Calcium Score Improves Framingham Algorithm

An elevated calcium score corresponded to a significantly increased risk of events.

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 computed tomography, 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 having either high or low risk. Dr. Vliegenthart Proença presented the data here 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 actually improve risk classification in the population.

The imaging analysis 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. Coronary calcification was measured by electron beam tomography, and Agatson's method was used to calculate calcium scores.

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.

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.

Including the calcium score moved 30% of patients to different risk categories.

DR. VLIEGENTHART PROENÇA

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."

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

"Actually, that is work in progress. At this moment there is no screening for coronary calcium in the Dutch population," Dr. Vliegenthart Proença explained.

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."

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 main finding that 20% of those patients actually have severe coronary disease is interesting and important to demonstrate, but not particularly surprising."

The studies were sponsored by University Medical Center Groningen.

Dr. Vliegenthart Proença reported having no potential inancial conflicts of interest. ■

Contrast Agent Restrictions Curb NSF at Two Care Centers

BY KERRI WACHTER

No new cases of nephrogenic systemic fibrosis occurred at two large tertiary care facilities after more restrictive policies on the use of gadolinium-based contrast agents were introduced.

Before the changes, the incidence of nephrogenic systemic fibrosis (NSF) was 1 in 33 in high-risk patients. In patients on dialysis, the incidence of NSF was 1 in 35, according Dr. Ersan Altun, a radiologist at the University of North Carolina in Chapel Hill, and his coauthors.

'The absence of NSF cases in the postadoption period may reflect the effect of the use of different GBCAs and the adoption of restrictive GBCA policies.'

"The absence of NSF cases in the postadoption period may reflect the effect of the use of different GBCAs [gadolinium-based contrast agents] and the adoption of restrictive GBCA policies on the incidence of NSF," they wrote (Radiology 2009;253:689-96).

In 2006, reports to the Food and Drug Administration suggested a strong association between NSF and gadolinium-based contrast agents used in MRI. The exact mechanism remains unknown; however, gadolinium contrast agents vary in their dissociation rates and dissociation of the gadolinium ion from the chelating ligand may be a risk factor, the researchers said.

Cases of NSF were documented at two tertiary care centers for three periods: before the adoption of restrictive GBCA policies and a change in agents, during the transition period, and after the adoption of these changes.

The new policies included careful screening of patients for risk factors for NSF such as renal disease, hypertension, dialysis, and diabetes before they underwent gadolinium-enhanced MRI. If GBCA-enhanced imaging was unavoidable in a patient deemed to be at high risk, a half dose of gadobenate dimeglumine was used. The policies also specified greater use of other types of imaging that do not require contrast agents. In addition, gadolinium-enhanced MRI was not performed in pregnant women unless maternal survival was at stake, was not performed in any patient twice within 48 hours unless absolutely necessary, and was not done twice within 48 hours in any patient deemed to be at high risk of NSF.

The researchers used patient records at center A and ICD-9 codes for acute renal failure and chronic kidney disease (stages 3-5) to identify patients who were at risk for NSF and underwent gadolinium-enhanced MRI. At center B, the researchers used ICD-9 codes and patient records to identify dialysis patients who underwent gadolinium-enhanced MRI.

Before adoption of the changes, both centers used gadodiamide (Omniscan, GE Healthcare Inc.). After the adoption of the revised policies, both centers used either gadobenate dimeglumine (Multihance, Bracco Diagnostics Inc.) or gadopentetate dimeglumine (Magnevist, Bayer Healthcare Pharmaceuticals Inc.). Gadobenate was used for all MRI studies of adults, patients younger than 1 year, and pediatric patients at risk for the development of NSF. Gadopentetate was used for pediatric patients 1 year and older who were not at risk for NSF. Both agents have lower dissociation rates than gadodiamide.

NSF was diagnosed by clinical findings and histopathologic evaluation of deep-skin biopsy. The temporal relationship/interval between the administration of gadolinium-based contrast and onset of NSF was determined for each patient.

At center A, 35 patients with NSF were identified in the preadoption period; of these, 28 underwent gadolinium-enhanced MR only at center A and received only gadodiamide. The benchmark incidence of NSF at center A was 1/1,750 and the NSF incidence in high-risk patients was 1/33.

At center B, 14 patients with NSF were identified in the preadoption period; of these, 9 underwent gadolinium-enhanced MR only at center B and received only gadodiamide. The benchmark incidence of NSF at center B was 1/1,803 and the NSF incidence in dialysis patients was 1/35.

There were no cases of NSF in the transitional and postadoption periods at either center.

One coauthor received funding from GE Healthcare, Bayer Healthcare Pharmaceuticals, and Bracco. ■