Bivalirudin, Unfractionated Heparin Equal for PCI

BY MITCHEL L. ZOLER
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CHICAGO — Bivalirudin was no better than unfractionated heparin for treating troponin-negative patients with angina who underwent percutaneous coronary intervention and received a full loading dose of clopidogrel before their procedure, in a randomized study with more than 4,500 patients.

Although treatment with bivalirudin led to significantly fewer major bleeding episodes, this benefit was balanced by a trend toward fewer ischemic events among the patients treated with unfractionated heparin. The net result was that for the study's primary end point—a composite of death, MI, need for urgent revascularization, and major bleeding events—the two drugs performed nearly identically, Dr. Adnan Kastrati reported at the Innovation in Intervention (i2) Summit.

The implications are that in this treatment situation, compared with bivalirudin, "unfractionated heparin may be a better choice [because of its lower] cost, but in certain patient subgroups one drug may be better than the other," such as patients with an increased risk for bleeding, said Dr. Kastrati, director of interventional cardiology at the Heart Center in Munich.

But another expert disagreed and said that the results showed an outright advantage for bivalirudin because it caused fewer major bleeds. "The composite end point was numerically in favor of bivalirudin, there was no [significant] increase in ischemic events [with bivalirudin], and major bleeds were reduced. The results show that bivalirudin is the antithrombotic of choice" in the type of patients enrolled in the study, commented Dr. Harvey White, professor of cardiology at the University of New Zealand in Auckland.

But Dr. Kastrati warned against overinterpreting the bleeding result. "The main message should be based on the primary end point, not the individual end points," he said.

In the primary end point of ISAR-REACT 3, bivalirudin and unfractionated heparin performed nearly identically.

DR. KASTRATI

The Intracoronary Stenting and Antithrombotic Regimen-Rapid Early Action for Coronary Treatment (ISAR-REACT) 3 trial enrolled patients at six centers in Germany and one U.S. center. Eligible patients had either stable or unstable angina, had no elevation of serum troponin, and were scheduled for PCI. Their average age was 67 years, and about three-quarters were men. All patients received a loading dose of 600 mg of clopidogrel (Plavix) 2 hours or more before their procedure began as well as at least 325 mg of aspirin, a regimen that has recently become the standard pretreatment for patients undergoing PCI.

Patients were randomized to either of two study treatments. A 0.75-mg/kg bolus of bivalirudin, followed by a 1.75-mg/kg per hour infusion, was administered to 2,289 patients. The control arm of 2,281 patients received a 140-U/kg bolus of unfractionated heparin, followed by placebo infusion. (This heparin dose is commonly used in Europe; a 100-U/kg bolus dose is more prevalent in the United States, Dr. Kastrati noted.) About 83% of the patients received a drug-eluting stent.

Following their procedure, all patients received 75-150 mg/day clopidogrel until they were discharged from the hospital, and then maintained on a 75-mg/day dosage for at least 6 months. All patients also received 80-325 mg/day aspirin indefinitely.

During the first 30 days after treatment, the incidence of the combined primary end point of death, MI, need for urgent revascularization, or a major bleeding event was 8.3% in the bivalirudin patients and 8.7% in the unfractionated heparin patients, a nonsignificant difference, reported Dr. Kastrati at the meeting, cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Intervention.

Major bleeds were defined by criteria first used in a 2003 study, the Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE)–2 trial. Patients were considered to have a major bleed if they met any of four criteria: intracranial, intraocular, or retroperitoneal bleeding; clinically overt bleeding resulting in a drop in hemoglobin of at least 3 g/dL; a fall of hemoglobin by at least 4 g/dL due to any cause; or transfusion with at least two units of packed red blood cells or whole blood. The incidence of major bleeds was significantly less with bivalirudin, as was the rate of minor bleeds, and major bleeds by the criteria used in the Thrombolysis in Myocardial Infarction (TIMI) trials (see table).

ISAR-REACT 3 was funded in part by Nycomed Pharma, which markets bivalirudin (Angiomax) in Europe. Dr. Kastrati said that he and his coinvestigators had no other relevant financial relationships. Dr. White has served as a consultant to and has received speaker fees and research support from The Medicines Company, the U.S. marketer of bivalirudin. ■

30-Day Outcomes for Percutaneous Coronary Intervention

Measure	Bivalirudin (n = 2,289)	Unfractionated heparin (n = 2,281)
Minor bleeds using primary study criteria	6.8%*	9.9%
Major bleeds using primary study criteria	3.1%*	4.6%
Major bleeds using TIMI criteria	0.5%*	1.0%
Composite ischemia outcome (death, myocardial infarction, or need for urgent revascularization)	5.9%	5.0%
Composite primary outcome (ischemia outcomes plus incidence of major bleeds)	8.3%	8.7%

* Statistically significant difference between treatment arms.
Source: Dr. Kastrati

Drug-Eluting Stents Hold No Edge in Transplanted Hearts

BY MITCHEL L. ZOLER
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BOSTON — Drug-eluting stents worked no better than bare-metal stents for preventing restenosis in heart transplant patients in a review of 80 stents placed at one U.S. center.

"In [heart transplant] patients with focal lesions, we saw no advantage to using drug-eluting stents, compared with bare-metal stents," Dr. Proddutur R. Reddy said at the annual meeting of the International Society for Heart and Lung Transplantation.

Speculating why the sirolimus-eluting coronary stents used at his center did not perform as usual and cut restenosis, compared with bare-metal stents, Dr. Reddy suggested that the systemic immunosuppressive treatment received by all of the transplant patients might reduce systemic inflammation and thereby diminish the risk of in-stent restenosis regardless of the stent type used.

The review also found no differences in survival or the incidence of major adverse coronary events during 1 year of follow-up, but because of the small number of patients, it would not be expected to show any differences in clinical outcomes.

Since 1999, 42 patients who had received a heart transplant at Loyola University Medical Center in Maywood, Ill., subsequently underwent a percutaneous coronary intervention with one or more stents for treatment of focal stenoses. The series included placement of 56 sirolimus-eluting stents and 24 bare-metal stents, said Dr. Reddy, a cardiologist at the medical center. There were no significant differences in the demographic or clinical characteristics of patients getting the two different stent types, although a larger percentage of the patients getting bare-metal stents had diabetes, compared with those who received drug-eluting stents. A larger percentage of patients who received drug-eluting stents had more complex coronary lesions, and the average coronary diameter in the drug-eluting stent group was smaller.

A year after stent placement, the rate of binary restenosis (50% stenosis or greater) was 23% in both subgroups.

The study did not have commercial support, and Dr. Reddy said that he did not have any financial disclosures relative to the study. ■

IVUS-Guided Drug-Eluting Stents Less Prone to Thrombosis

WASHINGTON — Drug-eluting stents implanted using intravascular ultrasound guidance might be less susceptible to later stent thrombosis, Dr. Probal Roy reported at a symposium sponsored by the Cardiovascular Research Institute at Washington Hospital Center.

His single-center observational study found that IVUS-guided stents were 35% less likely to develop stent thrombosis by 1 year than were stents placed with angiographic guidance alone.

"IVUS guidance should be considered for routine use during drug-eluting stent implantation in patients who are at increased risk for these events," said Dr. Roy of the Washington (D.C.) Hospital Center.

Dr. Roy and his colleagues examined outcomes in 1,786 patients (mean age 66 years) who received drug-eluting stents during 2003-2006. IVUS guidance was performed in 884 patients; angiographic guidance alone was used in the rest. Groups were matched for age, gender, cardiovascular risk factors, clinical presentation, left ventricular ejection fraction, and angiographic features. IVUS was performed either preintervention, post intervention or both, at the discretion of the operator. There were no significant differences in in-hospital outcomes between the two groups.

However, at 30 days, significantly fewer patients in the IVUS group experienced definite stent thrombosis than did those in the angiography-only group (0.5% vs. 1.4%, respectively). This difference remained significant at 1 year, when rates of definite stent thrombosis were 0.7% in the IVUS group, compared with 2% in the angiographic guidance group. "Freedom from stent thrombosis was largely driven by reductions in subacute stent thrombosis," Dr. Roy said.

—Michele G. Sullivan