

Consider Using Statin Therapy for Most Diabetics

BY SHARON WORCESTER

Southeast Bureau

Statin therapy is a safe and cost-effective option for reducing the risk of major vascular events in patients with diabetes and should be considered for almost all diabetics, findings from a recent meta-analysis show.

In all, 14 randomized trials of statin therapy involving 18,686 individuals with diabetes and 17,220 without diabetes were included in the meta-analysis, which was conducted by the Cholesterol Treatment Trialists' Collaborators.

During more than 4 years of follow-up, 3,247 major vascular events, which were defined as the composite outcome of myocardial infarction, coronary death, stroke, or coronary revascularization, occurred in the trial participants.

Statin therapy in the diabetic patients was associated with a 9% proportional reduction in all-cause mortality per mmol/L reduction in LDL cholesterol, and was associated with a statistically similar 13% reduction in all-cause mortality in those without diabetes. This finding was due mainly to a significant reduction in vascular mortality (rate ratio of 0.87) in those with diabetes; there was no apparent effect on nonvascular mortality (rate ratio of 0.97) in this population, the investigators reported (*Lancet* 2008;371:117-25).

Furthermore, both those with and without diabetes had a 21% proportional reduction in major vascular events per mmol/L reduction in LDL cholesterol. In the diabetic patients, the effects of statin therapy were similar regardless of whether they had a history of vascular disease and regardless of other baseline characteristics, including type of diabetes, age, sex, treated hypertension, body mass index, systolic or diastolic blood pressure,

smoking status, and estimated glomerular filtration rate.

In addition, reductions in major coronary events, coronary revascularization, and stroke were seen in those with diabetes (rate ratios of 0.78, 0.75, and 0.79, respectively), and the effect of statins on each of these outcomes was similar in diabetic and nondiabetic patients.

At 5 years, 42 fewer diabetic patients per 1,000 treated with statins had major vascular events, the collaborators found.

Statin therapy given in moderate doses over the 5 years was not associated with an increased risk of cancer or nonvascular causes of death in the study participants.

The findings, which "show convincingly" the benefits of statin therapy for reducing the risk of major vascular events in a wide range of individuals with and without diabetes, indicate that "the cost effectiveness of treatment for a person at a specific absolute level of risk of major vascular events, irrespective of whether diabetes is present, will be much the same," the investigators wrote.

In a previous meta-analysis of 14 statin trials involving more than 90,000 patients, the researchers showed that a generic statin regimen producing a mean reduction of about 1 mmol/L was cost effective in those with as low as 1% risk of a major vascular event—suggesting that statin treatment would be cost effective in almost all diabetic patients, they noted.

Furthermore, "standard doses of a statin reduce LDL cholesterol by about 40%, which translates into a reduction of at least 1.5 mmol/L for many people with diabetes, so our results suggest that such an absolute reduction in LDL cholesterol would prevent about a third

of patients from having a major vascular event," they wrote. They concluded that statin therapy is likely to be inappropriate only in those in whom there are safety concerns (such as in pregnant women) or when there is a low short-term absolute risk of vascular disease (such as in children with type 1 diabetes).

Because the benefit seen with statin therapy is related mainly to the absolute reduction in LDL cholesterol achieved, it may be necessary to revise guidelines on statin therapy to ensure that a regimen sufficient to reduce LDL cholesterol substantially is considered for those with diabetes, they added.

In a commentary on the findings, Dr. Bernard M.Y. Cheung of the University of Birmingham, England, calls the collaborators' findings reassuring, but notes that statins "are not a panacea, and patients on statins are liable to other causes of morbidity and mortality" (*Lancet* 2008;321:94-5).

Treatment decisions should be based on the reduction in absolute risk—or the number needed to treat, rather than on relative risk reduction, he states, noting that in those with a high absolute cardiovascular risk, even a modest reduction in relative risk will provide meaningful clinical benefit. But he adds that other factors, such as life expectancy, concomitant disease, and quality of life also should be taken into consideration, and he stresses the continued importance of lifestyle.

"Apart from drug treatment, one must not forget the importance of lifestyle changes, such as cessation of smoking, healthy diet, and regular exercise," Dr. Cheung wrote. ■

Statin 'are not a panacea, and patients on statins are liable to other causes of morbidity and mortality ... one must not forget the importance of lifestyle changes such as [diet and exercise].'

New Diabetes Often Precedes a Diagnosis for Pancreatic Cancer

BY HEIDI SPLETE

Senior Writer

New cases of diabetes were significantly more common among pancreatic cancer patients before their cancer diagnoses, compared with controls, according to data from 736 pancreatic cancer patients and 1,875 controls.

Although previous studies have shown a link between existing diabetes and pancreatic cancer, the temporal relationship between the two diseases—and whether this relationship might be used to predict cancer—is not well understood, wrote Dr. Suresh T. Chari and colleagues at the Mayo Clinic in Rochester, Minn.

To determine the prevalence of new-onset diabetes in pancreatic cancer patients and the temporal association between these conditions, the researchers reviewed records of pancreatic cancer patients and control patients seen at the Mayo Clinic between January 15, 1981, and July 9, 2004.

They assigned two matched controls to each cancer case. The mean age of both patients and controls was 69 years, and approximately 50% of the subjects in each group were men.

A subject was considered to have diabetes if he or she had a fasting blood glucose level greater than 126 mg/dL or was taking diabetes medication. The proportion of cases and controls with diabetes was compared in each 12-month interval, starting with 60 months prior to a cancer diagnosis for cancer patients (*Gastroenterology* 2008;134:95-101).

Overall, significantly more pancreatic cancer patients met the criteria for diabetes, compared with controls, any time during the 60-month period before pancreatic cancer diagnosis (40% vs. 19%). But the proportions of individuals with diabetes were not significantly different between

the cancer group and the control group during the 12-month intervals from 60 months to 48 months and from 48 months to 36 months prior to cancer diagnosis.

In contrast, starting with 36 months before a cancer diagnosis, the prevalence of diabetes in the pancreatic cancer patients rose steadily for each 12-month interval, while the prevalence of diabetes in the controls remained relatively stable throughout the study period. New-onset diabetes was defined as diabetes with onset at 24 months or less prior to a cancer diagnosis.

Diabetes was more likely to be new onset in patients with pancreatic cancer than in controls (52.3% compared with 23.6%, respectively) among the subjects with diabetes for whom diabetes duration was known; this difference was highly significant.

"The very high prevalence of diabetes in pancreatic cancer and its close temporal association with the diagnosis of cancer provide strong epidemiologic evidence to support the notion that pancreatic cancer causes diabetes mellitus," the researchers wrote.

The findings support data from small clinical studies in which the removal of tumors from pancreatic cancer patients with diabetes has improved their glucose tolerance and reversed their metabolic defects.

But prospective studies are needed to show the benefits of screening older adults with new-onset diabetes for pancreatic cancer, and such screening would be helpful only if a type of new-onset diabetes that is associated with pancreatic cancer could be distinguished from type 2 diabetes, perhaps with the use of a biomarker test, the researchers noted.

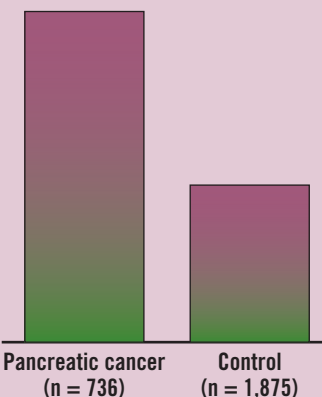
In an editorial that accompanied the article, Dr. Niels Teich, of the University of Leipzig in Germany wrote that there is a lack of practical criteria that could be used to rule out pancreatic cancer in new-onset diabetes patients (*Gastroenterology* 2008;134:344-5).

The study findings invite more research to determine whether new-onset diabetes in pancreatic cancer patients is different from new-onset type 2 diabetes mellitus in general, and whether new-onset diabetes could be an early sign of this cancer in otherwise asymptomatic persons, he noted.

"The data available today clearly suggest that diabetes mellitus can be both a longstanding cause of pancreatic cancer, and, as shown now, an early manifestation of the disease," Dr. Teich said. ■

The prevalence of diabetes in pancreatic cancer and its close temporal link with the diagnosis, suggests that pancreatic cancer might cause diabetes mellitus.

Proportion of Cases and Controls With Diabetes



Note: Based on patients (mean age 69 years) with diabetes during 60 months prior to cancer diagnosis.
Source: *Gastroenterology*