Diabetes, Late Thrombosis Cloud DES Picture

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ARLINGTON, VA. — Drug-eluting stents may have an advantage over bare-metal stents in major cardiac and cerebrovascular events, but the picture is less clear when it comes to diabetic patients and late thrombosis, according to data presented at a meeting sponsored by the Cardiovascular Research Institute at Washington Hospital Center.

Researchers in Argentina compared outcomes at 1, 2, 3, and 5 years' follow-up in patients with multivessel coronary artery disease (CAD) who were prospectively treated with drug-eluting stents—either the Cypher sirolimus or the Taxus paclitaxel stent in the Argentine Randomized Study: Coronary Angioplasty With Stenting Versus Coronary Bypass Surgery in Patients With Multiple Vessel Disease (ERACI) III—with similar cohorts of patients from the earlier ERACI II trial, which treated CAD patients with either bare metal stents or coronary artery bypass grafting (CABG).

"This multicenter, prospective, controlled study of patients with multivessel CAD treated either with sirolimus- or paclitaxel-eluting stents demonstrated a significant reduction of major adverse cardiac and cerebrovascular events [MACCE] and the need for repeat revascularization procedures when compared with our previous bare-metal data from ERACI II," said principal investigator Alfredo Rodriguez, Ph.D., of Otamendi Hospital in Buenos Aires.

The times at which thromboses were detected was telling: Three patients with BMS and none with DES were identified with in-stent thrombosis while in hospital.

A total of 225 patients treated with drug-eluting stents (DES) in five centers in Buenos Aires were prospectively enrolled in the ERACI III trial during 2002-2004. Just over a fifth of patients were diabetic (22%) and 37% had type-C lesions. They were compared with 500 patients from the earlier ERACI II, of whom 225 underwent CABG and 225 were treated with bare-metal stents (BMS). Of the combined group, 17% were diabetic and 15% had type-C lesions. Of the DES patients, 48% were treated with paclitaxel-eluting stents and 52% with sirolimus-eluting stents.

"DES versus bare metal and DES versus CABG are associated with lower MACCE at follow-up," said Dr. Rodriguez. The incidences of MACCE at 1 year were 22%, 20%, and 12% for patients with BMS, CABG, and DES, respectively, on the basis of a univariate analysis. There was no significant difference in the MACCE rate between the two drug-eluting stents.

Drug-eluting stents showed less benefit for diabetic patients in terms of MACCE at 1 year follow-up. In DES patients in ERACI III, there was a nonsignificant trend toward higher mortality in the 47 diabetic patients than in the 178 nondiabetic patients (23% and 9%, respectively). Diabetic patients had a higher incidence of acute myocardial infarction (9%) and repeat percutaneous coronary intervention or CABG (17%), compared with nondiabetic patients (1% and 7%, respectively). Researchers also looked at the incidence of in-stent thrombosis over time. Three BMS patients had in-stent thrombosis, compared with eight DES patients. The times at which thromboses were detected were even more telling: Three patients with BMS and none with DES were identified with in-stent thrombosis while in the hospital.

After hospital discharge and out to 3 years, no BMS patients had in-stent thrombosis. Three DES patients had stent thrombosis after discharge, but still in the first 30 days. Another three in this group developed stent thrombosis in the first year, and one other patient developed stent thrombosis by the 3-year follow-up. Three of the DES patients with stent thrombosis had MIs and three died. Dr. Rodriguez reported no conflicts of interest. ■

Thrombin Inhibition in ACS

Bivalirudin *from page 1*

versity in Durham, N.C. Another indication that the study did not focus entirely on the types of high-risk patients enrolled in past studies was that their incidence of ischemic complications during the first 30 days after treatment was about 7.5%, substantially lower than the 12%-15% rates seen in high-risk patients in previous studies.

In other studies, treatment with a IIb/IIIa inhibitor involved a trade-off between a reduction in ischemic events and an increased risk of bleeding. "If 40% of the patients don't have high-risk ACS, then in those patients you get the risk [of increased bleeding] without the benefit," said Dr. Peterson in an interview. "It's not surprising that drugs that work by reducing ischemic events didn't benefit" patients.

Dr. Peterson said that despite the new results, treatment with a IIb/IIIa inhibitor remains the standard of care for high-risk ACS patients with an elevated level of serum troponin who undergo angiography and may be treated with PCI.

The Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial was designed by Dr. Stone and his associates to address two questions. First, the study compared bivalirudin alone with two other antithrombotic regimens that included a IIb/IIIa inhibitor. The study also examined whether, in patients who received a IIb/IIIa inhibitor, it made a difference if the drug was given early, to all patients, or was deferred and administered only to the approximately 55% of patients who actually underwent PCI.

The study enrolled 13,819 patients at 448 centers in 17 countries. More than half of the patients were treated in the United States. The study was sponsored by The Medicines Company, which markets the synthetic direct-thrombin inhibitor bivalirudin (Angiomax). Dr. Stone is a consultant to The Medicines Company.

All of the patients were treated with aspirin; clopidogrel treatment was recommended, but was administered according to local practices. The patients were randomized equally between the three treatment groups: bivalirudin alone, bivalirudin plus a IIb/IIIa inhibitor, and unfractionated heparin or enoxaparin and a IIb/IIIa inhibitor. Patients who received a IIb/IIIa inhibitor during initial treatment were treated with either epifibatide or tirofiban. Those who had their treatment deferred until they underwent PCI primarily received either epifibatide or abciximab, with a small percentage receiving tirofiban.

The primary end point was the incidence during the next 30 days of ischemic events—death, myocardial infarction, or need for revascularization because of ischemia. The rate of major bleeding events was another primary end point, as was the composite incidence of ischemic events and major bleeds. The results showed no significant difference in ischemic events, which occurred in 7.3%-7.8% of patients, proving bivalirudin alone is not inferior to treatments with a IIb/ IIIa inhibitor, said Dr. Stone, professor of medicine and director of cardiovascular research and education at Columbia University in New York. Major bleeding events occurred in 5.7% of patients treated with heparin or enoxaparin and a IIb/IIIa inhibitor, 5.3% of patients treated with bivalirudin and a IIb/IIIa inhibitor, and in 3.0% of patients treated with bivalirudin alone, a statistically significant reduced rate in the bivalirudin group.

The results of the second analysis, which compared upfront use of a IIb/IIIa inhibitor in all patients against deferred use only in the 55% of patients who underwent PCI, showed that the efficacy of both approaches was similar. The incidence of ischemic events was 7.1% in patients who received immediate treatment with a IIb/IIIa inhibitor, and 7.9% in patients who received the drug only before having PCI, a difference that was not statistically significant for superiority, but fell slightly short of proving that deferred use of a IIb/IIIa inhibitor was not inferior.

The deferred strategy led to a 4.9% incidence of major bleeds, significantly less than the 6.1% rate in patients who got immediate treatment with a IIb/IIIa inhibitor. In the composite analysis of both major bleeds and ischemic events, the two strategies were completely equal, each producing an 11.7% event rate.

The "most important" implication from this analysis is that both strategies for administering a IIb/IIIa inhibitor were inferior to the net clinical outcome of bivalirudin alone, which had a composite event rate of 10.1% for major bleeds and ischemic events, Dr. Stone said.

"One thing that bivalirudin has done consistently [in prior studies] is reduce the rate of bleeding complications, so the difference in bleeding here is not surprising," said Dr. Kirk Garratt, director of interventional cardiovascular research at Lenox Hill Hospital in New York. ■

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