Long-Term Prognostic Value of Coronary Calcification Detected by Electron Beam Computed Tomography in Patients Undergoing Coronary Arteriography

To the Editor:

The paper by Keelan et al 1 addresses an important issue, namely how to define which patients with symptomatic coronary artery disease (CAD) are at risk for future events. They argue that coronary artery calcification (CAC) provides incremental prognostic value after clinical risk factors and coronary arteriography are included in the analysis, and indeed, only age and CAC were predictive in their model.

Several issues need to be addressed before accepting this conclusion. The authors used several methods of quantifying CAC. Quartile analysis was done, but no data are provided on the number of patients at risk in each quartile, and apparently this analysis did not reach significance. Log transformation was used to analyze the data and was found significant in the Cox model. Lastly, a score of 100 formed the basis of their survival curve analysis, which did yield a P<0.01. However, except for P value, on what basis was this value selected? From the clinician’s standpoint, a CAC of 100 has an excellent sensitivity of 77%; what the authors fail to highlight is a very low positive predictive value of 10%. This problem is not uncommon with noninvasive testing in general with regard to predicting future events in patients with CAD. 2 Also, patients were selected based on having undergone arteriography. The authors indicate that 54 patients underwent revascularization during the index admission. This suggests that the results of coronary arteriography were used to make important clinical decisions. Would CAC have been significant if assignment to therapy had not already been made based on arteriography? One suspects not.

Monty M. Bodenheimer, MD
Professor of Medicine
Albert Einstein College of Medicine
New Hyde Park, NY


Response

We thank Dr Bodenheimer for his comments on our article. 1 He indicates that “no data are provided on the number of patients at risk in each quartile, and apparently this analysis did not reach significance.” By definition, one-fourth of all participants (288/4=72) were in each quartile. The Results section reported the number of events in each quartile and the results for increasing quartiles. The P value was 0.07, which was not statistically significant.

He asks, “a score of 100 formed the basis of their survival curve analysis... on what basis was this value selected?” We selected 100 based on the literature. Detrano et al 2 found coronary event-free survival was significantly higher among patients undergoing angiography with a coronary artery calcification (CAC) score <100 than among patients with a CAC score ≤100. Arad et al 3 found that a CAC score >100 was a significant predictor of future hard events with sensitivity, specificity, and odds ratio (95% CI) of 89%, 77%, and 25.8 (5.9 to 113.0) among 1173 asymptomatic patients with 19 months of follow-up time. Rumberger et al 4 stated that a score of 100 indicated “definite, at least moderate plaque burden” with “non-obstructive CAD highly likely...” Rumberger et al further indicated that a score of 100 has “moderately high implications for CV risk.” 4 The literature thus supports 100 as a threshold value.

Dr Bodenheimer correctly points out the low positive predictive value with a CAC score of at least 100. However, the negative predictive value associated with a score of >100 is 96%, quite high. In the Discussion section of our paper, 1 we stated that future events are unusual in patients with small amounts of calcification. In fact, only 1 of 87 patients with a CAC score <20 (negative predictive value of 99%) had a hard event during almost 7 years follow-up. 1

Finally, we indeed used an angiographic subset of patients to understand coronary artery anatomy in relation to calcification and cardiac events long term. We examined only hard events, either cardiac death or nonfatal myocardial infarction, to reduce bias imposed by angiography and by clinician judgment. Coronary arteriography was conducted in these patients for clinical indications and treatment decisions. To address his concerns about these treatment decisions, we repeated the analyses in a patient subset excluding those undergoing revascularization before or during the index admission. The inferences were similar to those in the larger sample, and the log-transformed CAC score remained a significant and stronger predictor of future hard events than angiographic disease measures.

Paul C. Keelan, MB
Department of Cardiology
Glenard Hall
Dublin, Ireland

Khalid Ashai, MD
University of Minnesota
Minneapolis, Minn

John A. Rumberger, MD, PhD
Ohio State University
Preventive Imaging Technologies
Columbus, Ohio

Ali E. Denktas, MD
Patrick F. Sheedy, II, MD
Mayo Clinic
Rochester, Minn

Lawrence F. Bielak, DDS, MPH
Lama S. Jamjoum, PhD, MPH
Patricia P. Peyser, PhD
Department of Epidemiology
University of Michigan
Ann Arbor, Mich

Robert S. Schwartz, MD
Minnesota Cardiovascular Research Institute
Minneapolis Heart Institute and Foundation
Minneapolis, Minn

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Monty M. Bodenheimer

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