Screening Asymptomatic Diabetics for Ischemia Does Not Appear Warranted

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Patients with type 2 diabetes and no cardiac symptoms or prior coronary artery disease had a surprisingly low risk of nonfatal MI or cardiac death with or without routine screening in a study of 1,119 patients.

The 3% event rate over a 5-year period (or 0.5% per year) included cardiac death in 1.5% of 558 patients who were randomized to routine screening for silent ischemia, and 1.2% of 561 patients who were getting usual care. Nonfatal heart attacks occurred in 1.2% of the screening group and in 1.8% of the control group. The differences between groups were not statistically significant, Dr. Frans J. Wackers said at the annual scientific sessions of the American Diabetes Association.

The ADA recommends routine stress testing in patients with diabetes who have cardiac symptoms, are starting an exercise regimen, or have no cardiac symptoms but have multiple risk factors for coronary artery disease.

That approach appears to be sufficient. "Systematic screening for coronary artery disease cannot be recommended for asymptomatic patients with type 2 diabetes" based on results presented from the DIAD (Detection of Ischemia in Asymptomatic Diabetes) study, said Dr. Wackers, professor of diagnostic radiology and medicine at Yale University, New Haven, Conn.

The study enrolled adults aged 50-75 years with type 2 diabetes who had no known coronary artery disease, normal resting ECGs, and no stress testing in the prior 3 years. The screening group underwent adenosine myocardial perfusion imaging (MPI), which detected inducible ischemia in 22%. Except for the initial MPI in the screening group, diagnostic testing in both groups was at the discretion of the patients' physicians.

'Systematic screening for coronary artery disease cannot be recommended for asymptomatic patients.'

DR. WACKERS

Cumulative mortality at the 5-year mark was higher for patients with moderate to large defects detected on MPI (12%) than for patients with small or no defects detected (2% mortality for each) or for patients with nonperfusion abnormalities such as ischemic ECG changes (7%).

Screening results predicted cardiac outcomes, but the rates of cardiac events or mortality did not differ between groups. The mortality rate was 3% at 5 years.

The unexpectedly favorable 5-year prognosis probably reflects the benefits of contemporary strategies to optimize medical therapy, Dr. Wackers said.

"In the standard-care group, there was a fair number of stress tests and angiograms performed. I think clinicians made the right decisions," suggesting that routine screening is not needed, he said.

Patients in the standard-care group were more likely to get nonprotocol stress tests (30%) than were those in the screening group (21%). The proportion of those tests that identified abnormalities was similar between groups (24% of 118 additional tests in the screening group, and 26% of tests in 170 patients in the control group).

Coronary angiograms were as likely to be ordered for patients in the control group as in the screening group (12% vs. 14%), but were significantly more likely to identify abnormalities in the control group (44 of 66 angiograms, or 66%) than in the screening group (40 of 80 angiograms, or 50%). The use of oral medications increased in both groups over time, but did not differ between groups at baseline or at the end of the study.

Characteristics of the two groups were comparable. Patients had a mean age of 62 years and an 8-year history of diabetes. The baseline hemoglobin A_{1c} level was 7.1%. The cohort was 54% male, and 22% were ethnic minorities. The cohort probably is representative of the general population with type 2 diabetes. Patients were overweight, with a mean body mass index of 31 kg/m^2. No physical activity was reported by 34%, and 50% were unable to exercise. Diabetes treatment included oral medications in 63% and insulin in 22%. More than two cardiac risk factors were present in 60% of patients.

Dr. Wackers has received research support from Bristol Myers Squibb Medical Imaging and from Astellas Pharma, which makes cardiac imaging agents. ■

Impaired Fasting Glucose Boosts Stroke Risk

BY BRUCE JANCIN
Denver Bureau

COLORADO SPRINGS — Hyperglycemia was associated with a significantly increased stroke risk in a prospective study of 43,393 asymptomatic middle-aged men free of known cardiovascular disease and diabetes at baseline.

This finding raises the possibility that prevention and treatment of hyperglycemia could play a major role in stroke prevention, Dr. Xuemei Sui reported at a conference sponsored by the American Heart Association.

The men were seen for a preventive medical examination at the Cooper Clinic in Dallas during 1971-2003. During nearly 703,000 man-years of follow-up, the group collectively experienced 156 fatal and 456 nonfatal strokes.

The age-adjusted fatal stroke rate was 2.1 cases per 10,000 man-years in subjects with a normal fasting plasma glucose (FPG) of 80-109 mg/dL, 3.4/10,000 man-years in those with impaired fasting glucose as defined by an FPG of 110-125 mg/dL, and 4.0/10,000 man-years in subjects with undiagnosed diabetes as reflected in an FPG of 126 mg/dL or above.

Among men with an FPG of 110 mg/dL or more, each 10-mg/dL increment in FPG was associated with a 7% increased risk of total stroke events after adjustment for risk factors such as family history of cardiovascular disease, age, and body mass index, said Dr. Sui of the University of South Carolina, Columbia. ■

Pioglitazone Enhances Niacin's Effect in Raising Serum HDL

BY MITCHEL L. ZOLER
Philadelphia Bureau

CHICAGO — Adding pioglitazone to a niacin regimen boosted the rise in serum levels of HDL cholesterol in a controlled study of 72 patients with metabolic syndrome.

Although the finding needs to be replicated in a larger number of patients, it suggests that patients without diabetes but with metabolic syndrome and a low serum level of HDL cholesterol might benefit from combined treatment with pioglitazone and niacin, Dr. Richard L. Dunbar said while presenting a poster at the annual meeting of the American College of Cardiology.

This approach would nicely jibe with an emerging approach for treating patients with prediabetes with a thiazolidinedione, the drug class that includes pioglitazone (Actos), said Dr. Dunbar, a cardiologist at the University of Pennsylvania, Philadelphia. Adding a drug like pioglitazone may also blunt the tendency of niacin to trigger insulin resistance, which means that the combination can have multiple benefits, he said in an interview.

The study was funded in part by Kos Pharmaceuticals, which was subsequently acquired by Abbott. Abbott markets an extended-release formulation of niacin (Niaspan). Dr. Dunbar and his associates have no other financial relationship with Kos or Abbott.

The study enrolled patients with metabolic syndrome, including a low serum level of HDL cholesterol, but without diabetes. Their average HDL level at baseline was 37 mg/dL. Their average age was about 52 years, and about 75% were men.

All patients were titrated over 4 weeks to a 2-g/day dosage of extended-release niacin. They were then randomized, with 34 patients treated for 6 weeks with 30 mg/day pioglitazone, followed by 6 weeks on 45 mg/day. Thirty-eight patients were randomized to placebo instead of pioglitazone.

At the end of the niacin run-in, when all patients were only taking the maximum dosage of niacin, serum HDL cholesterol levels rose by an average of about 20% over baseline. After 6 weeks of treatment with 30 mg/day pioglitazone, the average HDL cholesterol level was 36% over baseline, compared with an average of about 20% over baseline in the placebo patients, a statistically significant difference.

After an additional 6 weeks of treatment with 45 mg/day pioglitazone, the average HDL cholesterol level was 24% over baseline, compared with an average of 11% over baseline in the niacin-alone group.

Women had greater increases in HDL cholesterol than men, and also received a greater boost from adding pioglitazone (see table).

As expected, treatment with pioglitazone had no discernible effect on levels of other serum lipids. Niacin treatment led to about a 10% drop in serum levels of LDL cholesterol, and about a 30% drop in triglyceride levels.

Also as expected, treatment with niacin alone worsened energy metabolism, leading to an average 8% rise in serum glucose, and an average 47% rise in serum insulin. In contrast, patients who took pioglitazone plus niacin had an average 1% rise in serum glucose and an average 12% drop in serum insulin levels. The differences in these measures between the two treatment arms were statistically significant. ■