Skin Test May Find Subclinical Atherosclerosis

Skin cholesterol level was tied to carotid intima-media thickness in asymptomatic CAD patients.

BY BRUCE JANCIN
Denver Bureau

ORLANDO, FLA. — A noninvasive point-of-care test that measures cholesterol in the skin is useful in identifying subclinical atherosclerosis in asymptomatic middle-aged adults, James H. Stein, M.D., reported at the annual meeting of the American College of Cardiology.

The PREVU Point of Care Skin Sterol Test, which recently became commercially available, may enable some patients deemed at intermediate cardiovascular risk on the basis of conventional risk factors to be spared the inconvenience and expense of referral for follow-up noninvasive or invasive testing aimed at further defining their risk, according to Dr. Stein.

"Because skin sterol is easy to measure, it may be a useful office-based tool for cardiovascular risk prediction," said Dr. Stein, codirector of the preventive cardiology program and director of the vascular health screening program at the University of Wisconsin, Madison.

"And in my opinion, we need to bring cardiovascular risk prediction back into the office, where the doctor and the patient interact. … What excites me about this test is, it at least holds out the potential that within 3-5 minutes, we can have an answer for the patient—or at least a little bit of guidance that helps push the patient and physician in the right direction," he said.

Dr. Stein reported on 81 consecutive asymptomatic patients with cardiovascular risk factors but without known vascular disease who were referred by their primary care physicians to the University of Wisconsin for B-mode ultrasound determination of their carotid artery intima-media thickness. The subjects' mean age was 56 years. Their average 10-year predicted risk of a cardiovascular event using the Framingham risk score was 7%, although that's clearly an underestimate, because 40% of participants in this study were already on lipid-lowering therapy. Carotid artery intima-media thickness is a well-validated marker for subclinical atherosclerosis.

Skin-tissue cholesterol level proved to be significantly and independently correlated with carotid intima-media thickness. The mean skin-tissue cholesterol value was 95.9 units.

After standard cardiovascular risk factors including age, gender, systolic blood pressure, blood glucose, and the ratio of total to HDL cholesterol were controlled for, each 10-unit increase in skin cholesterol was associated with a 59% increase in carotid intima-media thickness.

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DR. STEIN

Skin cholesterol as measured by the PREVU test had previously proved to be associated with the presence and extent of coronary artery disease in patients with angina or a positive exercise stress test.

The new study presented by Dr. Stein is the first to look at the skin test's utility in the setting where physicians find the need is greatest: as a simple, noninvasive means of improving risk prediction in patients with cardiovascular risk factors but not manifest CAD.

The PREVU test doesn't require a blood draw, pretest fasting, or a skin biopsy. The test measures cholesterol level colorimetrically in the skin of the patient's palm. The rationale for using the test as a marker for subclinical atherosclerosis is that as cholesterol accumulates in artery walls it also concentrates in other tissues—including the skin.

"I want to emphasize that the skin cholesterol test is really not meant in any way to replace traditional risk-factor assessment, including traditional cholesterol testing, or even some of the newer markers that are available. I think all these tests are complementary," the cardiologist said.

"What we're looking at here," he explained, "is an anatomic measure of the atherosclerotic disease process itself, rather than yet another marker that's associated with atherosclerosis. It's important not to think of the skin cholesterol test as a different way of measuring blood cholesterol—they're really two separate processes."

The study was funded by IMI International Medical Innovations, Inc., which developed the PREVU test, marketed by McNeil Consumer Healthcare. ■

Statins Boost Endothelial Function in Low-LDL CAD Patients

BY BRUCE JANCIN
Denver Bureau

ORLANDO, FLA. — Why do some individuals live well into their 90s free of heart disease despite an untreated serum cholesterol of 350 mg/dL, while on a daily basis cardiologists see numerous patients with normal or even low cholesterol who have advanced coronary disease at a relatively young age?

The answer appears to be that people differ in their vascular sensitivity to cholesterol. And that characteristic has major implications for treatment guidelines, which do not acknowledge these individual differences in sensitivity, Robert A. Vogel, M.D., said at the annual meeting of the American College of Cardiology.

This was the provocative implication of a new substudy of the previously reported Reversal of Atherosclerosis with Lipitor (REVERSAL) trial, said Dr. Vogel, professor of medicine and director of clinical vascular biology at University of Maryland, Baltimore.

The primary REVERSAL result was that intensive LDL-cholesterol lowering using 80 mg/day of atorvastatin (Lipitor) halted progression of coronary artery disease (CAD) as assessed by intravascular ultrasound during 18 months of follow-up. CAD continued to worsen in patients randomized to moderate LDL-cholesterol lowering with 40 mg/day of pravastatin (Pravachol). This finding paved the way for the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT TIMI-22) trial, which showed fewer cardiovascular events with 80 mg/day of atorvastatin than with 40 mg/day of pravastatin after hospitalization for acute coronary syndrome.

'If you get coronary disease and your LDL is low, it's because you're really sensitive to cholesterol.'

DR. VOGEL

The new REVERSAL substudy involved 214 participants with CAD whose endothelial function was assessed using the brachial artery flow–mediated dilation test at 21 medical centers. The purpose was to learn whether 3 months of intensive LDL lowering would improve endothelial function more than moderate LDL lowering. And, indeed, it did. Atorvastatin at 80 mg/day boosted flow-mediated dilation by 72%, while 40 mg/day of pravastatin increased it by 32%.

But the substudy also yielded a completely unexpected and counterintuitive finding: Those CAD patients with the lowest pretreatment LDL-cholesterol levels had the worst baseline endothelial function. And they also responded much more dramatically to intensive LDL lowering than did patients with higher LDL levels.

"We found in the overall trial that the difference between intensive and moderate therapy was concentrated in people who started with low cholesterol. As clinicians, we tend not to look at intensive therapy when the cholesterol is low to start out with. But we found in REVERSAL that those were the patients who actually benefited to the greatest degree," Dr. Vogel explained.

The presence of CAD in REVERSAL participants with low baseline LDL-cholesterol levels couldn't be accounted for by an increased prevalence of any of the traditional or novel cardiovascular risk factors. These patients differed from the others only in their low LDL levels and worse endothelial dysfunction.

"We think the explanation is that we're all different and that if you get coronary disease and your LDL is low, it's because you're really sensitive to cholesterol," he said.

"Your goal in cholesterol may be very different from my goal in cholesterol," he continued.

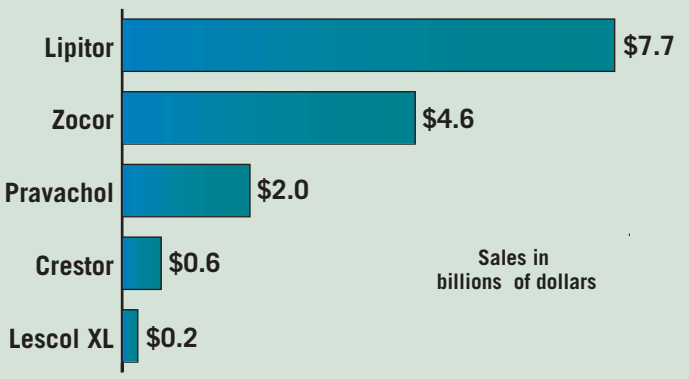
This is a reality the National Cholesterol Education Program guidelines will have to find a way to acknowledge, assuming the new REVERSAL finding is confirmed. But that doesn't mean measurement of endothelial dysfunction is likely to find its way into routine clinical practice as a risk-stratification tool.

"Measuring brachial artery blood flow is a complicated technique. We've been doing this now for 13 years. We have one technician who's been doing it the whole time. That's all he does. One of the disappointments in REVERSAL is we found the variability of even well-trained centers to be more than we would have expected," Dr. Vogel said.

"That makes doing clinical trials, let alone individual decision-making about patients, very, very difficult. At the present time, I don't see brachial artery ultrasound as a clinically oriented technique," he said. ■

DATA WATCH

Lipitor Sales to Retailers Led Statin Market in 2004



Note: Based on purchases, at wholesale prices, by retailers of prescription drugs. Total U.S. sales for statins were $15.5 billion.
Source: IMS Health

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