Skin Autofluorescence May Predict Mortality

BY KATE JOHNSON
Montreal Bureau

COPENHAGEN — Skin autofluorescence is a strong and independent predictor of mortality in patients with well-controlled type 2 diabetes, according to data presented at the annual meeting of the European Association for the Study of Diabetes.

The study was headed by Dr. Andries Smit, head of the vascular unit of the University Medical Center in Groningen, the Netherlands, and medical director and founder of DiagnOptics, which markets a skin autofluorescence (AF) measuring device called the AGE Reader.

Elevated levels of advanced glycation end products (AGEs) have been shown to predict cardiovascular complications better than blood sugar levels in patients with diabetes. Dr. Smit's group previously showed

The AGE Reader noninvasively detects advanced glycation end products.

that AGE levels can be measured in diabetic patients using skin AF (Diabetologia 2004;47:1324-30; Ann. N.Y. Acad. Sci. 2005;1043:290-8).

The current study involved 973 patients with type 2 diabetes (median duration 4.2 years) and well-controlled hemoglobin A_{1c} (HbA$_{1c}$). Skin AF levels were measured with the AGE Reader at baseline and a median of 3.2 years later. A total of 86 patients died during the study, 44 from cardiovascular disease, said Dr. Helen Lutgers, of the diabetes outpatient clinic, Isala Clinics, Zwolle, the Netherlands, who presented the study at the meeting.

In a Cox regression analysis, smoking, the presence of peripheral vascular disease, and skin AF predicted mortality, with relative risks of 2.17, 2.15, and 1.69, respectively, she reported, but blood sugar, blood pressure, and lipid parameters were not predictive. "This is a superior measurement to HbA$_{1c}$."

The AGE Reader measures skin AF noninvasively and can give results in 30 seconds, Dr. Smit said in an interview. "[It] gives incremental prognostic information … in type 2 diabetes at a fraction of the burden and cost of [other] tools."

The device is approved for marketing in Europe (at a cost of about $25,500). The company is waiting for Food and Drug Administration approval in the United States. U.S. physicians can order the equipment and use it as an investigational device, Dr. Smit said. ■

Consider Prediabetes Factors in Cardiovascular Assessments

BY KATE JOHNSON
Montreal Bureau

COPENHAGEN — Physicians should pay particular attention to prediabetes when considering a patient's cardiovascular health, according to new joint guidelines on diabetes and cardiovascular disease unveiled at the annual meeting of the European Association for the Study of Diabetes.

"The negative impact of dysglycemia is apparent before the onset of diabetes," said Dr. Eberhard Standl of the International Diabetes Research Unit, Munich, and vice president of the association (EASD). "There are signs of diastolic dysfunction with impaired glucose tolerance before the development of overt diabetes."

An executive summary of the joint guidelines, "Diabetes, Prediabetes, and Cardiovascular Disease," drafted by the EASD and the European Society of Cardiology (ESC), is expected to be published simultaneously in the official journals of both organizations—the European Heart Journal and Diabetologia—in November. The full 200-page text, which includes 72 recommendations, will appear in the European Journal of Cardiovascular Prevention and Rehabilitation, as well as on the EASD and ESC Web sites, Dr. Standl said at press briefing during the meeting. Pocket guidelines also are being prepared.

The guidelines reflect a growing recognition within both fields of the common co-occurrence of diabetes and cardiovascular disease.

An algorithm included in the document recommends that physicians assess cardiovascular health in all their patients with known or unknown cardiovascular disease, using electrocardiography, echocardiography, and exercise testing. Patients with positive findings should be referred to a cardiologist.

Cardiologists are advised to assess diabetic status in their patients using the oral glucose tolerance test (OGTT). Although testing is not recommended in all cardiology patients, the decision about who to test can be made using the Finnish Diabetes Risk Score (FIND-RISC), Dr. Standl said.

According to the EASD/ESC document, the OGTT is "the best method to diagnose previously unknown diabetes or prediabetes," compared with fasting glucose measurements.

However, a spokesman for the American Diabetes Association said although the OGTT recommendation will mean greater identification of diabetes cases, it raises the risk of noncompliance.

"The test is somewhat cumbersome and adds to the burden of so many things that need to be done with these patients," Dr. Vivian Fonseca said in an interview. Dr. Fonseca, professor of medicine at Tulane University, New Orleans, is drafting similar joint guidelines with the American Heart Association. ■

Low-Carb Diet Trumps Caloric Restriction in Type 2 Diabetes

BY JEFF EVANS
Senior Writer

WASHINGTON — Patients with type 2 diabetes may be able to improve glycemic control, weight loss, and cholesterol levels significantly more with low-carbohydrate diets than with diets emphasizing a caloric deficit, according to the results of two randomized trials presented at the annual scientific sessions of the American Diabetes Association.

Uncontrolled pilot studies of low-carbohydrate diets (ranging from 7% to 20% of total calories) in patients with type 2 diabetes have shown declines in HbA$_{1c}$ values ranging from 1.2 to 4.1 percentage points and decreases in weight of 7%-12% in up to a year of follow-up.

With such promising results in mind, Dr. Eric C. Westman and colleagues at Duke University, Durham, N.C., conducted a comparison of a low–glycemic index diet (LGI) with a low-carbohydrate, ketogenic diet (LCKD) in 97 type 2 diabetes patients, average age 50-51 years, who wanted to lose weight.

To be included in the trial, patients had to have no history of diabetic ketoacidosis, have an HbA$_{1c}$ of greater than 6% at screening, and be able to self-monitor blood glucose levels if on insulin or oral

hypoglycemic therapy. Patients were excluded if they had unstable cardiovascular disease (allowable if hypertension and hyperlipidemia were under control), kidney disease, or liver disease, or were pregnant or breast-feeding.

Participants in each group received exercise recommendations and nutritional supplementation (a multivitamin, chromium 1,000 mcg/day, and vanadyl sulfate 60 mg/day) and attended group meetings. The LGI diet consisted of an individualized 500-kcal reduction per day in energy intake, deriving 55% of energy from low-glycemic carbohydrates, whereas people on the LCKD restricted their carbohydrate intake to less than 20 g per day.

Among the 50 participants who completed the 24-week study, HbA$_{1c}$ levels improved significantly more in the LCKD group (8.8% to 7.3%) than in the LGI group (8.3% to 7.8%). When dropouts were included in analyses using the last observation, the LCKD group still had a significantly greater, albeit smaller, HbA$_{1c}$ improvement than the LGI group did

(8.4% to 7.6% vs. 8.3% to 8%).

In a multivariate regression model, treatment group was independently predictive of change in HbA$_{1c}$ after weight loss was controlled for "suggesting that [the LCKD] diet, even beyond weight loss, had an effect on HbA$_{1c}$," said Dr. Westman, professor in the department of medicine at Duke University.

By the end of the trial, 18 of the 29 people who completed the LGI diet had eliminated or reduced the number of medications they were on, compared with 20 of 21 individuals in the LCKD group. Body weight changed significantly more among LCKD participants (107 kg to 97 kg) than in LGI participants (104 kg to 98 kg).

Both groups had similar improvement in total and low-density lipoprotein cholesterol as well as triglycerides. LCKD participants had a significant 5.5% increase in high-density lipoprotein cholesterol (HDL-C), compared with no change in the LGI individuals.

The study was funded by the Robert C. Atkins Foundation. Dr. Atkins is credited with popularizing a low-carbohydrate diet.

In a multivariate regression model, treatment group was independently predictive of change in HbA$_{1c}$ after weight loss was controlled for.

In a separate 2-year trial, an interim analysis of 6 months of data showed that a diet restricted to about 70 g of carbohydrates (half from fruit and milk) significantly improved weight and waist circumference in patients with type 2 diabetes, compared with a diet with a 500-kcal per day calorie restriction, reported Dr. Michael E. Daly, a diabetologist at the Royal Devon and Exeter NHS Trust, Exeter, England.

Six-month data were available for 206 of 259 (80%) patients randomized in the trial. This 20% dropout rate was lower than that of other low-carbohydrate studies, Dr. Daly said (N. Engl. J. Med. 2003;348:2074-81; 2082-90). Participants had an average age of 59, a mean weight of 99 kg, and a mean BMI of 35 kg/m^2.

Significantly more weight loss occurred in carbohydrate-restricted patients (3.7 kg) than in those on the energy-deficit diet (1.2 kg). Both diets improved body fat percentage, HbA$_{1c}$, total cholesterol:HDL cholesterol ratio, triglycerides, and blood pressure, but no differences emerged between the two groups on any of these measures. In both groups, calcium excretion declined to a similar extent and microalbumin excretion did not change substantially (Diabet. Med. 2006;23:15-20). ■