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Multicenter Epidemiological Studies of Atherosclerosis Imaging

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Abstract

Cardiovascular disease is the leading cause of death and disability. Conventional cardiac risk factors do not fully explain the level of cardiovascular risk, incidence of coronary artery disease, and coronary events. Risk stratification and therapy based solely on these conventional risk factors may overlook a population who would benefit from lifestyle and risk factor modification. Thus, research has recently focused on improving risk assessment with new tools in an effort to better identify subjects at highest risk and in need of aggressive management. Cardiovascular imaging, both in coronary and extracoronary arterial beds, has proven to be very helpful in this regard. In this article, we review the current literature from multicenter epidemiology studies on the utility of noninvasive imaging modalities for risk stratification in the context of conventional risk factor evaluation.

Keywords

atherosclerosis; cardiovascular risk; magnetic resonance imaging; computed tomography; epidemiology; coronary calcium; carotid arteries; intima-media thickness

The burden of coronary heart disease (CHD) in the United States remains enormous, even though associated mortality rates fell by more than 40% between 1980 and 2000.¹ The lifetime risk of CHD is substantial,² and the condition is often silent or may strike without warning, underscoring the importance of prevention. Epidemiological studies continue to expand our understanding of the importance of both novel and established cardiovascular risk factors in the population.

Estimation of individual patient risk is a key element in decisions about the initiation of drug therapy, and the Framingham risk score (FRS) has been extensively evaluated as a predictor of future cardiovascular events in asymptomatic individuals.³ Although FRS is widely used, traditional cardiovascular risk factors (male sex, systolic blood pressure, total and high-density lipoprotein cholesterol, smoking, and diabetes mellitus) have a poor performance in predicting asymptomatic subjects who will or will not develop CHD.⁴ There is increasing realization that our traditional approaches to risk assessment result in a substantial detection gap.⁵ Recent developments in the measurement of cardiovascular structure and function make imaging of other aspects of subclinical disease and measuring functional aspects of the vasculature in population-based studies feasible and accurate, providing specific, detailed information that relates more directly to pathology.⁶ In this review, we focus on the utility

of noninvasive imaging modalities for risk stratification in addition to conventional risk factor evaluation.

CARDIOVASCULAR MAGNETIC RESONANCE

Over the last several years, cardiovascular magnetic resonance (CMR) has undergone rapid evolution, and tremendous advances in pulse sequence design, scanner hardware, and coil technology have resulted in a progressive expansion of applications.^{7,8} These improvements have led to the recognition of CMR as the reference standard for the evaluation of ventricular mass, volumes, regional and global function, and myocardial infarction (MI) and viability.⁹ The Multi-Ethnic Study of Atherosclerosis Study (MESA, <http://www.mesa-nhlbi.org/>) is the first epidemiology study that has used CMR in a large cohort to evaluate left ventricular (LV) mass, volume, and incident cardiovascular events.⁶

Left and Right Ventricular Reference Values

With the increased use of CMR in the routine evaluation of the heart, there exists a need for normative CMR reference values to distinguish health from disease. It is also important to study the associations of sex and race on LV/right ventricular (RV) structure and function, because normal values may vary with these variables. In a study of 800 MESA participants, free of symptomatic cardiac problems at baseline recruitment, Natori et al¹⁰ presented the range of the LV indices based on sex, age, and ethnicity using fast gradient echo sequence (FGRE). The results show, first, LV volumes and mass were significantly greater for men than for women; second, LV mass normalized by body surface area did not significantly decrease with age for either sex; third, LV volumes and volume indexes tended to decrease slightly with age for both sexes; and, fourth, the Asian American participants in general had lower values for LV mass and volumes than other ethnic groups even when adjusted for body surface area. Tandri et al¹¹ reported the reference value of RV structure and function from 500 asymptomatic MESA subjects using the same FGRE sequence. Right ventricular indices have similar characteristics as those of LV indices.

The traditional FGRE has been proven to be accurate in the assessment of ventricular volume, mass, and function.^{12,13} However, the steady-state free precession (SSFP) sequence has inherent advantages in speed and contrast-to-noise ratio compared with FGRE.¹⁴ SSFP images have greater contrast at the endocardial border with less blood flow dependence and greater fat-to-myocardial contrast at the epicardial border. These properties lead to significant differences between mass and volume measures between the 2 methods.¹⁵ Nevertheless, this issue was solved by Malayeri and his colleagues.¹⁶ They compared the SSFP and FGRE pulse sequences for measuring the LV mass and volumes. Left ventricular end-diastolic volume (EDV) and LV end-systolic volume (ESV) were significantly higher for the SSFP. Stroke volume was not different between the 2 sequences. Ejection fraction and LV mass were significantly lower using SSFP. There was a highly linear relationship between FGRE and SSFP for key LV function parameters. The results allow conversion of previous FGRE data to the current SSFP method.

Left Ventricular Mass in Relationship to Cardiovascular Events

The Framingham Heart Study^{17–19} and other population-based studies^{20–23} have shown that increased LV mass, known as LV hypertrophy, is an independent predictor of cardiovascular events. The predicting value of LV hypertrophy for cardiovascular events holds for individuals with or without prior known CHD and heart failure.^{17–20} Reduction of LV mass as a result of therapeutic intervention reduces cardiovascular events,^{24–27} indicating that LV mass is an important subclinical marker of cardiovascular disease.²⁸ Large epidemiological studies of LV geometry and systolic function have generally relied on echocardiography.

^{17,29,30} Cardiovascular magnetic resonance provides accurate and reproducible measurement of LV mass, volumes, and systolic function; is not limited by acoustic windows as is echocardiography; does not rely on geometric assumptions about the shape of the ventricle; and does not require exposure to ionizing radiation.^{31,32} Thus, CMR is an appropriate noninvasive technology for investigating subclinical alterations in LV size and systolic function.

Heckbert et al³³ reported the association of traditional cardiovascular risk factors with LV indices in asymptomatic populations. Higher systolic blood pressure and body mass index (BMI) were associated with larger LV mass and volumes; current smoking and diabetes were associated with greater LV mass, lower stroke volume, and lower ejection fraction. For each SD increase in the systolic blood pressure (21 mm Hg), the increase in LV mass was 13.5 g (8.0%) in men and 6.9 g (5.5%) in women younger than 65 years. For those 65 years or older, the LV mass increase was 12.9 g (7.6%) for men and 7.2 g (5.8%) for women per SD of systolic blood pressure. The average LV mass increased 11.7 g for each SD (5 kg/m²) increase in the BMI, 7.7 g for current smoking, and 3.5 g for diabetes. In addition, the proportion of variability within all the CMR measurements explainable by traditional cardiac risk factors was small. Furthermore, the association of risk factors with CMR measurements did not differ significantly across racial/ethnic groups.

The relationship between LV mass/geometry measured by CMR and the incidence of cardiovascular events was reported by Bluemke et al³⁴; 4968 MESA participants underwent CMR and were followed up for a median of 4 years. There were 216 total cardiac events. In this ethnically diverse population free of symptomatic cardiovascular disease at baseline, the left ventricular end-diastolic volume and LV mass determined by CMR were strongly associated with cardiovascular events (Fig. 1). Elevated LV mass in most individuals was accommodated over the 4-year period of follow-up, with only the top 5% of the cohort showing increased risk (hazard ratio, 8.6) for incident heart failure in adjusted models. Concentric remodeling (defined by elevated LV mass-volume ratio), rather than elevated ventricular mass, was predictive of incident non-heart failure cardiovascular events, specifically stroke and CHD.

Regional Cardiac Function With Traditional Risk Factors

It has been shown that subclinical LV dilation and systolic dysfunction are independent predictors of heart failure.³⁵ Myocardial tagging by CMR provides objective measurements of myocardial motion and deformation, allowing for a detailed quantification of regional cardiac function.^{36–38} Rosen et al³⁹ examined segmental LV function in more than 1100 MESA subjects. The principal variable evaluated was circumferential strain, the shortening of the myocardium in the circumferential direction, which is the orientation of LV myocardial fibers in the midwall (Fig. 2). Circumferential strain was evaluated by vascular territory using short-axis images of myocardial segments attributed to the left anterior descending, circumflex, and right coronary perfusion territories. The authors found overall that circumferential strain was reduced in subjects with diastolic hypertension relative to normotensive subjects after adjustment for age, sex, calcium score, and other variables, but not in those with borderline systolic or isolated systolic hypertension. Similarly, current cigarette smoking was associated with reduced strain, and there was a dose-response relationship to pack-years smoked. This relationship is strongest with the combination of diastolic blood pressure and cigarette smoking. Diabetes and lipid abnormalities had no demonstrable effects. The results demonstrate apparent regional myocardial dysfunction in subjects with the cardiovascular risk factors of diastolic hypertension and/or smoking despite the absence of clinically manifest disease. In addition, reduced LV regional systolic and diastolic function has been observed in subjects who are free of cardiovascular disease but have other risk factors, such as moderately reduced creatinine clearance,⁴⁰ elevated

plasma total homocysteine,⁴¹ and increased circulating inflammation marker, C-reactive protein.⁴² These novel observations challenge the very structure of conventional clinical reasoning about the distinction between risk factor and disease.⁴³

Coronary Artery Wall Imaging

Black blood coronary arterial wall MRI has been developed to directly assess coronary artery lumen diameter and wall thickness as a measure of plaque burden.⁴⁴⁻⁴⁶ There is a good correlation between MRI measured coronary wall thickness and matched histopathology sections for human coronary artery specimens and in vivo animal models.⁴⁷ Good reproducibility has also been demonstrated.^{48,49} Because of motion of the coronary arteries along with small size of the arteries, the coronary artery wall (<1-mm diameter) is at the threshold limit of identification with CMR. The improved depiction of the coronary artery wall is related with coronary rest period and atherosclerotic plaque burden measured by coronary artery calcium (CAC) and inversely related to heart rate.⁵⁰

In the MESA population, which is free of clinical cardiovascular disease, subjects with 2 or more cardiovascular risk factors had significantly greater maximum coronary wall thickness than those with 1 or no risk factors. This relationship was also present even in subjects without coronary calcification by computed tomography (CT) scan. In addition, coronary artery wall thickness showed better correlation with carotid intimal-medial thickness than CAC score.⁵¹ Miao et al⁵² studied the coronary artery wall thickness, lumen area, and outer contour area and compared the result with CAC. In 179 asymptomatic individuals without history of CHD, CMR showed positive coronary wall remodeling,⁵³ one of the earliest manifestations of atherosclerosis. Positive remodeling is characterized by compensatory enlargement of both the outer wall of the vessel as well as the lumen (Fig. 3). Coronary artery calcium score was positively associated with increased arterial wall thickness before and after adjustment for age and sex. Technically, coronary wall MRI is very challenging, with only about 80% of participants who completed the protocol had interpretable images. With further development, MRI has potential as a noninvasive method for assessing plaque burden and coronary artery size.

CORONARY ARTERY CALCIFICATION

Coronary atherosclerosis develops early on in life, and there is accumulation of calcium in the early stage of plaque formation, as early as the fatty streak.⁵⁴ Histological studies have shown high correlation between the areas of the total atherosclerotic plaque and calcification.⁵⁵ The presence and extent of coronary calcium rise with age from 5% of middle-aged to more than 50% in an elderly cohort and almost 100% by the eighth decade.^{56,57} Radiographically detectable CAC is a marker of subclinical CHD.^{58,59} There has been considerable interest in the potential use of measurements of CAC in models of risk prediction.

Reference values of coronary calcium distribution in subjects without clinical cardiovascular disease (or treated diabetes) became available from the MESA study, allowing for improved interpretation of the degree of coronary calcification according not only to age and sex, but also to ethnicity. McClelland et al⁶⁰ provided a CAC score reference values web tool (<http://mesa-nhlbi.org/CACReference.aspx>). This tool provides the estimated probability of nonzero calcium, and the 25th, 50th, 75th, and 90th percentiles of the calcium score distribution for a particular age, sex, and race. Additionally, if an observed calcium score is entered, the program will provide the estimated percentile for this particular score.

CAC and Prediction of CHD Events in Asymptomatic Subjects

The core issue surrounding this subject is whether measurement of CAC can predict CHD events in asymptomatic subjects and whether it is better than or adds value to conventional risk factor and risk models.

The prognostic implications of CAC in different ethnic groups were confirmed in 6722 asymptomatic participants in MESA.⁶¹ Subjects were followed up for a median of 3.8 years. In comparison with those with no coronary calcium, the adjusted risk of a coronary event was increased by a factor of 7.7 in those with CAC scores between 101 and 300 and by a factor of 9.7 in those with a CAC scores greater than 300 (Fig. 4). Among the 4 racial and ethnic groups, a doubling of CAC score increased the risk of a major coronary event by 15% to 35% and the risk of any coronary event by 18% to 39%. The areas under the receiver operating characteristic curves for the prediction of both major and any coronary events were higher when CAC score was added to standard risk factors. It has been demonstrated that CAC score was strongly predictive of incident CHD and provided predictive power beyond standard risk factors. In addition, this was true for all ethnic groups included.

The Prospect Army Coronary Calcium project is a prospective cohort study of US army personnel to examine the incremental value of CAC score beyond FRS for CHD.⁶² A total of 2000 men and women aged 40 to 50 years underwent CT and measurement of cardiovascular risk factors. Initial follow-up was 3 years, and coronary calcium was found in 22.4% of men and 7.9% of women. Coronary calcium was associated with an 11.8 times increased risk for incident CHD in a Cox model, which controlled for Framingham risk. A major problem with this study is that there were only 9 acute events in men and none in women.

In the Cooper Clinic Study, follow-up information was available for 10,746 self-referred men and women aged 22 to 96 years who underwent electron beam CT as a part of a preventive health examination.⁶³ Risk factors were self-reported. During a mean follow-up of 3.5 years, 81 hard events (CHD death and nonfatal MI) and 287 total events (hard events plus coronary revascularization) occurred. CAC score was positively associated with rates of total CHD events. The association remained significant after adjustment for CHD risk factors. CAC score was associated with CHD events in participants with no baseline risk factor and in both younger (<40 years) and older (>65 years) subjects.

The PREDICT study is a prospective cohort study designed to evaluate CAC score as a predictor of cardiovascular events in type 2 diabetes.⁶⁴ A total of 589 patients with no history of cardiovascular disease and with established type 2 diabetes had CAC score measured, as well as other risk factors. Participants were followed up for a median of 4 years, and first CHD and stroke events were identified as primary end points. There were 66 first cardiovascular events (including 10 strokes). CAC score was a highly significant, independent predictor of events, with a doubling in CAC score being associated with a 32% increase in risk of events (29% after adjustment) (Fig. 5). Only systolic blood pressure and insulin resistance predicted primary end points independently of CAC score. Measurement of CAC score proved to be a powerful predictor of cardiovascular events in asymptomatic patients with type 2 diabetes, which could enhance prediction provided by established risk models.

To examine the prognostic value of CAC score in an elderly population, CAC score was measured in 1795 asymptomatic subjects (mean age, 71 years), with a mean follow-up of 3.3 years in the Rotterdam Heart Study.⁶⁵ The risk of CHD events increased with increasing CAC score. The multivariate adjusted risk ratio for coronary event was 3.1 for CAC score 101 to 400, 4.6 for CAC score 401 to 1000, and 8.3 for CAC score greater than 1000, all

compared with scores of 0 to 100. Risk prediction based on cardiovascular risk factor improved when CAC score was added to the model. Coronary artery calcium score was found to be a strong and independent predictor of CHD in the elderly, improving on the power of conventional risk factors.

Progression of CAC

Coronary artery calcium, once established, typically progresses with time. The largest study on progression is that reported from the MESA. Kronmal et al⁶⁶ reported the follow-up CAC score from 5756 participants with an average of 2.4 years between scans. The incidence of CAC increased steadily across age, regardless of sex and race. The incidence of newly detectable CAC averaged 6.6% per year, ranging from less than 5% annually in those younger than 50 years to greater than 12% in those older than 80 years. Median annual change in CAC for those with existing calcification at baseline was 14 Agatston units for women and 21 Agatston units for men. Most traditional risk factors were associated with both the risk of incident coronary calcification and the progression of calcification including age, male sex, white ethnicity, hypertension, BMI, and diabetes family history. Baseline CAC score was an important determinant of progression. Whites had more incident CAC and CAC progression than the other 3 racial/ethnic groups.

In the PREDICT study, 202 of the original cohort of 625 asymptomatic type 2 diabetes subjects had a repeated scan with a mean interval of 4 years.⁶⁷ A total of 170 showed progression, whereas in 32, CAC score did not progress or regressed. Baseline score was the most important predictor of progression. Other predictors were systolic blood pressure, waist-hip ratio, waist circumference, male sex, age, urine albumin-creatinine ratio, and statin therapy. When baseline CAC score was included, the only independent predictors were systolic blood pressure and urine albumin-creatinine ratio and waist circumference.

Chung et al⁶⁸ reported the 95% repeatability limits for CAC on repeated scans in 3380 subjects in the MESA study. The limits varied with BMI and initial calcium score. The required change in Agatston score that would represent a definite change in the patient (rather than measurement error) was 68 for an initial score of 100 and 169 for an initial score of 400.

Gopal et al⁶⁹ performed follow-up CT studies of patients with a negative coronary calcium scan at baseline at a minimum of 12 months later (mean, 4 years). A total of 62% of their patients never developed coronary calcium, and only 3% had an increase of more than 50 Agatston units, suggesting that patients with an initial coronary calcium score of zero do not need follow-up evaluation before 5 years after the initial scan.⁶⁹

Ethnic Differences in CAC

The prevalence and extent of CAC differ between racial groups, but studies have produced conflicting results. In the Army Coronary Calcium project, CAC was measured in 999 participants with a mean age of 42 years. Coronary artery calcium was twice as prevalent in white (19.2%) compared with African American individuals (10.3%), despite African American participants having a 3-fold greater prevalence of risk factors.⁷⁰ In the Dallas Heart Study, CAC was studied in 1289 men and women, and the prevalence of CAC did not differ significantly between African American and white participants.⁷¹ Information from the MESA study provides probably the most definitive information in this area. In this multiethnic population study, CAC was measured in 6814 white, African American, Hispanic, and Chinese subjects with a mean age of 62 years. After adjustment for risk factors, CAC was greatest in whites followed by Chinese and Hispanics, with the lowest in African Americans.⁷² Despite some conflicting data, CAC tended to be lower in those of

African Caribbean descent than in other ethnic groups. However, the prognostic value of CAC was as great if not greater in those with African Caribbean origins as in the others.

CAC and Myocardial Perfusion

Clinical studies showed that the prevalence of stress-induced ischemia increased with CAC burden among patients with CHD.^{73,74} Whether an association between CAC and abnormal myocardial perfusion exists in subjects without a history of CHD remains largely unknown. Wang et al⁷⁵ reported on a subset of 222 subjects from the MESA study who underwent both CAC and adenosine stress MRI to assess myocardial perfusion reserve. They found that perfusion reserve was inversely associated with the presence and severity of coronary calcification, suggesting that this was a manifestation of subclinical coronary atherosclerosis in the absence of symptoms in these patients.⁷⁵

CAC Screening

Evidence has accumulated that CAC screening can be a useful tool to improve risk prediction for asymptomatic subjects with intermediate pretest probability and for symptomatic patients at low pretest probability of disease. This view has been embraced by experts and by large professional organizations such as the European Society of Cardiology,⁷⁶ the American College of Cardiology,⁷⁷ and American Heart Association.⁷⁸ The American Heart Association has endorsed that asymptomatic individuals with an intermediate FRS may be reasonable candidates for CHD testing using CAC as a potential means of modifying risk prediction and altering therapy. On the other hand, it believes there is little to be gained by CAC testing in patients with a low FRS. Furthermore, patients with a high FRS should be treated aggressively and thus should not require additional testing, including CAC scoring, to establish this risk evaluation.

ULTRASOUND OF CAROTID

Ultrasound of the carotid artery is used to assess both carotid artery plaque and thickening of the intima and media of the vessel wall. Carotid intima-media thickness (IMT) is a phenotype for early atherosclerosis. Because it can be measured relatively simply and noninvasively, it is well suited for use in large-scale population studies. Ultrasonic measurements correlate well with histology,⁷⁹ and increased IMT is associated with vascular risk factors and the presence of advanced atherosclerosis.⁸⁰ A number of longitudinal studies have examined the relationship between IMT and future cardiac events.

In middle-aged asymptomatic subjects of the Atherosclerosis Risk in Communities study,⁸¹ ultrasound evidence of markedly increased carotid overall mean IMT (average of IMT measures in common carotid, bifurcation, and internal carotid on both sides above the 95th percentile) was associated with increased CHD risk in men and women, after adjustment for age and race. The relationship was monotonic, and the strength of the association was reduced by including major CHD risk factors, but remained elevated at higher IMT.

Five thousand fifty-eight elderly subjects (>65 years old) without clinical cardiovascular disease in the Cardiovascular Health Study were followed up for a median of 6.2 years.⁸² The incidence of cardiovascular events correlated with measurements of carotid IMT. The relative risk of MI or stroke increased with IMT (Fig. 6). The adjusted relative risk for the quintile with the highest thickness as compared with the lowest quintile was 3.87. The association between cardiovascular events and IMT remained significant after adjustment for traditional risk factors, showing increasing risks for each quintile.

Five thousand fifty-six subjects of the Carotid Atherosclerosis Progression Study were followed up for a median 4.2 years.⁸³ This study showed that baseline carotid IMT predicted

future vascular events and death in a population with a wide age range at study entry (19–90 years). Furthermore, the hazard rate ratios associated with increased IMT were similar for the different arterial sites at the carotid bifurcation (ie, CCA-, BIF-, or ICA-IMT), and for the different clinical end points studied (ie, MI, stroke, or combined end point). Interestingly, the hazard rate ratios were significantly higher in younger (<50 years old) than in older subjects (>50 years old).

COMPARISON BETWEEN DIFFERENT TECHNIQUES

In apparently healthy individuals, the number of imaging tests revealing extensive atherosclerosis correlated with the Framingham score. However, there were frequent discrepancies between estimated risk and disease burden, and different modalities agreed poorly with one another, highlighting the challenge of inferring information of one vascular bed from the status of another. In a stratified sample of Framingham Heart Study participants free of clinical cardiovascular disease, Kathiresan et al⁸⁴ evaluated subclinical atherosclerosis by 4 different imaging techniques: abdominal and thoracic aortic plaque burden by CMR, CAC and TAC by electron beam computed tomography, and carotid IMT by ultrasonography. Correlations across atherosclerotic measurements in the various major vascular beds were low, and subclinical atherosclerosis tests identified different participants at risk. In subjects with an intermediate Framingham CHD risk score, a substantial proportion (14% of men, 25% of women) had a high atherosclerosis test value on more than 2 imaging tests. These results suggested that a combination of imaging tests may be useful in risk stratification, and this hypothesis needs testing in larger studies.

CONCLUSIONS

The need for improved methods to screen for CHD is well recognized, because traditional risk factor analysis predicts roughly only 50% of the patients who will develop manifestations of the most lethal chronic disease process affecting our population. New noninvasive imaging techniques are evolving rapidly and helping toward a better definition of arterial architecture and physiological health. Large-scale multicenter clinical trials demonstrate that those imaging techniques provide additional prognostic information independent of traditional risk factors, including the FRS in asymptomatic subjects. Further research will better define their ultimate value and possibly lead to revolutionary breakthroughs in our ability to image and more effectively treat this important disease.

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FIGURE 1.

Cumulative event rates for CHD events by quartiles of LV mass-volume ratio. Reprinted from *J Am Coll Cardiol*, Vol 52, Bluemke DA, Kronmal RA, Lima JA, et al. The relationship of left ventricular mass and geometry to incident cardiovascular events: the MESA (Multi-Ethnic Study of Atherosclerosis) study, 2148–2155, Copyright 2008, with permission from Elsevier. Figure 1 can be viewed online in color at www.topicsinmri.com.

FIGURE 2.

Myocardial tagging. End-diastolic (A) and systolic (B) tagging short-axis images at the midventricular level shows deformation of tag lines parallel to myocardial contraction. The graphic (C) demonstrates quantification of normal circumferential strain changes in the septum (blue line) and lateral wall (pink line) during the cardiac cycle by time. Reprinted from *Semin Roentgenol*, Vol 44, Turkbey EB, Dombroski DA. Cardiac magnetic resonance imaging: techniques and clinical applications, 67–83, Copyright 2009, with permission from Elsevier. Figure 2C can be viewed online in color at www.topicsinmri.com.

FIGURE 3.

A 73-year-old male participant with increased wall thickness and preservation of lumen area. A, Magnetic resonance angiogram (MRA) shows no significant stenosis in the proximal portions of the coronary arteries. Multiplanar reconstruction (MPR) of the MRA of the left main coronary artery (LM) (B) and the right coronary artery (RCA) (D) shows a normal lumen in cross sections. Coronary wall magnetic resonance image of the corresponding arterial cross sections (C and E) shows eccentrically thickened arterial walls. Reprinted from *J Am Coll Cardiol*, Vol 53, Miao C, Chen S, Macedo R, et al, Positive remodeling of the coronary arteries detected by magnetic resonance imaging in an asymptomatic population: MESA (Multi-Ethnic Study of Atherosclerosis), 1708–1715, Copyright 2009, with permission from Elsevier.

FIGURE 4.

Unadjusted Kaplan-Meier cumulative-event curves for coronary events among participants with CAC scores of 0, 1 to 100, 101 to 300, and more than 300. A shows the rates for major coronary events (MI and death from CHD), and B shows the rates for any coronary event. The differences among all curves are statistically significant ($P < 0.001$). Reprinted with permission from Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med*. 358:1336–1345, Copyright © 2008. Figure 4 can be viewed online in color at www.topicsinmri.com.

FIGURE 5.

Proportions of patients with an event with increasing time since recruitment into the PREDICT study in successive coronary artery calcification score categories (Agatston units). Reprinted from Elkeles RS, Godsland IF, Feher MD, et al. Coronary calcium measurement improves prediction of cardiovascular events in asymptomatic patients with type 2 diabetes: the PREDICT study. *Eur Heart J*. 2008;29:2244–2251, by permission of Oxford University Press.

FIGURE 6.

Unadjusted cumulative event-free rates for the combined end point of MI or stroke, according to quintile of combined IMT. Reprinted with permission from O'Leary DH, Polak JF, Kronmal RA, et al. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med.* 340:14–22, Copyright © 1999.