Bivalirudin and Heparin Prove Equal for PCI

BY MITCHEL L. ZOLER
Philadelphia Bureau

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 (see box), 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, myocardial infarction, 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.

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

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. The study was funded in part by Nycomed Pharma, which markets bivalirudin (Angiomax) in Germany and other European countries. Dr. Kastrati said that he and his coworkers on this study had no other financial relationships relevant to the study. Dr. White has served as a consultant to and has received speaker fees and research support from The Medicines Company, which markets bivalirudin in the United States.

'In certain patient subgroups, one drug may be better than the other.'

DR. KASTRATI

Eligible patients had either stable or unstable angina, had no elevation of serum troponin, and were scheduled for percutaneous coronary intervention (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 during PCIs, but a 100-U/kg bolus dose is commonly used in the United States, Dr. Kastrati noted. About 83% of the patients received a drug-eluting stent, about 10% were treated with balloon angioplasty, and about 7% received a bare-metal 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, myocardial infarction, need for urgent revascularization, or a major bleeding event was 8.3% in the bivalirudin patients and 8.7% in the patients treated with unfractionated heparin, a difference that was not statistically significant, reported Dr. Kastrati at the meeting, cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Intervention. ■

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

Obesity Linked to Higher Morbidity After Coronary Bypass

BY MITCHEL L. ZOLER
Philadelphia Bureau

TORONTO — Obesity was linked to an increased risk for postsurgical complications in a study of more than 11,000 patients who underwent coronary artery bypass surgery.

But in this series, obesity did not result in a significantly increased risk for postsurgical mortality, Dr. Mahboob Alam said at the 14th World Congress on Heart Disease.

Obesity also was linked to a significant 38% reduced risk for repeat operations for postoperative bleeding, an unexpected finding that requires further study to understand, said Dr. Alam, a cardiologist at Baylor College of Medicine, Houston.

The retrospective study included 11,417 consecutive patients who underwent coronary artery bypass surgery at St. Luke's Episcopal Hospital in Houston during 1996-2006.

The series included 2,257 patients (20%) who were obese, which is defined as having a body mass index of 30 kg/m^2 or greater.

The nonobese patients were older, with an average age of 64 years, compared with an average age of 61 among the obese patients.

But the obese patients had more comorbidities, with higher rates of unstable angina, coronary artery disease, hypertension, heart failure, and diabetes.

Obesity did not result in a significantly increased risk for postsurgical mortality.

DR. ALAM

The primary end point for the analysis was mortality during the first 30 days following bypass surgery. Although a multivariate analysis showed that the obese patients had an 8% increased risk for death, this difference was not statistically significant relative to the mortality risk in the nonobese patients, Dr. Alam reported at the congress, which was sponsored by the International Academy of Cardiology.

The multivariate analysis showed that obesity was linked with significant increases in the rate of several new-onset morbidities, compared with the rates in nonobese patients, after the patients in both groups underwent coronary artery bypass surgery.

These new-onset morbidities included a 43% increased rate of renal insufficiency in the obese patients, compared with the nonobese patients, a 71% increased rate of myocardial infarction, a 46% rise in respiratory failure, a 2.9-fold increased rate of sternal wound infections, and a 2.1-fold boost in the rate of leg wound infections, Dr. Alam said.

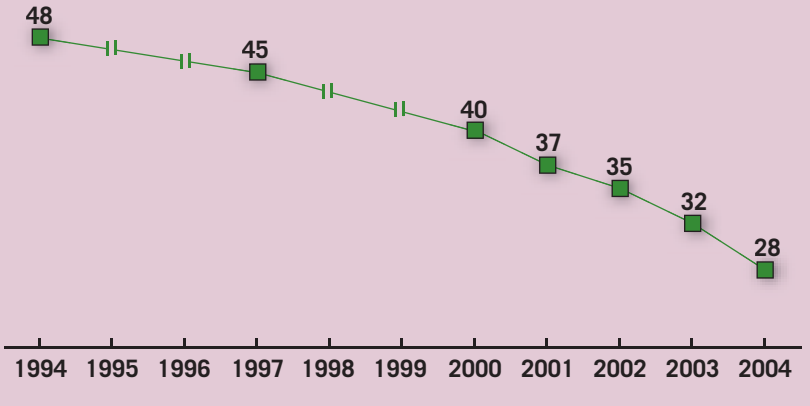
In addition, obesity was linked with a significantly increased duration of postoperative hospitalization after coronary artery bypass surgery.

Although the nonobese patients spent an average of 10.5 days in the hospital, in contrast, the obese patients spent an average of 11.85 days in the hospital after undergoing coronary artery bypass surgery, Dr. Alam reported at the congress. ■

DATA WATCH

Inpatient Mortality From Coronary Artery Bypass Graft Declining

(per 1,000 admissions)



Source: Healthcare Cost and Utilization Project