ONE MINUTE CONSULT

BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: Which patients may benefit from coronary artery calcification scoring?

RYAN J. CHAUFFE, DO
Department of Medicine, Division of Cardiovascular Disease, University of Florida, Gainesville

DAVID E. WINCHESTER, MD, MS
Department of Medicine, Division of Cardiovascular Disease, University of Florida, Gainesville

When added to a risk model score, calcification scoring can improve estimation of coronary risk in asymptomatic patients at intermediate risk

A: ALTHOUGH WE STILL HAVE NO evidence from randomized trials that patients have better outcomes if we measure the calcification in their coronary arteries, a growing body of evidence shows that we can estimate risk more accurately than with a risk model score alone if we also score coronary artery calcification in asymptomatic patients, especially those at intermediate risk.

See related editorial, page 374

Current guidelines[1] recommend using the Framingham Risk Score or a similar tool to estimate coronary risk in asymptomatic patients, but these tools have only modest accuracy. Calcification scoring is accurate, inexpensive, quick, widely available, low-risk, and does not appear to increase medical costs afterward. In addition to improving risk stratification, it may also encourage patients to adhere better to drug therapy and lifestyle modification.

HOW IS CORONARY ARTERY CALCIFICATION MEASURED?

Calcification of the coronary arteries is synonymous with atherosclerosis. It can easily be detected with computed tomography without contrast (**FIGURE 1**), and the amount can be quantified with a scoring system such as the volumetric score or the Agatston score. The latter, which is more commonly used, is based on the product of the area of the calcium deposits and the x-ray attenuation in Hounsfield units.

Scores can be roughly categorized (with some overlap owing to data from different studies) as:

- Low risk: 0 Agatston units (AU)
- Average risk: 1–112 AU
- Moderate risk: 100–400 AU
- High risk: 400–999 AU
- Very high risk: 1,000 AU.[2]

The actual test takes only a few seconds, and the patient can usually be out the door in 15 minutes or less. It does not require iodinated contrast and the radiation dose is minimal, usually less than 1 mSv, equivalent to fewer than 10 chest radiographs.[3]

The cost is typically between $200 and $500. The test is usually not covered by health insurance, but this differs by insurer and by state; for example, coverage is mandated in Texas, and the test is covered by United Healthcare.

WHAT IS THE EVIDENCE IN FAVOR OF CALCIFICATION SCORING?

Cohort studies with long-term follow-up show that calcification scoring has robust prognostic ability. A pooled analysis of several of these studies[2] showed that a higher score strongly correlated with a higher risk of cardiac events over 3 to 5 years. Compared with the risk in people with a score of 0, the risk was twice as high in those with a score of 1 to 112, four times as high with a score of 100 to 400, seven times as high with a score of 400 to 499, and 10 times as high with a score greater than 1,000.[2]

doi:10.3949/ccjm.80a.12066

A cohort study of more than 25,000 patients had similar conclusions about the magnitude of risk associated with coronary calcification.[4] It also found that the 10-year risk of death was 0.6% in patients with a score of 0, 3.4% with a score of 101 to 399, 5.3% with a score of 400 to 699, 6.1% with a score of 700 to 999, and 12.2% with a score greater than 1,000.

Although progression of coronary artery calcification may predict the risk of death from any cause,[5] the clinical utility of serial measurements is not yet apparent, especially since statin therapy—our front-line treatment for coronary disease—has not been shown to slow the progression of calcification.

Improving the accuracy of risk prediction

If a patient's 10-year coronary risk is intermediate (10% to 20%), calcification scoring can reclassify the risk as low or high in about 50% of cases and can improve the accuracy of risk prediction.[6–8]

For example, Elias-Smale et al[6] evaluated the effect of calcification scoring in 2,028 asymptomatic patients, with median follow-up of 9.2 years and 135 coronary events observed. Adding the calcification score to the Framingham model significantly improved risk classification, with a net reclassification improvement (NRI) of 0.14 ($P < .01$). (NRI is a measure of discriminatory performance for a diagnostic test; higher is better.[9]) Reclassification was most robust in those at intermediate risk, 52% of whom were reclassified, with 30% reclassified to low risk and 22% reclassified to high risk.

Erbel et al[7] reported data from the Heinz Nixdorf Recall study, which used calcification scoring to estimate the NRI in 4,129 patients followed for 5 years. During this time there were 93 coronary deaths and nonfatal myocardial infarctions. The addition of the calcification score to the Framingham risk model resulted in an NRI of 0.21 ($P = .0002$) for patients with a risk of 6% to 20% and 0.31 ($P < .0001$) for those with a risk of 10% to 20%. Erbel et al also estimated the C statistic (area under the receiver operating characteristic curve; the maximum value is 1.0 and the higher the value the better) for the addition of the calcification score to the Framingham risk model and to the Adult Treatment Panel (ATP) III algorithm. They reported a significant increase of 0.681 to 0.749 with the Framingham model and 0.653 to 0.755 with the ATP III algorithm.

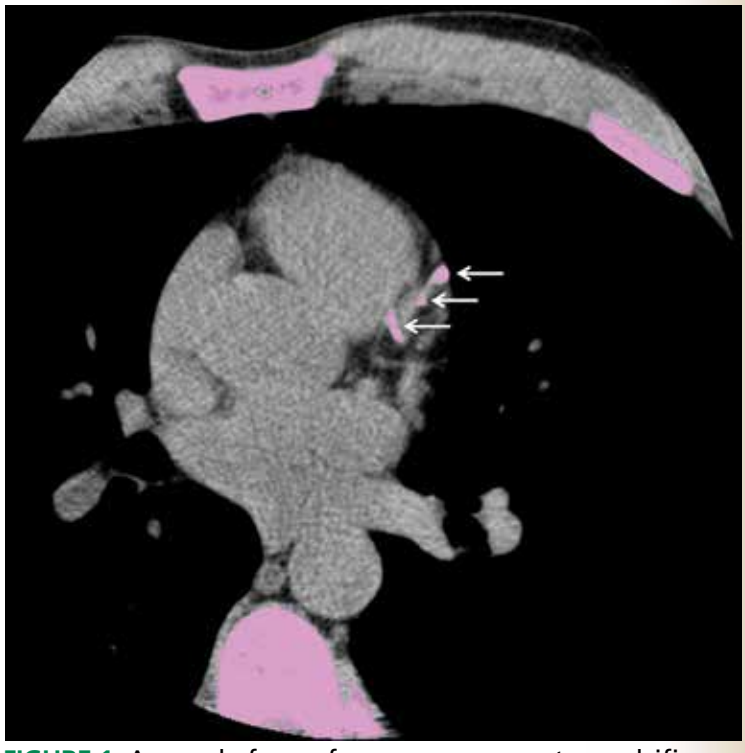

FIGURE 1. A sample frame from a coronary artery calcification score study. All structures above the threshold density that defines calcification are pink. Arrows indicate calcification within the left anterior descending coronary artery. The interpreting physician uses software to define the areas of calcification in each coronary vessel and sums them to yield a coronary artery calcification score.

Polonsky et al[8] studied a cohort of 5,878 participants from the Multi-Ethnic Study of Atherosclerosis (MESA) and estimated the event risk using a model based on Framingham risk characteristics. When the calcification score was added to the prediction model, 26% of the sample was reclassified to a new risk category. In intermediate-risk patients, 292 (16%) were reclassified as high risk, and 712 (39%) were reclassified as low risk, achieving an NRI of 0.55 (95% confidence interval 0.41 to 0.69; $P < .001$). In addition, the C statistic for the prediction of cardiovascular events was 0.76 for the model based on Framingham risk characteristics and increased to 0.81 ($P < .001$) with the addition of calcification scoring.

TABLE 1

Effects of coronary artery calcification scoring on cost and patient adherence

COHORT STUDIES	YEAR	NO. OF PATIENTS	COMPARISON	VARIABLE	ADJUSTED ODDS RATIO	*P* VALUE
Kalia et al[10]	2006	505	Highest vs lowest CAC quartile	Statin use	9.26	< .0001
Orakzai et al[13]	2008	980	Highest vs lowest CAC quartile	Aspirin use	2.98	< .001
				Improved diet	2.66	< .001
				Increased exercise	2.03	< .001
Taylor et al[12]	2008	1,640	Any CAC vs 0	Statin use	1.37	< .001
				Aspirin use	1.25	< .001
Nasir et al[11]	2010	6,814	CAC > 400 AU vs 0	Lipid-lowering drug use	1.53	< .001
				BP-lowering drug use	1.55	< .001
				Aspirin use	1.32	< .001
RANDOMIZED TRIAL	**YEAR**	**NO. OF PATIENTS**	**COMPARISON**	**VARIABLE**	**OUTCOME**	***P* VALUE**
Rozanski et al[14]	2011	2,137	CAC scoring vs control	Medical costs	$904 vs $712	.09
				Change in SBP, mm Hg	–7 vs –5	.02
				Change in LDL, mg/dL	–17 vs –11	.04
				Change in waist circumference, inches	0 vs 1	.01
			CAC > 400 AU vs 0	Exercise 3 or more times per week	47% vs 32%	.03
				Change in weight, lb	–3 vs 1	< .001
				Change in LDL-C, mg/dL	–29 vs –12	< .001
				Change in SBP, mm Hg	–9 vs –4	< .001

AU = Agatston units; BP = blood pressure; CAC = coronary artery calcification; LDL-C = low-density lipoprotein cholesterol; SBP = systolic blood pressure

Improving adherence and care

Knowing that a patient has a higher calcification score, physicians are more likely to prescribe lipid-lowering and antihypertensive drugs (TABLE 1),[10–12] and patients with a higher score are also more often adherent to recommendations regarding diet and exercise.[13]

Rozanski et al,[14] in a randomized controlled trial, showed that measuring coronary artery calcification did not increase downstream medical spending. A modest improvement in systolic blood pressure (P = .02), serum low-density lipoprotein level (P = .04), and waist circumference (P = .01) was observed in patients who had their calcification measured. Patients with the highest scores had the greatest improvement in coronary risk factors, including blood pressure, cholesterol, weight, and regular exercise.

On the other hand, other analyses have suggested that imaging tests are not effective for motivating behavioral changes. This topic deserves more research.[15]

Less utility in symptomatic disease

Coronary artery calcification scoring has less clinical utility in patients who already have coronary symptoms. Villines et al[16] described a cohort of 10,037 patients with coronary symptoms who underwent calcification scoring and computed tomographic coronary angiography and found that stenosis of greater than 50% was present in 3.5% of those who had a score of 0 and in 29% of those with a score higher than 0. Therefore, a score of 0 does not rule out obstructive coronary heart disease if the patient has symptoms. Conversely, these patients may still have coronary artery calcification even if perfusion stress imaging is normal,[17,18] and calcification scoring may have a role in the evaluation of equivocal stress tests.[19]

CALCIFICATION SCORING GUIDELINES

In their most recent (2010) joint guidelines for assessing risk of coronary heart disease in asymptomatic patients,[20] the American College of Cardiology and the American Heart Association say coronary artery calcification scoring:

- Is recommended for asymptomatic patients at intermediate 10-year risk (10% to 20%) of coronary heart disease (class IIa recommendation, level of evidence B)
- May be acceptable for asymptomatic patients at low to intermediate risk (6% to 10%) (class IIb recommendation)
- Is discouraged for those at low risk (< 6%) (class III recommendation).

The most recent (2010) criteria for the appropriate use of cardiac computed tomography[21] provide similar recommendations. Specifically, coronary artery calcification scoring with noncontrast computed tomography was rated as appropriate for patients at intermediate risk (10% to 20%) of coronary heart disease and for the specific subset of patients who are at low risk (6% to 10%) but who have a family history of premature coronary heart disease.

These recommendations are based on multiple lines of evidence that calcification scoring is a robust risk-predictor, can enhance risk estimates beyond traditional scoring strategies, and may—in theory—improve outcomes.

CALCIFICATION SCORING'S LIMITATIONS

The images used for measuring coronary calcification do predict risk of cardiovascular events, but they are not adequate to assess the severity of coronary stenosis. Further, calcification scoring often leads to incidental findings, which can cause anxiety and possibly lead to more imaging, entailing more radiation exposure and expense. And as noted, there are no randomized trial data demonstrating a reduction in cardiovascular events with the use of calcification scoring. ■

REFERENCES

1. **Redberg RF, Benjamin EJ, Bittner V, et al**. ACCF/AHA 2009 performance measures for primary prevention of cardiovascular disease in adults. J Am Coll Cardiol 2009; 54:1364–1405.
2. **Greenland P, Bonow RO, Brundage BH, et al**. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain. J Am Coll Cardiol 2007; 49:378–402.
3. **Winchester DE, Wymer DC, Shifrin RY, Kraft SM, Hill JA**. Responsible use of computed tomography in the evaluation of coronary artery disease and chest pain. Mayo Clin Proc 2010; 85:358–364.
4. **Budoff MJ, Shaw LJ, Liu ST, et al**. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. J Am Coll Cardiol 2007; 49:1860–1870.
5. **Budoff MJ, Hokanson JE, Nasir K, et al**. Progression of coronary artery calcium predicts all-cause mortality. JACC Cardiovasc Imaging 2010; 3:1229–1236.
6. **Elias-Smale SE, Proença RV, Koller MT, et al**. Coronary calcium score improves classification of coronary heart disease risk in the elderly: The Rotterdam study. J Am Coll Cardiol 2010; 56:1407–1414.
7. **Erbel R, Möhlenkamp S, Moebus S, et al; Heinz Nixdorf Recall Study Investigative Group**. Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. J Am Coll Cardiol 2010; 56:1397–1406.
8. **Polonsky TS, McClelland RL, Jorgensen NW, et al**. Coronary artery calcium score and risk classification for coronary heart disease prediction. JAMA 2010; 303:1610–1616.
9. **Pencina MJ, Agostino RB Sr, Agostino RB Jr, Vasan RS**. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Statist Med 2008; 27:157–172.
10. **Kalia NK, Miller LG, Nasir K, Blumenthal RS, Agrawal N, Budoff MJ**. Visualizing coronary calcium is associated with improvements in adherence to statin therapy. Atherosclerosis 2006; 185:394–399.
11. **Nasir K, McClelland RL, Blumenthal RS, et al**. Coronary artery calcium in relation to initiation and continuation of cardiovascular preventive medications: the Multi-Ethnic Study of Atherosclerosis (MESA). Circ Cardiovasc Qual Outcomes 2010; 3:228–235.
12. **Taylor AJ, Bindeman J, Feuerstein I, et al**. Community-based provision of statin and aspirin after the detection of coronary artery calcium within a community-based screening cohort. J Am Coll Cardiol 2008; 51:1337–1341.
13. **Orakzai RH, Nasir K, Orakzai SH, et al**. Effect of patient visualization of coronary calcium by electron beam computed tomography on changes in beneficial lifestyle behaviors. Am J Cardiol 2008; 101:999–1002.
14. **Rozanski A, Gransar H, Shaw LJ, et al**. Impact of coronary artery calcium scanning on coronary risk factors and downstream testing the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) prospective randomized trial. J Am Coll Cardiol 2011; 57:1622–1632.
15. **Hackam DG, Shojania KG, Spence JD, et al**. Influence of noninvasive cardiovascular imaging in primary prevention: systematic review and meta-analysis of randomized trials. Arch Intern Med 2011; 171:977–982.
16. **Villines TC, Hulten EA, Shaw LJ, et al; CONFIRM Registry Investigators**. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography. J Am Coll Cardiol 2011; 58:2533–2540.
17. **Schenker MP, Dorbala S, Hong EC, et al**. Interrelation of coronary calcification, myocardial ischemia, and outcomes in patients with intermediate likelihood of coronary artery disease: a combined positron emission tomography/computed tomography study. Circulation 2008; 117:1693–1700.
18. **Bybee KA, Lee J, Markiewicz R, et al**. Diagnostic and clinical benefit of combined coronary calcium and perfusion assessment in patients undergoing PET/CT myocardial perfusion stress imaging. J Nucl Cardiol 2010; 17:188–196.
19. **Schmermund A, Baumgart D, Sack S, et al**. Assessment of coronary calcification by electron-beam computed tomography in symptomatic patients with normal, abnormal or equivocal exercise stress test. Eur Heart J 2000; 21:1674–1682.
20. **Greenland P, Alpert JS, Beller GA, et al**. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults. J Am Coll Cardiol 2010; 56:e50–e103.
21. **Taylor AJ, Cerqueira M, Hodgson JM, et al**. ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac computed tomography. J Am Coll Cardiol 2010; 56:1864–1894.

***ADDRESS**: David E. Winchester, MD, MS, Department of Medicine, Division of Cardiovascular Disease, University of Florida, 1600 SW Archer Road, PO Box 100277, Gainesville, FL, 32610-0277; e-mail: dwinches@ufl.edu*