Drug-Eluting Stents Show Safety, Efficacy in AMI

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ATLANTA — Drug-eluting coronary stents were at least as safe and effective as bare-metal stents for treating patients with an acute MI 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 (DESs) were safe when implanted in patients with an acute MI (AMI)—and in the case of sirolimus-eluting stents also showed a reduced need for target vessel revascularization during follow-up—the reaction of experts to the results highlighted the degree of uncertainty about the safety of DESs in this clinical setting.

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DR. STONE

"The data for drug-eluting stents in acute MI is 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." Dr. Stone is the principal investigator for HORIZONS AMI.

But other experts contend that they are comfortable using DESs 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 DESs are used during primary PCI. It is also possible, but not yet proved, that the extra cost for DESs is balanced by a reduced rate of rehospitalization, said Dr. Bates. But the ability of DESs 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 DESs, such as in narrow coronary arteries or for long lesions.

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 stent thrombosis rates of 3.4% throughout all 12 months of follow-up, and 0.3% 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. Patients were directed to take aspirin and clopidogrel daily for at least 6 months after stent placement, said Dr. Spaulding.

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 AMI 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 who received a paclitaxel-eluting stent, the incidence of the end point was 8.7%, compared with 12.6% in the 310 patients who received 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. In this study, patients treated with the drug-eluting stent had both a 26% reduced rate of death or MI and a 32% reduced rate of need for revascularization.

The 1-year rate of stent thrombosis was 1% in both treatment groups. Stent thrombosis after the first 30 days following treatment occurred in two patients who received paclitaxel-eluting stents and in none of the patients who received bare-metal stents. Patients were directed to remain on aspirin and clopidogrel for at least 6 months after stent placement. ■

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THE ECS IMPACTS THE METABOLISM OF LIPIDS AND GLUCOSE[1-3]	• ECS overactivity may be associated with the development of cardiometabolic risk factors including: — Low HDL cholesterol — High triglycerides — High waist circumference — Elevated fasting glucose — Insulin resistance
THE ECS HELPS REGULATE PHYSIOLOGIC PROCESSES[1-4]	• The ECS consists of signaling molecules and their receptors, including the cannabinoid receptor CB_1[2] • Endocannabinoids bind to CB_1 receptors and trigger events that may have a negative impact on lipid levels and insulin sensitivity[1] • CB_1 receptors are located in sites such as muscle, the liver, the brain, and adipose tissue[1,2,4-6]
 RESEARCH CONTINUES TO INVESTIGATE THE ROLE OF CB_1 RECEPTORS IN MUSCLE*	• Reduced glucose uptake has been observed in isolated skeletal muscle of genetically obese, insulin-resistant animals
 ENDOCANNABINOIDS TARGET FATTY ACID PRODUCTION IN THE LIVER[3]	• May contribute to dyslipidemia and insulin resistance[3,7]
 PRESENT IN MULTIPLE AREAS OF THE BRAIN[2]	• Hypothalamus integrates signals from adipose tissue and other peripheral tissues[8,9]
 ADIPOSE TISSUE—MORE THAN SIMPLY A FAT STORAGE DEPOT	• Produces factors active in the metabolism of lipids and glucose[10] • Low levels of adiponectin negatively affect glucose and free fatty acids[1,10]
EXPLORING THE EFFECTS OF THE ECS	• This newly discovered physiologic system provides new opportunities for understanding cardiometabolic risk

*Data from animal model only.

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3-Vessel CAD: More Stenting Than Surgery

ATLANTA — Since the introduction of drug-eluting stents in the U.S. market in 2003, percutaneous coronary intervention has become the predominant mode of revascularization in patients with non–ST-elevation acute coronary syndromes and triple-vessel disease in community practice, according to fresh national registry data.

Meanwhile, the use of coronary artery bypass graft (CABG) surgery in such patients has declined significantly, although the proportion managed medically has remained steady at one-fourth, Dr. Prospero B. Gogo Jr. reported at the annual meeting of the American College of Cardiology. Many surgeons and interventional cardiologists have suspected as much but Dr. Gogo was able to fill in the big picture by drawing on a large data set.

He analyzed the cases of more than 103,000 patients who presented with non–ST-elevation acute coronary syndromes from January 2002 through June 2005 at the 365 hospitals participating in the CRUSADE quality improvement registry. Of the total, 80% of patients underwent coronary angiography during their index hospitalization, and 25,068 proved to have triple-vessel coronary artery disease.

A particularly interesting observation from the CRUSADE data is the marked temporal shift in the means of revascularization in acute coronary syndromes patients with triple-vessel disease. Before the introduction of drug-eluting stents, the distribution was roughly 50/50. Since the introduction, it has been a very different story. Whereas 49% of such patients revascularized in 2002 underwent coronary artery bypass graft surgery, that proportion had fallen to 40% by the first half of 2005.

In the same period, the use of percutaneous coronary intervention (PCI) in such patients climbed from 51% to 60%. Of these patients, 80% received drug-eluting stents, said Dr. Gogo of the University of Vermont, Burlington.

By using a multivariate logistic regression analysis, Dr. Gogo and his coinvestigator, Dr. Harold L. Dauerman, identified a number of independent predictors suggesting that PCI is being used rather than CABG. For example, they found that patients who were cared for by a cardiologist while they were in the hospital were 51% more likely to undergo PCI than were those who were not under a cardiologist's care. They also found that PCI was used preferentially in patients with a history of previous revascularization, whether by surgery or PCI, and in those with transient ST elevation on their ECG.

Randomized comparative trials of contemporary drug-eluting stents and surgery in patients with triple-vessel disease would help ascertain whether this trend reflects a decrease in the use of complete revascularization in the drug-eluting stent era, said Dr. Dauerman, professor of medicine at the university. CRUSADE is funded by multiple pharmaceutical companies.

—Bruce Jancin