

# Coronary Calcium Score May Underestimate CV Risk

BY BRUCE JANCIN  
Denver Bureau

ORLANDO, FLA. — Reference norms for coronary artery calcium may be significantly lower than previously believed, Axel Schmermund, M.D., said at the annual meeting of the American College of Cardiology.

This new finding means that a fair number of patients deemed not to have a clinically significant amount of coronary artery calcium (CAC) on electron beam computed tomography (EBCT) for the detection of subclinical atherosclerosis may in truth have more than the average amount for their age—and thus may be at increased risk, explained Dr. Schmermund of the West German Heart Center at the University of Essen.

Until now, the reference standards applied throughout the world in using EBCT for the measurement of CAC as a means of stratifying coronary risk have relied principally on data from four large prospective U.S. studies. The studies involved subjects referred by their physicians or self-referred for EBCT, and hence are subject to several major types of bias.

Dr. Schmermund presented baseline data from the 4,259-subject Heinz Nixdorf RECALL (Risk Factors, Evaluation of Coronary Calcium and Lifestyle) study, the first large prospective study of CAC measurement in an unselected population. “Our subjects were strictly unselected. We approached them,



not the other way around,” he noted.

The investigators found the distribution of CAC scores in their German population-based study differed significantly from that in the U.S. studies.

“Compared with American values, the Heinz Nixdorf values for the 50th percentile are all lower, at least in the higher age groups. There is an age shift of approximately 5 years,” Dr. Schmermund said.

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DR. SCHMERMUND

This means, for example, that a 67-year-old man with a CAC Agatston score of 150 would be below the age-matched median using the widely cited American reference cohorts—but above the median value using the Heinz Nixdorf data as the reference norm.

Dr. Schmermund said it would be a mistake for American physicians to rely on German CAC EBCT reference data to estimate the cardiovascular risk of U.S. patients, since the two populations differ in various ways. But the Heinz Nixdorf data raise a red flag regarding reliance on reference data that are based on referral populations.

The good news, he added, is that soon American physicians will for the first time have coronary artery calcium reference data obtained prospectively from an unselected, unbiased U.S. population, when the baseline data from the large prospective ongoing National Institutes of Health-sponsored Multiethnic Study of Atherosclerosis (MESA) are published. ■

# Myocardial Perfusion Proposed as First-Line Prognostic Test in Women

BY BRUCE JANCIN  
Denver Bureau

ORLANDO, FLA. — Myocardial perfusion imaging substantially restratifies women with a moderate or high Duke Treadmill Score on exercise stress testing, Justin B. Lundbye, M.D., said at the annual meeting of the American College of Cardiology.

“In this subset of women with intermediate to high pretest likelihood of coronary artery disease [CAD] based on Duke Treadmill Score, we feel that consideration should be given to utilization of exercise myocardial perfusion imaging as the first-line test,” asserted Dr. Lundbye of Hartford (Conn.) Hospital.

Current ACC/American Heart Association guidelines recommend exercise stress testing (EST) alone for women with an intermediate or high pretest probability of CAD. But because of the nature of EST, many women will have false-positive results. Perfusion imaging



reliably subclassifies women into two groups: those who require further testing and those who do not, he said.

He reported on 1,020 women with an intermediate or high pretest likelihood of significant CAD who underwent EST and technetium-99 sestamibi myocardial perfusion imaging. During a mean 2.4 years of follow-up, women with a moderate Duke Treadmill Score of -10 to +4 (high risk to moderate risk) had a 3% annual rate of all-cause mortality, nonfatal MI, or coronary revascularization performed more than 2 months after their EST. In those who had an abnormal imaging study, the combined annual event rate was 17%. In those with a normal perfusion imaging study, it was 2%.

**Perfusion imaging subclassifies these women into two groups: those who require further testing and those who do not.**

DR. LUNDBYE

In women with a high-risk treadmill score of -11 or less, the annual event rate was 12%. Those with an abnormal perfusion scan had an annual event rate of 28%, while those with a negative scan had a rate of 4%. ■

# CAC Is Imperfect Measure of Atherosclerosis in Diabetics

BY MIRIAM E. TUCKER  
Senior Writer

WASHINGTON — Even without evidence of coronary calcium on CT, a large proportion of diabetic patients are still at risk for atherosclerosis, Liviu Klein, M.D., said at a conference on cardiovascular disease epidemiology and prevention sponsored by the American Heart Association.

“Diabetics are clearly at risk for atherosclerosis. Some people believe that CAC [coronary artery calcium] is a perfect tool for discrimination, but it’s not. ... My concern is that the absence of CAC will be used as a reason not to treat,” Dr. Klein, a fellow in cardiovascular epidemiology and prevention at Northwestern University, Chicago, said in an interview.

About 30% of diabetic adults aged 45 and older without clinically manifest coronary heart disease have no CAC (score of 0) on CT. No previous study compared other markers of atherosclerosis in that subgroup with those of nondiabetics without CAC. The first-ever study to do so is a part of the Multi-Ethnic Study of Atherosclerosis (MESA), a population-based cohort of 6,814 African American, white, Chinese, and Hispanic adults aged 45-84 without symptoms or history of cardiovascular disease.

A total of 350 (34%) of the diabetic participants and 2,825 (49%) of the nondiabetic participants had CAC scores of 0 on coronary CT. Diabetic subjects were older than nondiabetics (61 vs. 57 years) and were more likely to be African American (44% vs. 28%) or Hispanic (34% vs. 23%). Average body mass index (BMI), waist circumference, and triglyceride and LDL-cholesterol levels were also higher in the diabetics than in the nondiabetics, Dr. Klein reported.

On B-mode carotid ultrasound, the diabetic patients had significantly higher common and internal carotid intimal medial thickness (IMT) than did nondiabetics, both before and after adjustment for age, gender, ethnicity, and traditional risk factors for atherosclerosis, including blood pressure, cholesterol level, BMI, smoking, socioeconomic status, and use of statins and aspirin.

After adjustment, common carotid IMTs were 0.84 mm for the diabetics and 0.81 mm for the nondiabetics; internal carotid IMTs were 0.98 mm and 0.86 mm, respectively. Levels of intercellular adhesion molecule-1, E-selectin, interleukin-6, and C-reactive protein were all significantly greater in the diabetic group, indicating a greater burden of atherosclerosis, Dr. Klein said.

Mean ankle-brachial index did not differ significantly between the two groups either before or after the same adjustments, nor were there differences in levels of the plaque instability mark-

ers matrix metalloproteinase (MMP)-3, MMP-9, or soluble CD40 ligand.

Whether diabetic patients without a history of myocardial infarction have the same risk of CHD events as nondiabetic patients with a history of MI remains controversial, despite two sets of evidence-based guidelines issued by the National Heart, Lung, and Blood Institute categorizing diabetes as a “risk equivalent” for coronary heart disease and advising that all individuals with diabetes receive intensive CHD risk factor management (JAMA 2001;285:2486-97 JAMA 2003;289:2560-72).

However, conflicting data have appeared both before and since the dissemination of those two documents (the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults and the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure).

One recent study, for example, found that diabetic patients without MI had a lower risk of CHD events and mortality from cardiovascular disease than did nondiabetic patients with MI, but stroke risk was similar between the two groups (Circulation 2004;109:855-60), while another suggested that 5-year survival among diabetics without CAC is similar to that of nondiabetic subjects without CAC (J. Am. Coll. Cardiol. 2004;43:1663-9).

But, according to Dr. Klein, there are multiple problems with these and similar studies.

First, they have not accounted for the fact that mean CAC differs among individuals of different races. In particular, African Americans and Hispanics have lower mean CAC values than do whites, despite having higher MI rates. “We don’t really know what the calcium score means,” he said.

Moreover, these new data from MESA show that even if someone with diabetes has a CAC of 0 now, that person is likely to have a significantly higher atherosclerotic burden, compared with a nondiabetic. “If you wait until a diabetic has CAC, you will have missed the chance to prevent diabetes complications. ... It’s not so much an issue of mortality as it is of morbidity,” Dr. Klein said at the meeting, also sponsored by NHLBI.

As it is, fewer than 25% of diabetics receive appropriate treatment for cholesterol, hypertension, and glucose. That number could drop significantly if physicians use a CAC score of 0 on CT as a threshold for intensive treatment, he noted. “The problem is the more tools you have, the easier it is to just get the test rather than committing yourself to lifestyle modification. ... But in diabetics, who clearly have atherosclerosis, you have to treat them.” ■