

Does coronary artery calcification scoring still have a role in practice?

TO TRY TO IDENTIFY AND TREAT people who are at highest risk of cardiovascular events, including death, we use comprehensive risk-prediction models. Unfortunately, these models have limited accuracy and precision and do not predict very well.

See related article, page 370

Attractive, then, is the idea of using a noninvasive imaging test to *measure* coronary atherosclerosis before it causes trouble and thereby individualize the risk assessment. Noncontrast computed tomography (CT) can measure the amount of calcification in the coronary arteries, and therefore it can estimate the coronary atherosclerotic burden. It seems like an ideal test, and calcification as a marker of subclinical atherosclerosis has been extensively investigated.

However, despite more than 2 decades of use and data from hundreds of thousands of patients, the test remains poorly understood. Many physicians seem to use it solely as a means of placating “worried well” patients and do not truly appreciate its implications. Others proceed to ordering CT angiography, a more expensive test that involves the added risks of using higher x-ray doses and iodinated contrast, even when a correctly interpreted calcification score would provide ample information.

In this issue of the *Cleveland Clinic Journal of Medicine*, Chauffe and Winchester review the utility of coronary artery calcification scoring in current practice. We wish to supplement their review by suggesting some considerations to take into account before ordering this test:

doi:10.3949/ccjm.80a.12162

- *Does the patient have symptoms of coronary artery disease, and what is his or her risk-factor profile?* Baseline patient characteristics are important to consider if we are to use this test appropriately.
- *How should the result be interpreted, and does the ordering physician have the confidence to accept the result?*

■ BEST USED IN ASYMPTOMATIC PATIENTS AT INTERMEDIATE RISK

Many large retrospective and prospective registries have demonstrated the predictive value of coronary artery calcification in diverse cohorts of patients without symptoms.

In three prospective registries—the Multi-Ethnic Study of Atherosclerosis¹ (MESA) with 6,722 patients, the Coronary CT Angiography Evaluation for Clinical Outcomes² (CONFIRM) with 7,590 patients, and the Heinz Nixdorf Recall (NHR) study³ with 4,129 patients—most of the patients who had heart attacks had a calcification score greater than 100. And conversely, data from more than 100,000 people show that the absence of calcification (ie, a score of 0) denotes a very low risk (< 1% over 5 years).^{1–6}

The pretest probability of coronary artery disease needs to be considered. The data clearly indicate that a Bayesian approach is warranted and that coronary artery calcification scoring should mainly be done in patients at intermediate or low-intermediate risk. Trials have shown that calcification scoring will reclassify more than 50% of intermediate-risk patients into the high-risk or low-risk category.³

The implications of these findings were eloquently assessed in the Justification for the Use

Many physicians seem to use coronary artery calcification scoring solely as a means to placate ‘worried well’ patients

of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER). In this trial, it was estimated that for patients with no calcification who would otherwise fulfill the criteria for treatment with a statin, 549 patients would need to be treated to prevent one coronary event, compared with 24 similar patients with a calcification score greater than 100.⁷

Although such analyses have potential shortcomings, in this era of greater concern about how to allocate finite resources, using a simple, inexpensive test to individualize long-term treatment is an attractive idea. Further, measuring calcification does not appear to increase testing “downstream” and indeed reduces it as compared with no calcification scoring. It also results in better adherence to drug therapy and lifestyle changes.

Because calcification scoring provides additional prognostic data and accurately discriminates and reclassifies risk, the American College of Cardiology and the American Heart Association have awarded it a class IIa recommendation for asymptomatic patients at intermediate risk, meaning that there is conflicting evidence or a divergence of opinion about its usefulness, but the weight of evidence or opinion favors it.⁸

■ **ITS ROLE IS MORE CONTROVERSIAL IN SYMPTOMATIC PATIENTS**

Perhaps a less established and more controversial use of coronary artery calcification scoring is in patients who are having coronary symptoms. In patients at high cardiovascular risk, this test by itself may miss an unacceptable number of those who truly have significant stenoses.⁹ However, when the appropriate population is selected, there is substantial evidence that it can be an important means of risk stratification.

In patients at low to intermediate risk, the absence of calcification indicates a very low likelihood of significant coronary artery stenosis, as demonstrated in the Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter (CONFIRM) registry.¹⁰ In the 10,037 symptomatic patients evaluated, a score of 0 had a 99% negative predictive value for excluding stenosis greater than 70% and was associated with a 2-year event

rate less than 1%. These data were supported by a meta-analysis of nearly 1,000 symptomatic patients with a score of 0, in whom the 2-year event rate was less than 2%.⁴

Taken together, these data suggest that the absence of coronary calcification in people at low to intermediate risk indicates a very low likelihood of significant stenotic coronary artery disease and foretells an excellent prognosis.

These data have already been incorporated into the British National Institute for Health and Clinical Excellence (NICE) guidelines, in which calcification scoring is an integral part of the management algorithm in patients with chest pain who are at low risk.

■ **WHY NOT JUST DO CT ANGIOGRAPHY?**

But why bother with coronary artery calcification scoring when we can do CT angiography instead? The angiography scanners we have today can cover the entire heart in a single gantry rotation. Dual-source scanners provide temporal resolution as low as 75 ms, and sequential, prospective electrocardiographic gating and iterative reconstruction can routinely achieve scans with doses of radiation as low as 3 mSv that provide coronary artery images of exquisite quality.

On the other hand, calcification scoring is fast and easy to perform and poses less potential harm to the patient, since it uses lower doses of radiation and no contrast agents. In addition, the quantification is semi-automated, so the results can be interpreted quickly and are reproducible.

In the CONFIRM trial, prediction by CT angiography was no better than calcification scoring in asymptomatic patients, so it is not recommended in this population.² In symptomatic patients, the CONFIRM trial data suggest that almost 1,000 additional CT angiography procedures would need to be done to identify one myocardial infarction and more than 1,500 procedures to identify one patient at risk of death missed by calcification scoring of 0 in patients at low to intermediate risk.¹¹

Chauffe and Winchester nicely summarize the limitations of calcification scoring. However, we would emphasize the potential impli-

This test should mainly be done in patients at intermediate or low-intermediate risk

cations of the above findings. Appropriately utilized, calcification scoring is safe, reproducible, and inexpensive and helps individualize treatment in asymptomatic patients at low to intermediate risk, thereby avoiding under- and overtreatment and potentially reducing downstream costs while improving compliance.

In patients at low to intermediate risk who

present with chest pain, documenting the absence of calcification can rationalize downstream testing and reliably, quickly, and safely permit patient discharge from emergency departments. In a time of increasing costs and patient demands and finite resources, clinicians should remain cognizant of the usefulness of evaluating coronary artery calcification. ■

REFERENCES

1. **Budoff MJ, McClelland RL, Nasir K, et al.** Cardiovascular events with absent or minimal coronary calcification: the Multi-Ethnic Study of Atherosclerosis (MESA). *Am Heart J* 2009; 158:554–561.
2. **Cho I, Chang HJ, Sung JM, et al; CONFIRM Investigators.** Coronary computed tomographic angiography and risk of all-cause mortality and nonfatal myocardial infarction in subjects without chest pain syndrome from the CONFIRM Registry. *Circulation* 2012; 126:304–313.
3. **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.
4. **Sarwar A, Shaw LJ, Shapiro MD, et al.** Diagnostic and prognostic value of absence of coronary artery calcification. *JACC Cardiovasc Imaging* 2009; 2:675–688.
5. **Blahe M, Budoff MJ, Shaw LJ, et al.** Absence of coronary artery calcification and all-cause mortality. *JACC Cardiovasc Imaging* 2009; 2:692–700.
6. **Graham G, Blahe MJ, Budoff MJ, et al.** Impact of coronary artery calcification on all-cause mortality in individuals with and without hypertension. *Atherosclerosis* 2012; 225:432–437.
7. **Blahe MJ, Budoff MJ, DeFilippis AP, et al.** Associations between C-reactive protein, coronary artery calcium, and cardiovascular events: implications for the JUPITER population from MESA, a population-based cohort study. *Lancet* 2011; 378:684–692.
8. **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.
9. **Gottlieb I, Miller JM, Arbab-Zadeh A, et al.** The absence of coronary calcification does not exclude obstructive coronary artery disease or the need for revascularization in patients referred for conventional coronary angiography. *J Am Coll Cardiol* 2010; 55:627–634.
10. **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: results from the CONFIRM registry. *J Am Coll Cardiol* 2011; 58:2533–2540.
11. **Joshi PH, Blahe MJ, Blumenthal RS, Blankstein R, Nasir K.** What is the role of calcium scoring in the age of coronary computed tomographic angiography? *J Nucl Cardiol* 2012; 19:1226–1235.

.....
ADDRESS: Milind Y. Desai, MD, Department of Cardiovascular Medicine, J1-5, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail: desaim2@ccf.org