Fitness Can Reduce Mortality in Diabetes

BY BRUCE JANCIN
Denver Bureau

MUNICH — Middle-aged men with type 2 diabetes can reduce their long-term mortality risk by roughly 14% for each 1-MET increase they achieve in peak exercise capacity through improved physical fitness, according to a large epidemiologic study.

The findings provide a persuasive new impetus to advocate moderate-intensity physical activity in all patients with diabetes, regardless of their body mass index (BMI), Dr. Peter Kokkinos said at the annual congress of the European Society of Cardiology.

The survival benefit varies according to BMI category. A normal-weight man (with a BMI below 25 kg/m^2) reduces his adjusted mortality risk by 11% for every 1-MET gain in fitness, an overweight individual lowers his risk by 16%, and an obese man reduces his risk by 17%, Dr. Kokkinos reported.

A dose-response relationship between peak exercise capacity and survival was observed.

For example, a moderately fit, normal-weight diabetic man, defined in this study as one capable of achieving 5.1-8 METs on a treadmill exercise test using a Bruce protocol, had an adjusted 41% lower mortality risk than a normal-weight man with a low level of fitness.

A highly fit, normal-weight man who achieved more than 8 METs reduced his risk by 60%, explained Dr. Kokkinos of the Veterans Affairs Medical Center, Washington.

He reported on 2,690 men with type 2 diabetes who underwent an exercise stress test at the VA centers in Washington or Palo Alto, Calif., where the policy for 2 decades has been to routinely administer a stress test to all diabetic patients. Roughly 60% of patients were African American.

The purpose of the study was to learn whether the benefits of physical activity attenuate the well-documented deleterious effects of obesity in a diabetic population. This indeed proved to be the case.

During an average 7.2 years of follow-up after the stress test, there were 762 deaths: 172 among the 406 normal-weight patients, 334 among the 1,088 overweight men, and 256 among the 1,196 obese men.

Exercise capacity at baseline proved to the strongest predictor of mortality in a multivariate analysis that included the standard cardiovascular risk factors, age, and medications.

An overweight individual who scored in the moderately fit range on his exercise stress test had a subsequent adjusted 42% lower mortality risk than an overweight man with a low level of fitness, while a highly fit one had a most impressive 65% reduction in risk, Dr. Kokkinos continued.

For every 1-MET gain in fitness, an overweight individual lowers his adjusted mortality risk by 16%.

DR. KOKKINOS

The survival benefit of exercise capacity in obese type 2 diabetic men did not show the same strong, graded, dose-response relationship that it did in the overweight and normal-weight men.

Moderately fit obese subjects had a 52% lower mortality than those who couldn't achieve more than 5 METs.

However, then there was a leveling off or perhaps even a suggestion of a J-shaped curve, as highly fit obese men had only a 44% lower mortality.

Audience members commented that this wasn't an intervention study, and Dr. Kokkinos hadn't actually shown that patients with type 2 diabetes who increase their fitness level reduce their mortality.

He replied that that has already been shown to be the case in studies by him and others. What's new here is the size of the study and the demonstrated benefit across the full range of BMIs, Dr. Kokkinos added.

"If anything, I think this study actually underestimates the effects of exercise on mortality. The trend is that as we age, we are less likely to exercise. If you are fit today, you are likely not to be as fit 10 years later—yet that protection at time zero is carried forward," Dr. Kokkinos remarked.

One audience member, Dr. John H. Horgan of Beaumont Hospital, Dublin, called the VA study results "very impressive," adding, "I think we need to encourage our diabetic patients to enter exercise programs and be trained." ■

THE EFFECTIVE PHYSICIAN

Glycemia Management in Type 2 Diabetes

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Last month, a consensus panel representing the American Diabetes Association and European Association for the Study of Diabetes published revised recommendations for management of hyperglycemia in patients with type 2 diabetes (INTERNAL MEDICINE NEWS, Jan. 15, 2009, p. 1), based on data published since similar recommendations were first published in 2006 and updated in 2008 to address safety issues associated with thiazolidinediones.

Conclusions

Control of blood sugar, to levels as close as possible to normal, has been shown in multiple studies of patients with type 1 diabetes to reduce the microvascular complications of retinopathy, neuropathy, and nephropathy. Studies of intensive treatment of type 2 diabetes patients have, likewise, shown reductions in microvascular complications. Unfortunately, trials to date have not shown a reduction in cardiovascular disease with intensive glycemic control in patients with type 2 diabetes.

Many drugs are available for treatment of glycemia in type 2 diabetes, but not many studies have explored the differential effectiveness of individual agents or combinations of agents. Thus, comparisons and recommendations are made based on the relative efficacy, costs, and side effects of the drugs and the recommendations of the consensus panel.

Implementation

The American Diabetes Association recommends a hemoglobin A_{1c} level under 7%, and the International Diabetes Federation has established a goal of less than 6.5%. The consensus of the guideline group is that action to initiate or change treatment should be undertaken for any patient with an HbA_{1c} above 7%.

Patient education is important in diabetes management and should address diet, medication adjustment, glucose targets and how to reach them, the management of hypoglycemia, and self-monitoring.

Lifestyle interventions to decrease weight and increase activity levels should be included in the management plan for nearly all patients, and should be the first step in the management of all with new-onset type 2 diabetes. Unfortunately, these efforts alone are rarely successful in the long-term maintenance of glycemic control to target levels.

In conjunction with lifestyle changes, metformin therapy should be begun when type 2 diabetes is diagnosed unless contraindications exist. The dosage should be increased stepwise to a maximal effective dose over 1-2 months, as tolerated. The addition of other glucose-lowering drugs should be considered if symptomatic hyperglycemia persists.

If diet and exercise plus metformin does not allow the patient to achieve glucose goals within 3 months, step 2 treatment, including the addition of a second medication, is suggested. If the HbA_{1c} remains over 8.5%, or if extreme hyperglycemia is present even with metformin and lifestyle changes, the consensus group recommends adding an intermediate- or long-acting insulin (basal insulin). If the HbA_{1c} is lower than 8.5% but still above 7%, either insulin or a sulfonylurea may be added.

If the combination of lifestyle, metformin, and a sulfonylurea (or basal insulin) is ineffective in reaching glycemic targets, step 3 treatment, consisting of multiple injections of a short- or rapid-acting insulin with meals, is recommended. Discontinuation of the sulfonylurea and/or other insulin secretagogues is recommended with intensive insulin treatment. If the HbA_{1c} is near target levels (below 8%), adding a third oral agent instead of insulin may be considered but is not preferred, as it is usually more costly for the patient and is no more effective.

Treatment with alternative second-tier regimens may be warranted in selected patients, such as those who are at particular risk of hypoglycemia. If these alternative second-tier regimens are not tolerated or are ineffective, a sulfonylurea or basal insulin should be substituted.

Patients who have severely uncontrolled diabetes—including those with an HbA_{1c} higher than 10%, fasting glucose above 250 mg/dL, random glucose greater than 300 mg/dL, symptomatic diabetes, and/or diabetes with ketonuria—should be treated initially with insulin therapy in addition to lifestyle interventions. Rapid titration of insulin is most likely to achieve control quickly. Some of these patients may ultimately be able to control their diabetes with oral regimens, while others may be found to have unrecognized type 1 diabetes.

Amylin agonists, α-glucosidase inhibitors, glinides, and dipeptidyl peptidase-4–inhibiting drugs are not recommended for initial type 2 diabetes management in most patients, as they do not lower glucose better than the recommended agents, have limited data supporting their use, and/or carry excessive cost.

The consensus group recommends against the use of rosiglitazone because of data suggesting greater cardiovascular risks and increased risk of bone fractures in women.

Control of other risk factors for microvascular and cardiovascular complications of diabetes, such as hypertension and dyslipidemia, is recommended in accord with other published guidelines.

Reference

Nathan DM, et al. Medical management of hyperglycemia in type 2 diabetes: A consensus algorithm for the initiation and adjustment of therapy. Diabetes Care 2009;32:193-203.

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