Coronary Calcium Does Not Accurately Predict Near-Term Future Coronary Events in High-Risk Adults

To the Editor:

The article by Detrano et al1 concerning the predictive value of coronary artery calcium contains fundamental flaws in methodology that may invalidate their conclusions.

Their protocol differs significantly from the original protocol, which was designed to be sensitive to the presence of small amounts of calcium and to accurately reflect the quantity of calcium present.1,2 Multiple studies have shown that these goals were met surprisingly well.3 The differences in protocol can account for the lack of discriminative power found in their article, without criticizing the high-risk composition of their study group.4 Using 6-mm-thick slices, instead of 3 mm, increases the volume averaging inherent in CT scanning. Small calcified lesions may not meet the density threshold criteria for a calcified lesion with 6-mm-thick slices. There is also a 2-fold decrease in the number of lesions seen in 6-mm slices versus 3-mm slices, which decreases the calcium score by a factor of 2.

The use of an 8.16 mm³ threshold for defining a calcified lesion also significantly reduces sensitivity. This is 5X the original threshold. Lesions, which could have a potential contribution of 10 to the total calcium, could have a score of 0 with Detrano et al’s modifications. In combination with increased volume averaging, this higher volume threshold will have an even greater effect. It seems that a total calcium score in the range of 80 to 160 defines a high-risk group.5,6 The potential magnitude of score reduction using Detrano et al’s modifications are of the same order of magnitude.

The data presented support the assertion that the calcium scores are significantly lower than would be expected. With a mean age of 66±8 years, a median score of 44 and a tertile 1 score range of 0 to 3.4 were seen. Janowitz et al7 published similar data; in their 60 to 70 year age group, comparable numbers were a median score of 88, with the first tertile ranging from 0 to 24. This group would be expected to have lower scores than Detrano et al’s high-risk group. There is also no way to determine if patients classified by Detrano et al’s technique would fall into the same tertile groups using the standard protocol. By selectively eliminating smaller lesions, which may be a better predictor of future events than larger, more heavily calcified lesions, it seems that the superior predictive value of electron beam CT for future events is diminished. Attempting to improve reproducibility, Detrano et al have sacrificed the sensitivity and utility of the technique.

Unless one is familiar with coronary calcium quantification, it is difficult to distinguish the differences in protocols and the fact that the calcium scores reported are significantly different than those that would have been obtained by the Agatston-Janowitz scoring system. The data in this article should not be compared with the large body of existing literature concerning coronary artery calcium quantification by electron beam CT. At best, the conclusion should be that the scoring system used was unable to provide additional information over conventional risk factors in their high-risk population.

Warren R. Janowitz, MD
Miami Cardiac and Vascular Institute
Baptist Hospital of Miami
8900 North Kendall Drive
Miami, FL 33176-2197
Warren.Janowitz@worldnet.att.net


Response

Our prospective investigation1 demonstrated that the assessment of coronary calcium with electron beam computed tomography (EBCT) was equivalent to standard risk-factor stratification in determining the risk of a future coronary heart disease event in subjects with coronary risk factors.1 Both EBCT and risk-factor assessment were only moderately accurate for predicting future coronary events.

In our study, we used a 6-mm tomographic slice thickness image-acquisition protocol. Dr Janowitz states correctly that the 6-mm protocol we used is less sensitive for detecting coronary calcium than is the more commonly used 3-mm protocol. However, Dr Janowitz’s speculation that this reduced sensitivity will lead to reduced predictive accuracy is not supported by the literature or by the data we present below.

A major problem with EBCT involves its high rest variability.2 The 6-mm protocol we used demonstrates lower rest variability compared with the more commonly used 3-mm protocol.3 For this reason, we used the 6-mm protocol in our investigation. Like Dr Janowitz, we were concerned that improved rest reproducibility might come at the expense of prognostic accuracy. For this reason, we compared the prognostic accuracy of these 2 protocols in a cohort of 326 patients (derived from our full cohort), and we found that the prognostic accuracy of the 2 protocols was equivalent.4

Nevertheless, it would be helpful to determine whether our previous findings demonstrating an equivalent prognostic accuracy of the more reproducible 6-mm protocol and the more sensitive 3-mm protocol are confirmed in patients with a longer follow-up duration and more coronary events. We have now followed this subset of 326 subjects for 44 months. They have experienced a total of 16 hard coronary events (coronary death or nonfatal myocardial infarction) and 25 total coronary events, when revascularizations (coronary bypass or angioplasty) are included. All 326 subjects underwent, within 15 minutes, consecutive EBCT coronary calcium assessments using both the 3-mm and the 6-mm protocols. Subjects were divided into equal tertiles according to calcium score. The distribution of hard coronary events for the 3-mm scans was as follows: 4 in the lowest tertile (zero score), 4 in the middle tertile, and 8 in the highest tertile. The distribution of hard events for the 6-mm scans was as follows: 3, 6, and 7 in the 3 tertiles. These distributions are not significantly different from one another. When all events (including revas-
cicularizations) were included, the distributions for the 3-mm and 6-mm scans were 4, 6, and 15 and 3, 9, and 13, respectively; these distributions are not significantly different. These results confirm our previous conclusion\(^4\) that the more reproducible 6-mm protocol has a prognostic accuracy equivalent to the more sensitive 3-mm protocol in predicting future coronary heart disease events.

Furthermore, the rank correlation between the 6-mm and 3-mm derived calcium scores in these 326 subjects was 0.97. This high correlation means that both sets of scores, when sorted in ascending order, will rank the 326 subjects in an equivalent manner and, therefore, that the distribution of events by score will be similar, no matter how long the follow up or how many the end points.

Robert C. Detrano, MD, PhD
Division of Cardiology
Department of Medicine
Harbor-UCLA Medical Center and Saint John’s Cardiovascular Research
1124 West Carson Street
Building RB2
Torrance, CA 90502-2064
detrano@harbor4.humc.edu

Nathan D. Wong, PhD
Terence M. Doherty, BA
Robert M. Shavelle, PhD
Weiyi Tang, MD
Leonard E. Ginztom, MD
Matthew J. Budoff, MD
Kenneth A. Narahara, MD

Coronary Calcium Does Not Accurately Predict Near-Term Future Coronary Events in High-Risk Adults
Warren R. Janowitz

Circulation. 2000;102:e20-e21
doi: 10.1161/01.CIR.102.2.e20

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2000 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/102/2/e20

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/