

# Calcium Score Tweaks Framingham Algorithm

BY RICHARD HYER

CHICAGO — The Framingham Heart Study risk algorithm fails to identify a significant number of individuals at high risk of coronary heart disease, and its accuracy could be improved significantly by integrating coronary calcium scoring, according to a new study from the Netherlands.

“Coronary calcium scoring, detected by CT, is a promising way to improve cardiovascular risk prediction. Population-based studies have shown that the calcium score is a strong predictor of coronary events,” said Rozemarijn Vliegenthart Proença, Ph.D., of University Medical Center Groningen (the Netherlands).



This 7-year-long study of 2,038 patients, conducted at the medical center, is supported by outcomes data demonstrating that nearly two-thirds of patients who would be classified as intermediate risk should actually be reclassified as either high or low risk. The data were reported at the annual meeting of the Radiological Society of North America.

The study questioned whether adding the calcium score to known cardiovascular risk factors would improve risk classification in the population. It was embedded into the population-based Rotterdam Study, and 2,038 individuals aged 55-85 years were invited to participate.

“We assessed as clinical outcome coronary heart disease comprising nonfatal myocardial infarction, [coronary heart disease] mortality, coronary artery bypass grafting, and percutaneous coronary interventions,” Dr. Vliegenthart Proença said.

Investigators created two prediction models: one with variables of the Framingham risk score, fitted to this patient population, and the other including the calcium score. Risk estimates for coronary events were extrapolated to 10 years, the common time horizon for predicting cardiovascular risk.

“Then we calculated reclassification percentages to assess what the actual effect is of adding the calcium score to risk factors. Finally we compared the predicted risk, in the different categories, to the actually observed risk,” Dr. Vliegenthart Proença said.

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**DR. VLIEGENTHART PROENÇA**

Patients had a mean age of 70 years, and 1,171 (57%) were women. During the course of the study, 84 men and 45 women had a coronary event.

An elevated calcium score corresponded to significantly increased risk of events. Men with a calcium score over 400 had a sevenfold increased risk, compared with men who had a calcium score of 0-10. “When we adjusted for cardiovascular risk factors, these relative risks did not materially change,” Dr. Vliegenthart Proença said.

The strong association between the amount of coronary calcification and the risk of coronary heart disease was evident in the women’s cohort as well.

When the calcium score was included with the Framingham risk score, almost 30% migrated to different risk categories. Reclassification was most prominent in the intermediate Framingham risk category, where nearly two-thirds of men and women were reclassified as either lower or higher risk.

According to Dr. Vliegenthart Proença, this was one

of the study’s strengths. “Reclassification was based on the actual events. The observed risk in the different categories were calculated on the basis of our risk model, our prediction model, and on the basis of the actual events occurring in the different risk categories.”

A member of the audience questioned whether the Netherlands has used this data to change treatment recommendations.

“Actually, that’s work in progress. At this moment there is no screening for coronary calcium in the Dutch population,” Dr. Vliegenthart Proença said.

Session moderator Dr. Frank John Rybicki III of Harvard Medical School, Boston, agreed.

“This was an important study because it used actual patient outcomes with a follow-up of almost 7 years to then reclassify risk, integrating calcium score into the traditional methods of risk, which is the Framingham model. And it showed with outcomes that there is a positive influence integrating calcium with those more traditional risk factors. It pretty specifically shows that integration of the calcium score has a very high chance of being beneficial in determining one’s overall risk,” he said.

In a separate presentation, Dr. Vliegenthart Proença argued for noninvasive cardiac imaging of asymptomatic patients with peripheral arterial disease. A randomized, controlled trial of 231 such patients at her institution found that one in five were indicated for coronary revascularization.

Dr. Rybicki did not find this surprising. “A fifth of patients with peripheral arterial disease are also going to have significant coronary disease. We expect that.”

The studies were sponsored by University Medical Center Groningen.

Dr. Vliegenthart Proença had nothing to disclose. ■

## All-Cause Death

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dard has now been met, but he acknowledged that the study was observational and not a prospective, randomized trial. Nonetheless, the size and duration of the study, as well as the striking magnitude of beneficial effect, should be persuasive, said Dr. Budoff, program director of cardiology at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center.

In his study, 2,538 symptomatic patients referred for assessment of possible coronary disease and evaluated by coronary CT had a 52% reduced risk of all-cause death during an average 6.7-year follow-up compared with a similar group of 1,706 patients whose work-up did not include CT angiography.

“Increased awareness of coronary artery disease severity among people undergoing CT angiography may have contributed to their survival,” Dr. Budoff said. “Probable mechanisms include increased adherence to and use of anti-atherosclerotic therapies, such as statins, angiotensin-converting enzyme inhibitors, and anti-platelet drugs” such as aspirin, he added.

Dr. Budoff shows patients in his clinic who undergo coronary CT and have coronary calcium six images of their coronary arteries that depict the calcium deposits and stenoses. “I think that this is something that leads to compliance. It’s very black and white. Patients can see their plaque and stenosis and know they need

treatment,” he said in an interview. Patients also receive their calcium scores.

The 4,244 symptomatic patients in the study had an average age of 58 years, and 62% did not have known coronary artery disease. The patients who underwent coronary CT and those who received standard care without coronary CT imaging were treated in the academic cardiology clinic at Harbor-UCLA.

The two groups were matched by age, gender, the time when they were first seen, and their conventional cardiac risk factors.

All patients undergoing coronary CT had the examination covered by their insurance providers; none of the patients paid for the exam out of pocket. One factor that the study did not control for was socioeconomic status. The patients who did not undergo CT angiography may have been, as a group, somewhat poorer than those who had CT examinations, Dr. Budoff said.

During an average 80-month follow-up, the all-cause mortality rate was 3% in patients who had CT examinations and 11% in those who did not, a statistically significant difference. Mortality rates began to diverge between the two groups after about 3 years, and then continued to diverge.

In a multivariate analysis that controlled for age, gender, and coronary risk factors, patients who had standard care had a fourfold higher risk of dying than did those who had CT angiography.

Dr. Budoff has served on the speakers bureau for GE, a company that markets CT equipment. None of his associates had any financial disclosures. ■

## Several Questions Still Lack Answers

The study by Dr. Budoff contributes significantly to the growing number of studies that demonstrate the value of coronary CT. A 52% reduction in all-cause mortality over 6.7 years is impressive. A cost-benefit analysis would quite likely be favorable.

The fact that patients were shown images of their own coronary vasculature with objective evidence of disease is one potential compelling explanation of the results.

Studies have shown repeatedly, however, that even among patients who have sustained myocardial infarction and have undergone coronary revascularization, compliance with life-saving medications can be shockingly low.

While providing a plausible explanation, the findings in this non-randomized observational study need to be evaluated more precisely in a prospective fashion. While interesting, these results must be seen as hypothesis generating. There are many sources of confounding and bias that are not adequately addressed. For instance, did patients who underwent scanning have increased ac-

cess to drugs, increased frequency of follow-up, more consistent lab testing, greater access to cardiac rehabilitation, better social support networks, etc.?



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The standard for clinical trials is to have a randomized, controlled, prospective study. I consider it unlikely that this study will convince all health plans, especially federal ones, that coronary CT is the diagnostic

tool of choice in patients with symptomatic coronary disease. Cost-effectiveness will have to be proven and the benefits of coronary CT, compared with conventional stress testing or angiography, will have to be further defined. Settling these issues will require a committed clinical trial that will probably have to be funded by the private sector.

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