Diabetes Screening May Lower CV Event Risk

BY MIRIAM E. TUCKER

FROM THE ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

STOCKHOLM – Screening for prevalent type 2 diabetes in primary care identified people at high modifiable cardiovascular risk, but subsequent intensive multifactorial treatment improved cardiovascular outcomes by only an insignificant 17% over routine care in a large 5-year randomized study.

Nevertheless, "when compared to no screening and no diabetes treatment, screening and either early routine diabetes care or intensive multifactorial treatment are likely to reduce cardiovascular morbidity and mortality by nearly half," Dr. William H. Herman, who was not involved in the research, commented at the annual meeting of the European Association for the Study of Diabetes.

Indeed, the difference between the intensive intervention and routine treatment groups is not the main point of the ADDITION study, said Dr. Herman, professor of medicine at the University of Michigan, Ann Arbor, who served as the independent commentator on the study.

"The reality is that once people were labeled with diabetes they achieved much better risk factor control. … During the time this community-based study was being conducted, there were major national and international initiatives to improve diabetes care, and they clearly had an impact on blood pressure, cholesterol, smoking, and glycemia," Dr. Herman said in an interview. "It's the combination of screening, diagnosis, and treatment that seemed to have an impact."

Miriam E. Tucker/Elsevier Global Medical News

Dr. William H. Herman (left) and Dr. Simon Griffin discussed the treatment-phase results of the European ADDITION study.

As part of the Anglo-Danish-Dutch Study of Intensive Treatment in People With Screen Detected Diabetes in Primary Care (ADDITION), 76,308 people aged 40-69 years without known diabetes were screened in Denmark, Great Britain, and the Netherlands.

The screening results showed that individuals with screening-detected type 2 diabetes and included in the ADDITION study had an elevated and possibly modifiable risk of coronary heart disease (CHD). Specifically, the median estimated 10-year risk of CHD was 11% in women and 21% in men (Diabetologia 2008;51:1127-34).

Dr. Simon Griffin of the Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, England, presented the 5-year ADDITION outcome results for 1,379 randomized to routine care and 1,678 who received intensive multifactorial intervention. At baseline, patients were aged 60 years and had a mean body mass index of 32 kg/m^2. Before diabetes diagnosis, less than half – about 40% – were on antihypertensive medication and only 15% were on statins, despite having a mean blood pressure of 150/86 mm Hg and mean LDL cholesterol levels of 131 mg/dL.

The intensive intervention included lifestyle education (dietary modification, increased physical activity, and smoking cessation) and intensive treatment of blood glucose, blood pressure and lipids, and prophylactic aspirin with or without motivational interviewing.

Over the 5-year study period, treatment with antihypertensive medication, statins, and aspirin increased dramatically in both groups, although to a slightly greater degree in the intensive treatment group. At 5 years, statin use was 68% for the routine care group and 78% for intensive treatment, daily aspirin was used by 40% and 69%, and glucose-lowering medication by 54% and 64%, respectively, Dr. Griffin reported.

The proportion of patients achieving targets for blood pressure, cholesterol, and glycemia – targets that changed over the study period based on national guidelines – increased in both groups but was slightly greater with intensive treatment.

The primary outcome composite of cardiovascular mortality, nonfatal MI, nonfatal stroke, revascularization as a first event, and amputation did not differ significantly between the routine and intensive treatment groups at 8.5% vs. 7.2%, with a hazard ratio of 0.83.

All-cause mortality, a secondary outcome, also did not differ significantly, with a hazard ratio of 0.91, Dr. Griffin said.

Dr. Griffin noted that mortality in both groups was low, and even in the routine care group it was lower than that of the general diabetes population in Denmark and only slightly higher than the age-matched Danish general population.

The ADDITION study was funded by unrestricted grants from Novo Nordisk A/S (main industry sponsor), ASTRA Denmark, Pfizer Danmark, Glaxo-SmithKline, Pharma Denmark, SERVIER Danmark, A/S HemoCue Danmark, and A/S Novo Nordisk Scandinavia AB. Research funds also were contributed by the Danish Council for Strategic Research, Danish Research Foundation for General Practice, Danish Centre for Evaluation and Health Technology Assessment, the Aarhus University Research Foundation, Novo Nordisk Foundation, the National Board of Health, the Danish Medical Research Council, the Danish Diabetes Association, the A.P. Møller Foundation for the Advancement of Medical Science, the Bernhard and Marie Kleins Trust, the Centre for Innovation in Nursing Education, the County of Aarhus, and the Danish Council of Nursing.

Dr. Griffin said he has received lecture fees from GSK, Unilever, Eli Lilly, and MSD. Dr. Herman stated that he had nothing to disclose. ■

Meta-Analysis Finds No Evidence of Statin-Cancer Link

BY MITCHEL L. ZOLER

FROM THE ANNUAL CONGRESS OF THE EUROPEAN SOCIETY OF CARDIOLOGY

VITALS

Major Finding: No increased risk for cancer or cancer death occurred in patients who were treated with statins, compared with those treated by placebo or lower statin dosages.

Data Source: Meta-analysis of 26 randomized, controlled trials of statins that each enrolled at least 1,000 patients who were followed for at least 2 years.

Disclosures: Dr. Emberson said he had no disclosures.

STOCKHOLM – Data from 170,000 patients in 26 randomized trials may finally dismiss the idea that low cholesterol levels during statin therapy play a role in causing cancer.

"There is no evidence that cancer risk is increased when very low cholesterol concentrations are achieved with high-dose statins," Jonathan Emberson, Ph.D., said at the congress.

"There is no suggestion of an emergence of any hazard with longer duration of treatment, at least within a period of about 5 years. There is no evidence that low cholesterol increases cancer risk at any site or in any group of individuals. I think the question about statins has now probably been answered as well as it can be from the randomized trials," said Dr. Emberson, a statistician in the clinical trial service unit at the University of Oxford (England).

Follow-up for the patients in the trials ran 5-6 years, producing "extremely reassuring" results for long-term safety, he said in an interview.

Concern that very low serum cholesterol levels – hence statin therapy – might boost cancer incidence has not had a big impact on statin use. But every now and then over the past 20 years, "a trial threw out a random result that raised a new hypothesis," he said. For example, in 1996, the CARE (Cholesterol and Recurrent Events) trial, which compared 40-mg pravastatin with placebo for secondary prevention in more than 4,000 patients followed for an average of 5 years, showed 12 cases of breast cancer during follow-up in the pravastatin arm, compared with one case in the placebo arm, a statistically significant difference (N. Engl. J. Med. 1996;335:1001-9).

"Random things happen all the time," Dr. Emberson noted. The CARE results showed "a significant excess, but what's important is, it wasn't supported by data from all the other statin trials. Occasionally, trials throw up hypotheses that can be tested. We attempted to systematically test all of those hypotheses using all of the data."

The 26 statin trials in the meta-analysis included all those that were published through the end of 2009 with at least 1,000 patients followed for at least 2 years. In all, 21 trials compared a statin with placebo, and 5 compared a low statin dose with a higher statin dose. The 170,000 patients in all 26 trials developed 10,000 cases of cancer during follow-up, with more than 3,500 cancer deaths.

Statin treatment gave no hint of an influence on cancer rates in all 26 studies together, nor separately in the 21 studies in which it was compared with placebo, nor in the 5 in which high dose was compared with low dose. The results showed no sign of cancer increase when treated patients started with low serum levels of LDL cholesterol. There was no cancer impact with longer duration of statin use, no impact for various, specific cancer types, and no difference by age or by sex. The analysis showed no suggestion of an increased risk in the elderly. And no increased risk appeared for gastrointestinal cancers, another cancer type that gave a signal for higher risk in one of the trials.

"The value of our analysis is that we were able to systematically test all of the hypotheses that had been raised in a much larger data set than has previously been possible, and the results are very reassuring for the many millions of patients who take statins, at least for 5-6 years' duration." In addition, "results from studies that followed patients for longer than 6 years have not suggested any cancer concerns," Dr. Emberson said. ■