

# Cardiac Screening for Diabetics Still Controversial

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The question of whether all asymptomatic diabetic patients should be routinely screened for coronary artery disease—and if so, how—is still open, according to a consensus statement from the American Diabetes Association.

“Although the CAD-asymptomatic patient with diabetes is by definition at least at intermediate risk for cardiovascular disease events, it is difficult to support routine CAD screening for these patients,” the ADA document stated. “As previous recommendations for stratifying diabetic patients based upon the number of risk factors have not proven effective, the question remains whether there are individuals with diabetes in whom coronary artery imaging would seem particularly appropriate” (Diabetes Care 2007;30:2729-36).

Until more data become available, “we recommend testing for atherosclerosis or ischemia, perhaps with cardiac [computed tomography] as the initial test, be reserved for those in whom medical treatment goals cannot be met and for selected individuals in whom there is strong clinical suspicion of very high risk CAD,” said a six-member panel chaired by Dr. Jeroen J. Bax, of the department of cardiology at Leiden (the Netherlands) University Medical Center.

The new document updates the last ADA statement on the subject, published in 1998. Then, the advice was to base the decision to screen patients on risk-factor burden, baseline electrocardiogram findings, and whether there was clinical evidence of vascular disease at other sites. But the authors acknowledged their positions were based primarily on opinion, because few well-controlled clinical trial data were available at that time (Diabetes Care 1998; 21:1551-9).

Since then, there has been greatly increased recognition of the prevalence and impact of CAD in people with diabetes. More is known about the role of inflammatory risk markers, and the benefit of primary and secondary cardiovascular disease risk factor modification on cardiac outcomes has been proven in several prospective interventional trials. Evidence has accumulated regarding newer CAD diagnostic tools, such as CT angiography, coronary artery calcium scoring, and cardiac magnetic resonance imaging. But, so far, there are not sufficient data to provide a “robust evidence-based recommendation” for CAD testing in diabetic patients, the panel said.

At the same time, studies that have looked specifically at asymptomatic type 2 diabetes patients have not supported the 1998 recommendation to screen only those patients with two or more risk factors, they noted. Based on these issues, the panel addressed the following four questions:

► **Which patients with diabetes are at increased risk for adverse cardiovascular outcomes and should be screened?** The goal of screening would be to identify a group of patients with high cardiac risk in whom outcomes might be improved through more aggressive risk-factor modification, medical surveillance, or revascularization. Among asymptomatic

patients, potentially predictive clinical features include other atherosclerotic vascular disease; microalbuminuria and other chronic kidney disease; abnormal resting electrocardiogram; autonomic neuropathy; retinopathy; hyperglycemia; age older than 65 years and male gender; and the presence of multiple cardiac risk factors.

However, at least two trials have found that such risk factors do not always predict which patients will have abnormal screening tests. For example, the DIAD (Detec-

tion of Ischemia in Asymptomatic Diabetics) study showed that basing the decision to screen on clinical features alone would fail to identify 41% of patients with silent ischemia (Diabetes Care 2004;27:1954-61).

► **What are the implications of an early diagnosis of coronary ischemia or atherosclerosis?** Noninvasive imaging techniques are now available that can help define the degree of atherosclerosis and estimate the degree of narrowing in individual lesions.

However, the benefit of such images is

not clear in a patient who receives aggressive medical risk-factor reduction therapy, which is already recommended for patients with diabetes. Presumably, the idea of using imaging is to identify asymptomatic patients with more extensive disease, in whom further testing would be indicated to identify those with significant inducible myocardial ischemia who might in turn then undergo coronary angiography and subsequent revascularization.

But although some data suggest that pa-

*High expectations*

*for lowering*

very high triglycerides ( $\geq 500$  mg/dL)

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7. LOVAZA was well-tolerated in controlled studies. The most common adverse events reported were: eructation, infection, flu syndrome, dyspepsia, rash, taste perversion, and back pain.
8. Please see full prescribing information.

References: 1. Lovaza Prescribing Information. Liberty Corner, NJ: Reliant Pharmaceuticals, Inc; 2007. 2. Data on file, Reliant Pharmaceuticals, Inc. 3. Ginsberg HN. Insulin resistance and cardiovascular disease. *J Clin Invest*. 2000;106:453-458. 4. Stalenhoef AFH, de Graaf JD, Wittekoek ME, Bredie SJH, Demacker PNM, Kastelein JJP. The effect of concentrated n-3 fatty acids versus gemfibrozil on plasma lipoproteins, low density lipoprotein heterogeneity and oxidizability in patients with hypertriglyceridemia. *Atherosclerosis*. 2000;153:129-138. 5. Garg R, Vasamreddy CR, Blumenthal RS. Non-high-density lipoprotein cholesterol: why lower is better. *Prev Cardiol*. 2005;8:173-177.



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tients with ischemia involving 10% or more of the left ventricle have a better outcome after revascularization than do those on medical therapy alone, other data—such as those from the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) study, in which one-third of the 2,287 patients had diabetes—have cast doubt on the superiority of revascularization over medical treatment (Am. Heart J. 2006;151:1173-9).

► **What tests, or sequence of tests, should be considered? With what frequencies should testing be done?** The 1998 panel recommended that exercise ECG be used to screen patients believed to be at high risk,

followed by imaging only in patients with abnormal resting ECGs. Since then, studies have demonstrated the prognostic value of cardiac CT in asymptomatic patients, including those with diabetes.

Thus, although prospective trial data are still lacking, if “in the judgment of the clinician, an asymptomatic patient is a candidate for CAD testing, it is reasonable to apply cardiac CT for detection of coronary artery calcification, using either electron beam or multislice technology, as the first step,” the panel recommended.

Several studies have suggested that a coronary calcium score of 400 or greater is associated with a high likelihood of inducible

ischemia, including one study that looked specifically at asymptomatic patients with diabetes (Eur. Heart J. 2006;27:713-21).

Thus, if coronary calcium testing is performed, it “appears reasonable” to proceed with further testing in diabetes patients with coronary calcium scores greater than 400. Such further testing could be done with single photon emission tomography to assess myocardial perfusion, or with stress echocardiography to assess ischemic wall motion abnormalities, the panel said.

► **What further research is needed to evaluate the effectiveness of these recommendations?** As a first step, the development and testing of improved risk pre-

diction models against data available from national registries would be particularly helpful in capturing general population risk data, Dr. Bax and his associates said.

In the BARI 2D (Bypass Angioplasty Revascularization Investigation in Type 2 Diabetes) study, patients with type 2 diabetes and documented CAD have been randomized to immediate revascularization combined with aggressive medical management, or a program of aggressive medical management with delayed or no revascularization. This study will provide important insight to assist in the development of strategies for the treatment of asymptomatic patients. ■

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