

## News and Views From the Literature

### Coronary Artery Disease

#### Calcium Score of Zero: Not a Gatekeeper to Rule Out Coronary Artery Disease

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**The Absence of Coronary Calcification Does Not Exclude Obstructive Coronary Artery Disease or the Need for Revascularization in Patients Referred for Conventional Coronary Angiography**

Gottlieb I, Miller JM, Arbab-Zadeh A, et al.

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Coronary artery calcium measurements have emerged as a tool for risk stratification, as coronary artery calcification has been shown to be highly specific for atherosclerosis.<sup>1</sup> Conversely, the

absence of coronary artery calcification is associated with a very low risk of future cardiovascular events.<sup>2</sup> A recent statement by the American College of Cardiology and the American Heart Association suggested that a zero calcium score (CS 0) in symptomatic patients could act as a filter prior to invasive coronary angiography.

In this substudy of the CORE 64 (Coronary Evaluation Using Multi-Detector Spiral Computed Tomography Angiography Using 64 Detectors) trial, Gottlieb and colleagues<sup>3</sup> evaluated whether the absence of coronary calcium could rule out significant stenosis, obstruction, or the need for revascularization in patients referred for conventional angiography. This multicenter (n = 9) international observational study enrolled 291 patients (mean age 59.3 ± 10 years, 26.8% women) between November 2005 and January 2007. All patients underwent calcium scanning with 64-multidetector row computed tomography (MDCT) scanners using standard tube currents of 300 mA and voltage of 120 kV followed by coronary angiography within 30 days. End-points were defined as ≥ 50% luminal narrowing by quantitative coronary angiography or the need for revascularization within 30 days. The authors evaluated patients according to calcium score (CS > 0 vs CS 0); those with CS 0 were further evaluated by acuity of presentation (emergency department vs outpatient referral) and pretest probability of coronary artery disease (CAD). In addition, they report the diagnostic accuracy of CS 0 for detecting the absence of ≥ 50% coronary stenosis.

The authors found that the overall prevalence of ≥ 50% coronary stenosis by conventional angiography was 56%

in this cohort. Of the 291 enrolled patients, 195 (67%) had CS > 10, 24 (8%) had CS 1-10, and 72 (25%) had CS 0. In patients with CS > 10, significant stenosis was present in 138 patients (71%) and revascularization was performed in 85 patients (44%). A subset of 11 patients (46%) with CS 1-10 were found to have  $\geq 50\%$  stenosis and 6 patients (25%) subsequently underwent revascularization. Similarly, 14 patients (19%) with CS 0 were found to have  $\geq 50\%$  stenosis and 9 (13%) underwent revascularization.

### Calcium Score > 0

Patients with CS > 0 had significantly increased risk of  $\geq 50\%$  coronary stenosis with an odds ratio (OR) of 8.1 ( $P < .001$ ) as compared with those with CS 0, after adjustment for age, sex, race, hypertension, dyslipidemia, diabetes, family history of premature CAD, and hospitalization.

### Calcium Score 0

From the 291 patients, 25% (72 patients) had a CS 0. These patients were younger ( $55.9 \pm 9.9$  years vs  $60.5 \pm 9.8$  years;  $P = .001$ ) and more likely to be women (40.3% vs 22.4%;  $P = .003$ ) as compared with those with CS > 0. CS 0 was found to significantly decrease the likelihood of  $\geq 50\%$  coronary artery stenosis with an OR of 8.8 ( $P < .001$ ) after adjustment. The authors further delineated these patients based on  $\geq 50\%$  stenosis (19%),  $\geq 70\%$  stenosis (15%), and need for revascularization (12.5%). Of patients with CS 0 and obstructive CAD, 98% had single-vessel disease, 2% had 2-vessel disease, and none had 3-vessel disease. On a per-vessel basis, 12% (47/383) of vessels without calcium had  $\geq 50\%$  stenosis and 20% (13/64) of complete occlusion vessels had no calcium.

### Patient Presentation and Pretest Probability

Emergency department presentation was the only variable significantly associated with obstructive CAD in patients with a CS 0 (adjusted OR 4.7, 95% confidence interval, 1.13-19.75;  $P = .03$ ). Among patients with both CS 0 and low clinical probability of CAD ( $n = 8$ ), no obstructive CAD was detected. However, in patients with CS 0 and intermediate ( $n = 57$ ) to high ( $n = 7$ ) CAD probability, 21% and 29%, respectively, had at least one stenotic coronary lesion.

### Diagnostic Accuracy of Calcium Score 0

The accuracy of CS 0 to predict the absence of  $\geq 50\%$  coronary stenosis in a patient-based analysis is as follows: sensitivity of 45%, specificity of 91%, positive predictive value of 81%, and negative predictive value of 68%.

Similar results were reported in the vessel-based analysis.

The authors appropriately concluded that coronary CS 0 cannot be used as a gatekeeper in symptomatic patients because a noteworthy proportion of patients (19%) with CS 0 have  $\geq 50\%$  stenosis on invasive coronary angiography. Analysis of the composition of vulnerable plaques in acute coronary syndromes (ACS) has shown that culprit lesions have some component of noncalcified plaque, with 29% being exclusively noncalcified.<sup>4</sup> Thus, patients may develop symptomatic CAD and even ACS prior to the accumulation of calcium.

The findings of Gottlieb and colleagues<sup>3</sup> are important given the increasing role of computed tomography (CT) in the evaluation of CAD. The low sensitivity and negative predictive value of calcium scoring stands in contrast to the excellent diagnostic accuracy of CT angiography (CTA) and reinforces the value of CTA in the assessment of CAD. From the ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial, the sensitivity, specificity, and positive and negative predictive values of coronary CTA for the detection of  $\geq 50\%$  stenosis were 85%, 92%, 68%, and 99%, respectively.<sup>5</sup> The high negative predictive value highlights the role of coronary CTA as an effective tool to exclude significant coronary artery stenosis. Coronary CTA is of particular benefit in the setting of emergency department presentation as it was shown to have a sensitivity and negative predictive value for ACS of 100% in the ROMICAT (Rule Out Myocardial Infarction using Computer Assisted Tomography) trial.<sup>6</sup>

The results from this CORE 64 substudy are not surprising. Given that coronary calcium scoring was developed and validated for risk stratification in asymptomatic population-based cohorts such as the Framingham Heart Study and Multi-Ethnic Study of Atherosclerosis,<sup>7,8</sup> the clinical utility of coronary calcium scoring remains questionable in symptomatic patients. That said, in asymptomatic patients, absolute coronary calcium scores predicted cardiovascular outcomes better than age, sex, race, or ethnicity.<sup>9</sup> Moreover, asymptomatic patients with CS 0 have very low risk (0.47% over a mean of 50 months) for an adverse cardiovascular event in a meta-analysis of 64,873 asymptomatic patients.<sup>2</sup> Therefore, we suggest that the optimal use of calcium scoring is not triage or management of symptomatic patients, but rather as a prognostic and risk stratification tool in an asymptomatic cohort. ■

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