Coronary Calcium Flags Young Men at Cardiac Risk

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ORLANDO — Coronary artery calcium identified young men at relatively high risk for a coronary heart disease event even when their Framingham risk score was low, in a study with more than 1,600 men.

The new findings "challenge the notion that a coronary artery calcium [CAC] score is only useful for people with an 'intermediate' Framingham risk score" of 10%-20%, Dr. Allen J. Taylor, professor of medicine and chief of cardiology at Walter Reed Army Medical Center in Washington, said at the annual scientific sessions of the American Heart Association. "It's rational to drop the threshold [for a CAC score] to a Framingham risk score of 5%" in younger men, those aged 40 to 50 years.

Recommendations published last year by the American College of Cardiology and American Heart Association called for considering using CAC screening in people with a Framingham risk score (FRS) that shows a 10%-20% 10-year risk for a coronary disease event, but screening was not recommended in those with an FRS of less than 10% or more than 20% (J. Am. Coll. Cardiol. 2007;49:378-402). An FRS of less than 10% generally indicates a low risk for a coronary heart disease event over the next 10 years, an FRS of 10%-20% indicates intermediate risk, and an FRS of more than 20% shows high risk.

"The only thing [making those in the new study] low risk is that they're young. The FRS doesn't do it for people who are young because it only uses a 10-year horizon," said Dr. Philip Greenland, professor of medicine and dean for clinical and translational research at Northwestern University, Chicago.

Dr. Taylor's study used data collected in the Prospective Army Coronary Calcium Project, which began in 1998 and enrolled 2,000 healthy and asymptomatic men and women who were 40-50 years old at entry and underwent assessment with the FRS and CAC screening and have been followed for an average of almost 6 years. The new analysis focused primarily on the 1,640 men in the study, of whom 1,634 have full follow-up data. Average age at enrollment was 43, and average FRS was 4.6%. About a third had an entry FRS of less than 3%, a third had an FRS of 3%-5%, and a third had an FRS greater than 5%.

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DR. TAYLOR

The CAC score was obtained using electron beam CT. Any score greater than zero was considered abnormal; 22% of the men had a CAC score above zero at baseline. The average was 20.

During follow-up that ranged from 1 to 8 years, the men had 14 "hard" coronary events, as well as 8 cases of revascularization. The incidence of events was 4% in the 367 men with a positive CAC score at baseline, and 0.6% in 1,267 men without discernable CAC at baseline. In an unadjusted hazard ratio analysis, men with a positive CAC score were about sixfold more likely to have a coronary event, compared with men without discernable CAC. The incidence of events also was highest among the men with the largest FRS at baseline.

Additional analysis showed the impact of a positive CAC score on the rate of coronary events in people with a baseline FRS of 5% or greater. Those with coronary calcium had about a ninefold increased risk of an event, compared with those with an FRS of more than 5% but no calcium, a significant difference. A positive CAC score had no significant effect on coronary risk in those with a starting FRS of 5% or less.

Another analysis highlighted the prognostic role of the CAC score in this group. Even when they were controlled for baseline FRS, men with a CAC score of 10-44 had an almost 6-fold increased risk for an event, compared with those with no coronary calcium, and men with a CAC score of more than 44 had a 10-fold increased risk, compared with those with no coronary calcium. Both of these hazard ratios were statistically significant. A CAC score of less than 10 had no significant impact on the event rate. "The results show the independent value of CAC screening in young, middle-aged men," Dr. Taylor said. ■

Magnesium Plays a Role

Calcium *from page 1*

Following completion of a 5-year osteoporosis study (Am. J. Med. 2006;1119:777-85), Dr. Mark J. Bolland and his associates at the University of Auckland (New Zealand) reassessed their data to compare cardiovascular events.

The women were randomized to 1 g/day of elemental calcium (Citracal) or placebo. All of the 1,471 participants were postmenopausal for at least 5 years and older than age 55 years at baseline, and 10% of those were older than age 80 at baseline (BMJ 2008 Jan. 16 [doi:10:1136/bmj.39440525752.BE]).

Death, sudden death, myocardial infarction, angina, other chest pain, stroke, and transient ischemic attacks events were recorded every 6 months. In all, 336 women stopped taking the calcium and 296 stopped taking the placebo before the study end.

A total of 21 of the 732 women in the calcium group experienced 24 myocardial infarctions, a statistically significant difference, compared with 10 of the 739 in the placebo group who had 10 such events.

A composite end point of sudden death, myocardial infarction, angina, or chest pain was also higher in the calcium group (155 events among 87 women) compared with the placebo group (135 events among 93 women).

No significant differences were found in angina, chest pain, transient ischemic attack, stroke, or sudden death events between groups. There were 34 deaths in the calcium group and 29 in the placebo, a nonsignificant difference.

Family physician, Dr. Peter P. Toth, who is director of Preventive Cardiology at Sterling Rock Falls Clinic, Ltd. in Sterling, Ill., said in an interview that subgroup analyses are hypothesis-generating only and require confirmation in a prospective, randomized clinical trial, and as such, he does not think doctors should stop prescribing calcium supplementation.

"It is extremely difficult to draw any meaningful conclusions from this study. It is a single-center study with an exceptionally high dropout rate," said Dr. Toth, who is also a clinical associate professor at the University of Illinois College of Medicine in Peoria. "Given [its] limitations and the weak associations it is able to draw between calcium supplementation and risk for acute cardiovascular events, it requires confirmation in a larger, more representative sample of postmenopausal women."

"This study in no way proves . . . that supplemental calcium is vasculotoxic and convincingly increases risk for cardiovascular events," he said. "Clinical practice should not be changed by this study."

Dr. Steven Masley, a family physician in private practice in St. Petersburg, Fla. and clinical assistant professor at the University of South Florida agreed. "I don't think physicians should stop [prescribing calcium], but they have to dose it appropriately," he asserted.

But for cardiologist Dr. Rita F. Redberg, the findings are sufficient to stop prescribing the supplementation.

"It is an important finding because so many women are prescribed calcium supplements," she said in an interview. "I would not recommend calcium supplementation based on this finding.

In the calcium group, 21 of the 732 women had 24 MIs, compared with 10 of the 739 women in the placebo group who had 10 such events.

This raises enough concern. With any supplement, you have to show evidence of benefit without risk."

In the current study, the HDL/LDL cholesterol ratios improved among the 732 women who took daily calcium supplementation, compared with the 739 participants who took placebo, which suggests that a different mechanism spurred the increase in myocardial infarction.

"This is an interesting point. It shows that just improving cholesterol does not reduce the risk of a heart attack," said Dr. Redberg, a Robert Wood Johnson Foundation health policy fellow and director of women's cardiovascular services at the University of California, San Francisco. "It was the same finding with estrogen: It lowered LDL, increased HDL, but did not reduce the number of heart attacks in studies."

Dr. Redberg said she was not surprised by the elevated MI risk, citing research by Dr. Linda Demer, vice chair of medicine at the University of California, Los Angeles, which has indicated increased cardiovascular risk associated with calcium.

"It's called the calcium paradox. Women lose calcium from their bones as they get older and it ends up in their arteries and the lining of their vessel walls, leading to accelerated atherosclerosis," said Dr. Redberg, who is also a professor of medicine at the University of California, San Francisco. "This study is a confirmation of that hypothesis, that calcium can end up in the walls of your arteries."

The study authors noted that the mean age was 74 years and participants were white, which presented a possible limitation for generalizing results to other ages or racial groups.

However, Dr. Redberg, who was not involved in the study, said that the inclusion of older women in the study is a strength because they are the most likely to be prescribed calcium supplements. It is very unusual for studies to include people older than age 80, she added.

Both Dr. Toth and Dr. Masley, neither of whom was involved in the study, criticized the researchers for prescribing calcium supplementation alone.

"[There is no] information about background calcium intake from dietary and vitamin sources," Dr. Toth said. "Moreover, in the United States it is generally not customary to dose supplemental calcium without concomitant vitamin D therapy."

Not accounting for calcium intake from diet is a bigger issue that goes beyond this study, said Dr. Masley, who estimated that 80% to 90% of physicians routinely prescribe 1,000 mg calcium supplements without first assessing dietary intake. "This study slams home the point that you should not give calcium by itself."

Calcium can decrease already-low magnesium levels in many patients, "and when you block the magnesium levels … you would expect an increase in cardiac events," Dr. Masley said. "Some of the women in the study were probably overdosed on calcium, which likely worsened their low magnesium status. No one is supposed to get more than 1,500 mg/day, and some in the study were probably getting more than 2,000 per day."

Dr. Redberg said that if the elevated MI risk from calcium supplementation is validated, it raises a broader issue relating to the prevention of osteoporosis.

"First we had estrogen, then vitamin D and calcium, and the bisphosphonates, but all have been shown to have significant side effects or risk. It may be safest to prescribe diet and weight-bearing exercises to prevent osteoporosis because all the supplements seem to have some risk," he said. ■