# Depression, Diabetes Linked to CAD Mortality

BY JONATHAN GARDNER
*London Bureau*

Having both type 2 diabetes and depression puts patients with coronary artery disease at greater risk of death over a 4.5-year period than does either condition alone.

That finding emerged from a study presented at the American Psychosomatic Society meeting in Budapest, Hungary.

The more severe the depressive symptoms were in those patients with both coronary artery disease and diabetes, the greater their risk of death during follow-up.

Having high scores on the Beck Depression Inventory (BDI) increased the risk of dying during the follow-up period by 20%-30%, compared with patients with similar depression scores but without type 2 diabetes, according to investigators from Duke University, Durham, N.C. These findings suggest that physicians should screen for and treat depression in their patients with diabetes and heart disease.

"There is some sort of synergistic effect between type 2 diabetes and depression that we don't fully understand," lead researcher Anastasia Georgiades, Ph.D., said in a written statement. "In our analysis, we controlled for factors that could influence mortality, such as heart disease severity and age. For whatever reasons, these patients were still at higher risk of dying, and future research will aim to investigate the mechanisms for this association."

The study compared 325 patients with type 2 diabetes and 582 patients without the disease during hospitalization for a coronary angiography. Their depression symptoms were rated using the BDI. Approximately 25% scored at least 10 on the BDI, indicating depression, Lana Watkins, Ph.D., an investigator in the study, noted in an interview.

During the follow-up period of 4.5 years (median, 3 years), the researchers documented 135 deaths among the study participants. Among the depressed patients, 19% died, compared with 12% of those patients without depression, Dr. Watkins said.

The researchers found statistically significant associations between depressive symptoms and increased mortality and, separately, diabetes and increased mortality. The highest mortality was among patients with both diabetes and elevated BDI scores. The researchers did not publicize hazard ratios, however, because they said those statistics would overestimate the risk and create anxiety among patients.

"Patients with type 2 diabetes typically have an extensive self-care regimen involving special diet, medications, exercise, and numerous appointments with their doctor," Dr. Georgiades said in the statement. "It may be that such patients who are depressed might not be as motivated to carry out all these activities, thereby putting them at higher risk."

Physicians treating patients with heart disease and diabetes need to screen them for depression and treat as needed.

"Regular exercise has been shown to improve depression, too, so that might be an option," Dr. Watkins noted in an interview. "This could potentially improve depression and diabetes, and might be a good first choice for diabetics who would prefer not having to take additional medications." ■

# *Health Centers Undertreat CV Risk Factors in Diabetes Patients*

BY LESLIE SABBAGH
*Contributing Writer*

Undertreatment for hypertension and dyslipidemia is highly prevalent among diabetic patients who receive care at community-based centers, with only a small group having all their cardiovascular risk factors managed, according to an observational Italian study.

The authors wrote that there could be several possible explanations for this outcome, "including the complex and challenging nature of diabetes management and the low reimbursement rate for outpatient visits. …In fact, a short encounter with a high-risk and challenging patient does not adequately provide the time necessary for addressing adherence to complex care behaviors and assessment for optimal therapeutic effectiveness."

Dr. Furio Colivicchi of the S. Filippo Neri Hospital in Rome and colleagues prospectively evaluated 1,078 type 2 diabetes mellitus patients (571 men and 507 women) with a mean age of 67.6 years to assess how hyperglycemia, hypertension, and dyslipidemia are detected, treated, and controlled in urban community-based diabetic care clinics in Italy. The authors cited the lack of treatment and outcome data for these patients as a reason for conducting the study.

The researchers prospectively collected glycosylated hemoglobin, blood pressure, and cholesterol subfractions values and clinical and medication data to assess cardiovascular risk factor control. The mean time from the initial diagnosis to the inclusion visit was 11.6 years (Diabetes Res. Clin. Pract. 2007;75:176-83).

Despite a 66.6% hypertension prevalence in the study cohort, only 29.6% of patients met the treatment goal of systolic blood pressure less than 130 mm Hg. The goal of diastolic blood pressure less than 80 mm Hg was met in 38.6% of patients, and only 25.5% of patients met the treatment guideline for LDL cholesterol values less than 100 mg/dL.

Glycosylated hemoglobin values less than 7% were recorded in 57.8% of cases; the mean value for glycosylated hemoglobin in the study sample was 6.9%. The authors called these findings "far more satisfactory than those reported in other similar previous surveys, possibly expressing the fact that clinical management of diabetic patients in this setting of urban diabetic care clinics is mainly focused on glycemic control."

Undertreatment for hypertension and dyslipidemia in community-based centers was "highly prevalent in this survey, and only a very small group of diabetic patients had all cardiovascular risk factors comprehensively addressed," the authors noted. Consequently, "a high proportion of our patients were noncompliant with European guidelines."

They added that their results "underscore the major difficulties in following complex guidelines in our present health care system, rather than the lack of enthusiasm among health care providers to rigorously implement recommendations."

The authors advised their study should be "considered as a baseline measurement and an initial step paving the way for further quality improvement initiatives." ■

# Type 1 Diabetes Prevention Trials Evaluating β-Cell Loss

BY NANCY WALSH
*New York Bureau*

NEW YORK — A new generation of clinical trials is evaluating various ways of interrupting autoimmune β-cell destruction in type 1 diabetes, thereby preventing development of the disease, Dr. Carla J. Greenbaum said at a meeting sponsored by the American Diabetes Association.

Two studies begun in the early 1990s, the Diabetes Prevention Trial–Type 1 (DPT-1) and the European Nicotinamide Diabetes Intervention Trial (ENDIT), showed the feasibility of conducting large, well-designed, rigorously controlled clinical trials in patients at risk for diabetes. But the therapies tested—low-dose insulin injections, oral insulin, and nicotinamide—failed to delay or prevent the onset of type 1 diabetes, said Dr. Greenbaum, director of the diabetes research program at Benaroya Research Institute at Virginia Mason, Seattle.

Today, with significant advances in understanding of immune regulation and β-cell growth and development, multiple primary, secondary, and tertiary prevention trials are being conducted. These studies are needed because of the tremendous recent increase in the incidence of type 1 diabetes worldwide, including a 300% increase in type 1 incidence among children younger than 4 years, she said.

► **Primary prevention.** The goals of primary prevention studies are to identify patients who are genetically at risk because they have certain genetic mutations or because a close relative has the disease, to monitor those patients for the development of autoantibodies, and to intervene when antibodies appear.

In the randomized Trial to Reduce Insulin-Dependent Diabetes in the Genetically at Risk (TRIGR), the effects of cow's milk or soy-based formula in addition to breast-feeding is being evaluated in at-risk babies. A previous pilot study suggested that cow's milk was associated with a higher incidence of antibody development.

In the Nutritional Intervention to Prevent Diabetes (NIP) trial, anti-inflammatory omega-3 fatty acids are being given to mothers and infants to determine if this beneficial fatty acid can inhibit the initial autoimmune process.

► **Secondary prevention.** The goal in patients who already are antibody positive and in whom the autoimmune process is underway is to prevent the development of clinical disease, Dr. Greenbaum said.

ENDIT and DPT-1 were secondary prevention studies, and although unsuccessful, they provided data that have proved useful in the newer generation of prevention trials. In DPT-1, for example, although oral insulin was not effective overall, it was beneficial in a subset of patients who had very high levels of autoantibodies. This is now being tested again in patients considered most likely to benefit, she said.

► **Tertiary prevention.** For patients who already have clinical disease, the goal is to preserve β-cell function and thereby prevent both short- and long-term complications; of particular concern in the short term is severe hypoglycemia. Patients in the Diabetes Control and Complications Trial who had some residual β-cell function and who received intensive therapy had a 60% reduction in risk of hypoglycemia, Dr. Greenbaum said.

To prevent long-term complications and to stabilize pancreatic function, the concept of using immunotherapy is being explored. This premise was first tested in the 1980s with cyclosporine, and although the trial showed some benefit to patients, toxicity was a problem. The intention now is to find a tolerable drug or drugs that can be used for a short course that will "reset" the immune system so it stops attacking the pancreas, she said. Among the agents being evaluated are the newer immunosuppressants mycophenolate mofetil, thymoglobulin, daclizumab, and rituximab.

"We can cure diabetes in mice, but we can't yet cure it in people," Dr. Greenbaum said. "When I think about what cure is going to look like, multiple avenues are going to be needed." For patients who are genetically at risk, there may be dietary interventions, and for those who go on to develop autoimmunity, antigen-specific therapies may block β-cell destruction. In those who lose β-cell function, achieving a cure may involve tolerance induction, intermittent immunotherapy, and the use of β-cell growth factors and insulin sensitizers, she predicted.

Dr. Greenbaum concluded with a plea for clinicians to refer patients and relatives willing to participate in these trials. Information is available at www.diabetestrialnet.org and at 800-425-8361. ■