Study finds coronary calcium beats C-reactive protein for predicting heart attack and stroke risk

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The presence of calcium in coronary arteries is a much better predictor of heart attack and stroke than C-reactive protein among people with normal levels of LDL cholesterol, according to a study of more than 2,000 people led by a Johns Hopkins heart specialist.

Results of the study, published in the August 19, 2011 issue of *The Lancet*, have important implications for deciding whether cholesterol-lowering statin medication should be prescribed for people who have heart disease risk factors but normal levels of LDL, the so-called "bad" cholesterol. An estimated 6 million American adults fall into that gray-zone category.

The goal of the new study, which followed 2,083 people for six years, was to further refine who was at higher risk and, therefore, might benefit from taking statin medications. Conversely, the study also looked to define which groups may be at low risk and not in need of the drugs. The participants in the study were volunteers in the ongoing Multi-Ethnic Study on Atherosclerosis, known as MESA, which is an NIH-funded Hopkins-affiliated study.

"This was a direct comparison to see which patients with a normal LDL level of less than 130 mg/dL would have the greater risk of having a heart attack or stroke—those with evidence of calcium in coronary arteries, as determined on a cardiac CT test, or those with high levels of

C-reactive protein, which is measured in blood and is an indicator of inflammation somewhere in the body," says Michael J. Blaha, M.D. M.P.H, a cardiology fellow at the Johns Hopkins University School of Medicine and the Johns Hopkins Heart and Vascular Institute, who is the lead author of the study.

Blaha and colleagues found that 95 percent of the heart attacks, strokes or heart-related deaths in the study population occurred in people with some measurable calcium in their heart arteries. Meanwhile, 13.4 percent of those with the highest levels of coronary calcium (with scores greater than 100 on a calcium scoring test) had a heart attack or stroke during the study, whereas only 2 percent of those with high C-reactive protein in their blood, but no calcium buildup, had a heart attack or stroke.

In their study, the researchers determined that high levels of C-reactive protein in the blood, a score at or above 2 milligrams per liter, offered little predictive value after accounting for such risk factors as age, gender, ethnicity, hypertension, obesity, diabetes, smoking and a family history of heart disease.

"A calcium test directly looks for the disease we propose to treat with statins. Without measurable amounts of calcium, which indicates atherosclerosis, you are likely to be at very low risk in the short-term," explains Blaha.

This new study was designed to address some unanswered questions from a 2008 study called JUPITER, short for the Justification for the Use of Statins in Primary Prevention: An Interventional Tool Evaluating Rosuvastatin. That study found a 46 percent reduction in heart attacks among people with normal LDL cholesterol and a high level of C-reactive protein who took the statin medication rosuvastatin, which is marketed as Crestor.

JUPITER only included people with high C-reactive protein and none of those participants were tested to see whether they had evidence of calcium in their coronary arteries. So, Blaha says, it could not be determined from JUPITER whether people with low levels of C-reactive protein would benefit in the same way from statin therapy, or how the presence of coronary calcium may have affected the results.

All of the participants in the MESA trial had undergone coronary CT scanning, known as a calcium scoring test. Blaha and colleagues identified a group of participants in MESA who had high C-reactive protein levels and fit the criteria for JUPITER. The researchers also selected a group from MESA who had low levels of C-reactive protein. Then they were able to directly compare the prognostic importance of coronary artery calcium to C-reactive protein.

A statistical comparison of the results showed that among those with no measurable coronary calcium, it would be necessary to treat 549 patients with statin medication in order to prevent one heart attack. However, for those with high levels of coronary calcium buildup (with a calcium score greater than 100), the predicted number needed to treat to prevent one heart attack was only 24.

"Statin medications, which are a lifelong therapy, should not be considered the same as other preventive measures, such as diet and exercise, to reduce the risk of cardiovascular disease," says Roger Blumenthal, M.D., a cardiologist, professor of Medicine and director of the Ciccarone Center for the Prevention of Heart Disease at Johns Hopkins. He also was a co-investigator on the new study. "All drugs have the potential to cause side effects in some people, although with statins, the side effects are rare," he adds.

According to Blumenthal, "Many patients fall into the gray zone of being healthy with normal LDL cholesterol, but also having some risk factors,

including being overweight, having elevated blood sugar levels or a family history of heart disease. Our study provides clear evidence that high levels of calcium in coronary arteries will increase the risk of a heart attack or a stroke. And the risk increases with the amount of calcium, whether or not patients have high levels of C-reactive protein."

"While not everyone needs a calcium scoring test," Blaha says, "we believe looking for calcification in coronary vessels in certain patients makes sense in order to predict who may benefit from statin therapy because the test gets right to the heart of the disease we want to treat."

"Our data support recent American Heart Association guidelines, which say it is reasonable to order a coronary calcium scan for adults who are considered to be at intermediate risk of a heart attack over the next 10 years. A high coronary calcium score would indicate that statin therapy would likely be a useful strategy to lower that person's cardiovascular risk," according to Blumenthal.

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