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iNEWS

NEWS AND VIEWS

Imaging for Coronary Risk Assessment: Ready for Prime Time?

SINCE THE INTRODUCTION OF THE CONCEPT OF CARDIOVASCULAR RISK FACTORS in 1961 by the Framingham Heart Study investigators (1), clinicians and patients have been seeking better tools to assess the likelihood of future cardiovascular events. As our knowledge in this area has grown, so has the clinician's armamentarium, from a simple history and physical examination to laboratory testing and biomarkers and, most recently, to imaging of atherosclerotic plaque. However, the gold standard still remains the Framingham Risk Score (FRS), which ignores the strong correlations between abnormalities detected by these alternative methods and both incident and prevalent coronary artery disease (CAD).

For carotid intima media thickness, the ARIC (Atherosclerosis Risk In Communities) study first demonstrated such correlations in the 1990s (2), and recent preliminary data from the MESA (Multi-Ethnic Study of Atherosclerosis) regarding the predictive power of coronary artery calcification (CAC) (3) has again demonstrated a relationship between imaging results and outcomes while extending its validity across all ethnicities and both genders. Perhaps the ultimate noninvasive imaging tool for coronary disease, coronary artery computed tomography angiography (CTA), has had a recent boost with the presentation of the CORE 64 multisite results indicating the high accuracy of 64-slice CT in comparison with invasive coronary angiography (4).

However, although many risk scores are epidemiologically associated with prognosis, predictive power for events in individual patients is limited. Further, no risk assessment strategy—not FRS, not biomarkers (such as high-sensitivity C-reactive protein), not imaging—has ever been proven in a randomized trial to reduce cardiovascular events. The studies simply have not been done and, given the financial and logistic hurdles, are unlikely ever to be done. For some observers, this lack of evidence is a critical flaw, and precludes incorporation of imaging into routine care algorithms (5). For others, it is a minor detail, rendered even more insignificant given the unlikelihood of a randomized trial and by improvements in preventive therapies and risk assessment tools. For these individuals, it may be a case of precision versus pragmatism.

What is the future for atherosclerosis risk assessment by imaging? Must we perform randomized controlled trials of an imaging CAD risk assessment strategy using clinical endpoints to determine if imaging risk assessment really can save lives? Or do we have enough information already to recommend routine imaging in selected groups of asymptomatic individuals?

We have invited 2 experts to comment on the new imaging data supporting the relationships between imaging and outcomes and whether these will change how they perform risk stratification in their clinical practices. What do they have to say? Would you share your opinion with us? We encourage you to visit *iJACC-iNEWS* in Cardiosource and tell us what you think, using its *"Talk-Back"* feature. The opinions presented below are entirely of the authors and do not reflect or express the position of the American College of

Cardiology, *JACC: Cardiovascular Imaging*, or the editors.

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We Need More Evidence!

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NEW TECHNOLOGY HOLDS GREAT PROMISE in our ability to obtain noninvasive images of the coronary arteries. However, to justify its incorporation into clinical practice, cardiac imaging must go beyond pretty pictures to provide incremental and actionable data over current cardiac risk prediction. The cardiac risk factors described almost half a century ago by the Framingham investigators (1) are still accurate today; the FRS has proven to be invaluable in predicting and helping to prevent heart disease. Our focus for preventing heart disease should remain reducing these risk factors. Indeed, most of the reduction in coronary heart disease mortality in the last 2 decades is due to reduction of the cardiac risk factors that comprise the FRS. In particular, as shown recently, at least 44% of the decreased CAD mortality rate in the last 2 decades likely is attributable to favorable changes in risk factors—total cholesterol (24%), blood pressure (20%), smoking (12%), and physical inactivity (5%) (6). In contrast, there are no data to show that cardiac CTA is associated with any reduction in coronary heart disease mortality.

Although numerous studies have shown a high diagnostic accuracy for multislice cardiac CTA when compared with invasive coronary angiography, these data have been obtained in highly selected populations, technically difficult cases were excluded, and experienced physicians interpreted the images in high-volume centers. Similar diagnostic accuracy would be unlikely in routine use. More importantly, there are no studies showing effect of CT on prognosis or on clinical events. In the only randomized control trial to examine this issue, researchers found that using coronary calcification screening to motivate patients to make evidence-based changes in risk factors was not associated with improvement in modifiable cardiovascular risk at 1 year (7). Despite this lack of outcomes data, there has been a call for more "imaging for prevention" by the American Society of Nuclear Cardiology (8). There are serious risks to this approach. Recent data suggest that the increase in CT imaging from 3 million scans in 1980 to 62 million scans in 2005 may lead to as many as 3 million additional cancer cases in the next few decades (9).

The value of this new technology is an unanswered question. For imaging to be used for prevention, the objective must be more than simply beautiful pictures (10). The images must be shown to offer useful prognostic information incremental to the FRS. Computed tomography imaging data have no real value unless they lead to actions that improve outcomes over actions that already would be taken based on risk factors. Before we embrace the new imaging technology, we should insist on evidence that it will improve patient outcomes. In the absence of such evidence, to further the goal of prevention, we should continue to emphasize the measures we know for certain will reduce CAD and save lives, such as stanching the obesity epidemic (and its accompanying increase in diabetes), by increasing physical activity and heart-healthy diet adherence, reducing hypertension and hypercholesterolemia, and eliminating smoking.

Computed tomography imaging data have no real value unless they lead to actions that improve outcomes over actions that already would be taken based on risk factors.

Calcium Scores Refine Risk Prediction. . .

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AN ACCURATE DETERMINATION of cardiovascular disease risk in an asymptomatic adult can be very challenging. The conventional stratification by the FRS into the categories of low, intermediate, and high risk is based on estimation of the 10 year absolute risk of manifesting CAD. (11) This estimate is dominated by chronologic age and not true biologic age.

Risk stratification is fundamental in dictating the intensity of medical treatment. However, ambiguity lies in assessment of those assigned to the intermediate category (10% to 20% CA risk during the next decade). The preferred situation would involve refining such a person's risk to either a very low (<6% risk) or a high risk (>20%), where management guidelines and the evidence for them are clearer. Relevant details which may potentially help include a family history of premature CAD and components of the metabolic syndrome and other lifestyle factors not included in the FRS.

Coronary artery calcification scores can refine risk prediction in persons with an intermediate risk FRS. The

2007 American College of Cardiology/American Heart Association expert consensus document and the 2006 American Heart Association statement on cardiac CT outline the evidence supporting CAC scoring as providing significant incremental prognostic information on top of the FRS (11,12). However, some individuals with a high burden of subclinical atherosclerosis are sometimes inappropriately assigned to the "low-risk" category (<10% CAD risk), which often occurs in women <70 years and middle-aged men, who will often have an FRS <10% despite multiple risk factors (13).

The determination of CAC also may prove to be helpful in the treatment of selected persons who are classified as low risk by their FRS. The MESA investigators examined nondiabetic women (mean age of 60 ± 9 years) who were classified as low risk by the FRS and found that any CAC as compared with no CAC was strongly predictive of CAD events (6-fold increased risk) in fully adjusted models (4). Moreover, advanced coronary calcification (CAC score ≥300) was highly predictive of future CAD events and also identified a group of "low-risk" women who had an 8.6% absolute CAD risk during a 3.75 year period (14)!

. . .calcium scoring is a very reasonable option to refine risk assessment. . .

Previous studies demonstrate differing prevalences in CAC by ethnicity. Reference tables and graphics describing CAC distribution by ethnicity are now available from the MESA study. Recently, Nasir et al. (15) found CAC scores to be predictive of all-cause mortality in all ethnic groups, with a greater CAC score portending a worse outcome.

Accurate risk assessment and classification has important ramifications for management and treatment of patients. Reassignment from an equivocal "intermediate risk" to "high risk" qualifies an individual for more aggressive treatment with antiplatelet therapy, more rigorous lipid management, and even stricter blood pressure goals equivalent to those for persons with documented CAD. If the clinician is not certain that a particular patient with average or borderline risk factor levels needs to be on life-long aspirin and aggressive lipid-lowering therapy, coronary calcium scoring is a very reasonable option to refine risk assessment and help make that decision. Needless to add that the development of strategies for better characterization of atherosclerotic plaques, beyond calcium scoring, would substantially refine our quest for risk prediction.

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