Coronary Artery Calcium Helps Predict CHD

BY MARY ANN MOON

Adding the coronary artery calcium score to traditional risk factors significantly improved asymptomatic patients' risk classification for coronary heart disease, in an analysis of the Multi-Ethnic Study of Atherosclerosis.

"Incorporation of an individual's CACS leads to a more refined estimation of future risk of CHD events than [do] traditional risk factors alone," said Dr. Tamar S. Polonsky of Northwestern University, Chicago, and associates.

However, this finding "will need to be validated in additional populations" before CACS can be adopted into routine clinical practice, they noted. More importantly, it still hasn't been determined whether screening for subclinical disease using CACS actually improves patient outcomes, they cautioned.

In an editorial, Dr. John P.A. Ioannidis of the University of Ioannina (Greece) and Harvard School of Public Health, Boston, and Ioanna Tzoulaki, Ph.D., of Imperial College of Medicine, London, agreed that these study results, "no matter how promising, do not suffice to recommend this marker for widespread routine use."

In addition to the clinical utility of obtaining the CACS, the considerable cost of the procedure and its potential harms due to radiation exposure must be thoroughly examined. "The evidence to date suggests that while CACS is a promising tool, the verdict is not yet in as to whether it is ready for routine use, and much more is still left to do," Dr. Ioannidis and Dr. Tzoulaki wrote.

Dr. Polonsky and colleagues assessed CACS using data from the Multi-Ethnic Study of Atherosclerosis, a cohort study of more than 6,800 white, black, Hispanic, and Chinese Americans aged 45-84 years who had no known cardiovascular disease at enrollment in 2000-2002. For their study, the investigators included 5,878 of these subjects who had undergone CT scanning for coronary calcium assessment at baseline and who had been followed every 9-12 months for a median of 6 years.

There were 209 CHD events during follow-up, including 96 MIs, 14 CHD deaths, and 12 resuscitated cardiac arrests.

Adding CACS to the risk prediction model resulted in the reclassification of 26% of the sample. "Overall, 728 individuals in the entire cohort were reclassified to a higher risk category, with an event rate of 8.7%, and 814 were reclassified to a lower risk category, with an event rate of 2.7%," Dr. Polonsky and associates said (JAMA 2010;303:1610-6).

An important measure of a risk marker's usefulness "is whether it separates individuals into more clinically relevant risk categories. Ideally, a model would reclassify most of the individuals out of the intermediate-risk group and into the highest or lowest risk categories."

Accordingly, adding CACS to the risk prediction model placed 77% of the total study population into definitive highest risk or lowest risk categories, where treatment strategies are more straightforward, as opposed to the somewhat nebulous "intermediate risk" category. In comparison, only 69% of the study population were classified as highest or lowest risk when CACS was not added to the model, they noted.

There were three important caveats to the study's overall finding of improved risk prediction with CACS.

First, for patients who were reclassified from high to lower risk categories, it is questionable whether clinicians could safely decrease or withdraw preventive therapy. If they are going to continue treatment as usual regardless of CACS findings, then obtaining CACS in this patient group would be moot.

Second, patients in this study classified as low risk using CACS actually had an event rate that was higher than was predicted by the model. Therefore an important portion of patients thought to be at low risk did have a coronary event.

Third, nearly 60% of the coronary events in this study occurred in people who were not classified as high risk by either traditional risk factors or by CACS, the investigators noted. Thus, both methods of risk prediction may have underestimated risks for the majority of patients.

In their editorial, Dr. Ioannidis and Dr. Tzoulaki said that the study investigators "cautiously acknowledge that they analyzed a prospective cohort, not a randomized intervention trial. Thus, the authors have not yet demonstrated that the added accuracy in risk stratification can actually aid clinicians in better treating patients or improving their clinical outcomes" (JAMA 2010;303:1646-7). ■

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AAA Detection Increased to 59% With New Screening Tool

BY PATRICE WENDLING

CHICAGO — Researchers have developed a simple scoring system that detects large abdominal aortic aneurysms in a broader at-risk population—including women and those younger than 65 years—than do current screening criteria.

Based on an analysis of 3.1 million patients, the new scoring system estimated the prevalence of 5-cm or greater abdominal aortic aneurysms (AAA) in the United States to be 0.14%, or equivalent to 120,810 aneurysms. The current U.S. Preventive Services Task Force (USPSTF) guidelines would capture just one-third of these large aneurysms, whereas two-thirds would be identified with the new system, principal investigator Giampaolo Greco, Ph.D., said at the annual meeting of the American Surgical Association.

It would take 156 screenings with the current guidelines to get a single AAA vs. 85 screenings with this system.

DR. GRECO

"The score needs to be validated in another cohort, but if validated, we believe these results argue for fundamentally changing current screening policy," he said.

Dr. Gregorio Sicard called the findings a "landmark in the area of screening for vascular disease." Dr. Sicard, an invited discussant who is head of vascular surgery at Washington University in St. Louis, said that the current USPSTF guidelines have not been universally encouraged or adopted by vascular surgeons, and that utilization of Medicare's one-time ultrasound screening for AAA has been unsuccessful.

"Use of a strategy with this statistical model will significantly increase and clarify this controversy in which patients are best screened," he said.

The current USPSTF guidelines, which are designed to identify aneurysms greater than 3 cm in males aged 65-75 years who have ever smoked, are both too narrow and too broad, explained Dr. Greco of the department of health evidence and policy at Mount Sinai School of Medicine, New York. They exclude women, who account for 33% of the 20,000 deaths each year from ruptured AAA, and those younger than 65 years, who account for 10% of AAA deaths. They also identify smaller AAAs that are at a lower risk of rupture, thereby resulting in unnecessary anxiety in low-risk individuals.

Dr. Greco and his associates used multivariate logistic regression analysis to identify risk factors for AAAs in 3.1 million patients undergoing ultrasound screening for AAA by Life Line Screening from 2003 to 2008. Not surprisingly, smoking was found to have a profound influence on the risk for a 5-cm or larger AAA; the risk increased with quantity and duration of smoking and decreased following smoking cessation. Odds ratios ranged from 2.6 for smoking a half-pack or less per day for less than 10 years to 14.5 for smoking more than a half-pack per day for 35 years. The risk of AAA fell dramatically for those who quit smoking for 5-10 years (OR 0.8) and for more than 10 years (OR 0.5), reported Dr. Greco and senior author Dr. K. Craig Kent, chair of the surgery department at the University of Wisconsin in Madison.

Others at elevated risk included males (OR 7.7), those with a family history of AAA (OR 3.2), and those aged 85 years or older (OR 53.1).

Novel findings included a protective effect of exercising at least once per week (OR 0.8), consuming nuts at least four times per week (OR 0.9), and being of black (OR 0.7) or Hispanic (OR 0.7) ethnicity, Dr. Greco said.

Using these and other factors, the researchers developed a scoring system with a good predictive accuracy, as noted by a C statistic equal to 0.81. If AAA screening were performed on the 6.8 million at-risk individuals identified by current screening criteria, 33.7% of the large AAAs would be captured, he said. Based on a score of 36 on the new model, the number of individuals who would need to be screened would be reduced to 6.3 million and nearly 59.3% of AAAs would be identified. "It would take 156 screenings with the current guidelines to get a single AAA, whereas it would take 85 screenings with our scoring system to find one person with AAA," Dr. Greco said.

The risk of AAA fell dramatically for those who quit smoking.

DR. KENT

Alternatively, if the threshold were lowered to a score of 30, the same level of screening would bring the yield of detected AAAs to 84%, he added.

During a discussion of the findings, Dr. Sicard asked whether a separate scoring system should be developed for women, observing that the analysis contained very few women with large AAAs who were younger than 75 years. One attendee asked whether intervention should begin at a smaller aneurysm size in women, who present with rupture more often than do males and have greater in-hospital mortality. Dr. Greco said that a separate system for women would not be necessary, as they are included in the new model and the stringency of the test on smaller aneurysms is affected by lowering the score threshold. Ultimately, society would need to decide whether additional funds should be allocated to expand screening. A cost analysis is planned, Dr. Greco said in an interview. ■

Disclosures: *Dr. Greco and Dr. Sicard disclosed no conflicts of interest. Dr. Kent has been an investigator on various industry-sponsored trials. A study coauthor disclosed employment with Life Line Screening of America.*