Drug-Eluting Stents: Safe, Effective in Acute MI?

Studies compare patient outcomes with sirolimus- and paclitaxel-eluting models vs. bare-metal stents.

BY MITCHEL L. ZOLER
Philadelphia Bureau

ATLANTA — Drug-eluting coronary stents were at least as safe and effective as bare-metal stents for treating patients with an acute myocardial infarction in a pair of studies that each involved 600-700 patients.

One study compared the outcomes after 1 year in patients treated with sirolimus-eluting stents or bare-metal stents; the second report involved a comparison of paclitaxel-eluting stents with bare-metal stents after 1 year. The results were reported at the annual meeting of the American College of Cardiology.

Although the results from both trials seemed to show that drug-eluting stents were safe when implanted in patients with an acute MI (AMI)—and in the case of sirolimus-eluting stents also showed a reduced rate in the need for target vessel revascularization during follow-up—the reaction of experts to the results highlighted the degree of uncertainty about the safety of drug-eluting stents in this clinical setting. At least some experts thought that the new results involved too few patients to provide definitive proof.

"The data for drug-eluting stents in acute MI are very mixed. Some study results suggest safety. Others suggest possible harm," commented Dr. Gregg W. Stone, of the division of cardiology at Columbia University, New York. "I think we need results from a large, randomized, controlled study to understand the safety and efficacy of drug-eluting stents in the prothrombotic environment of acute MI. Such a trial is now being done, the HORIZONS [Harmonizing Outcomes with Revascularization and Stents] AMI study, which will enroll 3,400 patients."

The results from that study are expected next year, added Dr. Stone, who is the principal investigator for the HORIZONS AMI trial.

But other experts contend that they are comfortable using drug-eluting stents now for the primary treatment of acute MI. "I've used drug-eluting stents for primary PCI [percutaneous coronary intervention] for at least the past 2 years," said Dr. Eric R. Bates, a professor of medicine at the University of Michigan, Ann Arbor.

Speaking in a separate talk at the meeting, Dr. Bates acknowledged that results from the HORIZONS AMI trial will help settle the issue. But, he added, "for those who wish to use drug-eluting stents now, you can find some evidence to support it. For those who want to continue to use bare-metal stents, it's fair to do that until more evidence is forthcoming."

So far, there is no evidence that the risk of thrombosis is increased when drug-eluting stents are used during primary PCI. It is also possible, but not yet proved, that the extra cost for drug-eluting stents is balanced by a reduced rate of rehospitalization, said Dr. Bates. But the ability of drug-eluting stents to reduce the need for target vessel revascularization, compared with that of bare-metal stents, may be blunted in this setting because restenosis may not be that big a problem when bare-metal stents are used for primary PCI. This may mean that the best approach is selected use of drug-eluting stents, such as in narrow coronary arteries or for long lesions.

"I think we have the data to say now that it's safe to implant drug-eluting stents in patients with acute MI," commented Dr. John M. Hodgson, chief of academic cardiology at St. Joseph's Hospital and Medical Center, Phoenix. "We don't need to wait for the HORIZONS AMI results. But if a physician is not sure that the patient is willing to take clopidogrel for several months after PCI, it's acceptable to implant a bare-metal stent in that patient."

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DR. STONE

The study comparing sirolimus-eluting and bare-metal stents was done at 48 centers in Europe. The TYPHOON (Trial to Assess the Use of the Cypher Stent in Acute Myocardial Infarction Treated with Angioplasty) study was sponsored by Cordis Corp., which markets the sirolimus-eluting stent (Cypher). Patients entered the study if they first presented within 12 hours from the onset of symptoms of acute MI that required primary PCI in a native coronary artery. The study's primary end point was the rate of target vessel failure by 1 year after treatment—a composite of all target vessel–related death, recurrent MI, or need for target vessel revascularization.

The rate for this end point was 7.3% in 355 patients treated with a sirolimus-eluting stent and 14.3% in 357 patients treated with a bare-metal stent, a statistically significant difference, reported Dr. Christian Spaulding, of the Assistance Publique-Hôpitaux de Paris. This difference was driven primarily by a difference in the rate of need for revascularization, which was 5.6% in patients treated with a sirolimus-eluting stent and 13.4% in those who got a bare-metal stent.

Treatment with a sirolimus-eluting stent appeared safe, with a 3.4% rate of stent thrombosis throughout all 12 months of follow-up, and a 0.3% rate of stent thrombosis after the first 30 days following treatment. In the bare-metal stent group, the overall rate of stent thrombosis was 3.6%, which included a 0.6% rate after 30 days. In the trial protocol, patients were directed to take aspirin and clopidogrel daily for at least 6 months after stent placement, Dr. Spaulding said at the meeting.

The study of the paclitaxel-eluting stent (Taxus) was done at two hospitals in the Netherlands. The PASSION (Randomized Comparison of Paclitaxel-Eluting Stent Versus Conventional Stent in ST-Segment Elevation Myocardial Infarction) study did not have any industry support.

During 2003-2004, researchers enrolled patients with symptoms of acute MI who had a culprit lesion in a native coronary artery. The primary end point was the combined rate of cardiac death, recurrent MI, or need for target lesion revascularization during the first year of follow-up.

In the 309 patients receiving a paclitaxel-eluting stent, the incidence of the end point was 8.7%, compared with 12.6% in the 310 patients receiving a bare-metal stent. Although this was a 32% risk reduction associated with the paclitaxel-eluting stent, the difference was not statistically significant, reported Dr. Maurits T. Dirksen, a cardiologist at Onze Lieve Vrouwe Gasthuis Hospital, Amsterdam. ■

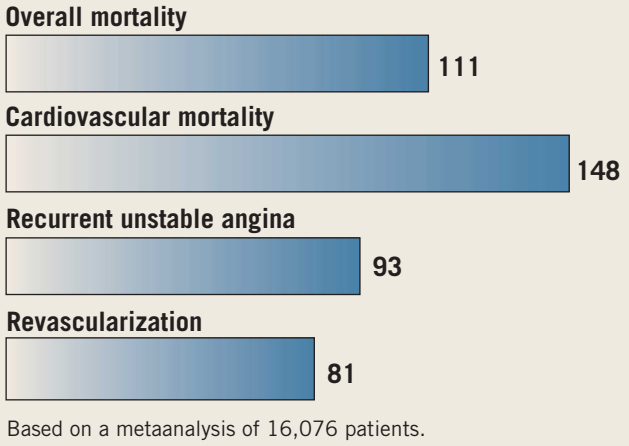
Early, Aggressive Use of Statins Lowers Post-ACS Mortality

BY BRUCE JANCIN
Denver Bureau

CHICAGO — Initiating high-dose statin therapy during hospitalization for an acute coronary syndrome brings significant survival benefit, Dr. Anthony A. Bavry said at the annual meeting of the Society for Cardiovascular Angiography and Interventions.

His metaanalysis of nine randomized clinical trials totaling 16,076 ACS patients showed that in-hospital initiation of high-dose statin therapy saved one life for every 111 patients treated for 15 months, which he termed a favorable number-needed-to-treat ratio. (See box.)

Number of ACS Patients Needed to Be Treated With Early High-Dose Statins to Prevent One Adverse Outcome



Note: Based on a metaanalysis of 16,076 patients.
Source: Dr. Bavry

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In addition to the observed 22% relative risk reduction in all-cause mortality—the primary end point in the metaanalysis—early, aggressive statin therapy also resulted in highly significant reductions of 25% for cardiovascular mortality, 16% for subsequent unstable angina, and 9% for surgical or percutaneous coronary revascularization procedures, said Dr. Bavry of the Cleveland Clinic Foundation.

In addition, there were favorable, albeit statistically nonsignificant, trends for fewer strokes, MIs, and cardiac arrests in the aggressive statin treatment group.

The metaanalysis was restricted to studies in which ACS patients were randomized to in-hospital initiation of maximal- or near-maximal–dose statin therapy or to a more conservative approach involving lower-dose statins or placebo.

If anything, the relative risk reductions with early, aggressive statin treatment found in the metaanalysis underestimate the true benefits in ACS patients, according to Dr. Bavry. That's because one of the largest trials included in the metaanalysis—the PROVE-IT (Pravastatin or Atorvastatin Evaluation and Infection Therapy) trial—featured 40 mg/day of pravastatin in the control arm, which would have been considered aggressive therapy in several of the other studies.

PROVE-IT was one of three atorvastatin trials totaling 7,200 ACS patients included in the metaanalysis. Trials of aggressive simvastatin and pravastatin were also featured. No significant differences in the benefits of aggressive statin therapy were noted based upon the specific statin used, he said.

At first glance, Dr. Bavry's metaanalysis would seem to conflict with the findings of a recently published metaanalysis led by investigators at the Basel (Switzerland) Institute for Clinical Epidemiology (JAMA 2006;295:2046-56). That study found no significant benefit in the composite end point of death, MI, and stroke at 4 months in more than 13,000 ACS patients enrolled in 12 randomized trials, some of which were also included in Dr. Bavry's metaanalysis.

The explanation for the divergent results may be that follow-up in the Swiss study wasn't long enough. At 4 months, the metaanalysis showed a nonsignificant 7% relative risk reduction in the combined end point in the aggressive statin treatment group. Similarly, Dr. Bavry's metaanalysis also showed nonsignificant trends in individual cardiac outcomes early on favoring aggressive statin therapy. ■

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