). Interobserver and intraobserver agreement were also very high (Kappa = 0.93 and 0.90, respectively).

CORONARY HEART DISEASE ASCERTAINMENT. At intervals of 9 to 12 months, a telephone interviewer contacted each participant to inquire about interim hospitalizations, cardiovascular outpatient diagnoses and procedures, and deaths. Trained personnel abstracted medical records, and 2 physicians independently classified the events using pre-defined

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