Statins Beneficial in Diabetes Patients With ACS

The data, however, highlight the need for additional strategies in this high-risk group of patients.

REVIEWED BY CHRISTOPHER P. CANNON, MD, AND SHAHEEDA AHMED, MD

Results from a subgroup analysis of the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT) TIMI 22 trial show significant reductions in acute coronary events among acute coronary syndrome (ACS) patients with diabetes who are treated with intensive statin therapy.

The data, recently published in the *European Heart Journal*, reveal that intensive lipid lowering among this patient population is indeed beneficial. Christopher P. Cannon, MD, from the cardiovascular division at Brigham and Women's Hospital and Harvard Medical School, and colleagues, wrote that the impact of intensive lipid lowering with statins in ACS patients with diabetes has not been well characterized.

STANDARD VERSUS INTENSIVE LIPID THERAPY

The trial tested standard therapy with pravastatin 40 mg (Pravachol; Bristol-Myers Squibb, New York, NY) versus intensive statin therapy with atorvastatin (Lipitor; Pfizer, New York, NY) among patients treated early in the post-ACS period, according to the report. Dr. Cannon and colleagues compared outcomes between patients with diabetes (n=978) and those without (n=3,184). Patients with diabetes were identified by history, fasting plasma glucose ≥126 mg/dL or Hb1Ac >7%.

The investigators found that the rate of acute coronary events, including death, myocardial infarction (MI) and unstable angina requiring rehospitalization among patients on intensive versus standard therapy was much higher in patients with diabetes, (21.1% vs 26.6%, HR=0.75, *P*=.03) than in those without (14.0% vs 18.0%, HR=0.76, *P*=.002). Although the relative risk reduction with intensive therapy was nearly the same in both groups, the absolute risk reduction was larger in patients with diabetes (5.5%) than in those without diabetes (4.0%).

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Despite intensive lipid-lowering intervention, however, the investigators noted that the majority of patients with diabetes did not reach the dual goal of LDL cholesterol <70 mg/dL and high-sensitivity C-reactive protein <2 mg/L.

Mean LDL was reduced by 44% from baseline among patients with diabetes assigned to atorvastatin versus an 18% reduction among pravastatin-assigned patients.

CLINICAL OUTCOMES IMPROVED

"Improved clinical outcomes were seen in patients with and without diabetes, but since [patients with diabetes] were at higher risk, more acute cardiac events (death, MI or unstable angina) were prevented with intensive therapy in those with diabetes (55 vs 40 per 1,000 patients treated without diabetes)," Dr. Cannon wrote.

Current clinical practice guidelines do not agree on target LDL numbers in patients with diabetes, they said. While the American College of Physicians supports statin therapy among patients with type 2 diabetes, it

does not specify an LDL goal. The American Diabetes Association suggests a target LDL of <100 mg/dL, and the National Cholesterol Education Program Adult Treatment Panel III Guidelines advocates an LDL of <100 mg/dL with the option to treat to <70 mg/dL in patients with diabetes.

"In our analysis, the LDL in both intensive and standard arms at 'baseline' was already in this range (<100 mg/dL), yet further LDL led to further reduction in cardiovascular events," Dr. Cannon and colleagues said. "In view of the very high event rate in patients with diabetes who did not achieve the dual goal even on intensive therapy, additional lifestyle (or drug) strategies are warranted to attain this goal." ■

Christopher P. Cannon, MD, is in the cardiovascular division at Brigham and Women's Hospital and the Harvard Medical School. Dr. Cannon received research grant support from Accumetrics, Bristol-Myers Squibb, Glaxo SmithKline, Merck, Pfizer, Sanofi-Aventis and Schering Plough. He may be reached at cpcannon@partners.org.

Ahmed S, Cannon CP, Murphy SA, Braunwald E. Acute coronary syndromes and diabetes: is intensive lipid lowering beneficial? Results of the PROVE IT-TIMI 22 trial. *Eur Heart J.* 2006;27:2323-2329.

STATINS REDUCE RISK OF MI, STROKE IN THOSE WITHOUT HEART DISEASE

Researchers from Brigham and Women's Hospital have found that among individuals without cardiovascular disease (CVD), taking statins regularly may reduce the risk of major cardiovascular events such as myocardial infarction (MI) and stroke, but may not reduce the risk for coronary heart disease or overall death. The findings were from a meta-analysis of previously published studies and were reported in the *Archives of Internal Medicine.*

Statins have been shown to reduce death and other negative outcomes associated with heart and cerebrovascular disease among those who already have these conditions, according to background information in the article. It is less clear whether these medications benefit those without CVD, according to a news release. Current national treatment guidelines recommend the use of statins in these patients based on their cardiovascular risk profile and LDL cholesterol level. For patients without CVD and normal LDL, statins are recommended only among those with diabetes two or more other cardiac risk factors that raise their 10-year risk of MI or other heart event to at least 10%.

Niteesh Choudhry, MD, PhD, and colleagues analyzed the results of seven previously published clinical trials that assessed the benefits of statins in a total of 42,848 patients, 90% of whom had no history of CVD. In each study, patients were randomized to statins or another form of care and were followed for at least 1 year, at least 100 major cardiovascular events occurred and ≥80% of the participants did not have CVD. Dr. Choudhry is in the division of pharmacoepidemiology and pharmacoeconomics at Brigham and Women's Hospital and is also an instructor in medicine at Harvard Medical School.

In total, 21,409 patients in the trials took statins and 21,439 were assigned to placebo. The average follow-up period for the studies ranged from 3.2 to 5.2 years; average age of the participants ranged from 55.1 to 75.4 years; and the proportion of men included ranged from 42% to 100%. In patients on statin therapy, there were 924 major coronary events such as MI compared with 1,219 among those in control groups — a 29.2% reduction in risk. Major cerebrovascular events, including stroke, occurred in 440 patients taking statins and 517 controls, a 14.4% lower risk.

Statin treatment was also associated with a 31.7% reduction in risk for nonfatal MI and a 33.8% reduction in the number of revascularization procedures.There were no statistically significant differences between the statin and control groups in the rates of patients who died from CVD or from all causes.

Assuming that individuals not taking statins have a 5.7% chance of having a major heart event over a 4.3-year period, statins can reduce that risk to 4%, the authors wrote. "Therefore, 60 patients would need to be treated for an average of 4.3 years to prevent one major coronary event." Similarly, 268 patients would need to be treated to prevent one stroke or other major cerebrovascular event; 61 to prevent one nonfatal MI; and 93 to prevent one revascularization procedure.

Statins are expensive and other therapies also may work to reduce risk, the authors concluded.

"Therefore, even though universal lipid-lowering therapy appears attractive, especially in an intermediate-risk primary prevention population, further studies are needed to clarify the cost-effectiveness of therapy in this group." ■

Thavendiranathan P, Bagai A, Brookhart A, Choudhry NK. Primary prevention of cardiovascular diseases with statin therapy: A meta-analysis of randomized controlled trials. *Arch Intern Med.* 2006;166:2307-2313.