Medical Tx Best for Stable Patients

Late PCI *from page 1*

OAT was a 217-site international study involving stable patients with a 100% occlusion 3-28 days post-MI, when they were randomized to PCI and stenting plus optimal medical therapy, or to optimal medical therapy alone.

The primary end point was the 4-year cumulative rate of death, repeat MI, or hospitalization for class IV heart failure. This end point was reached by 17.2% in the PCI group and 15.6% with medical management, a nonsignificant difference. No subgroup benefited from late PCI, including higher-risk patients with a large anterior MI, an ejection fraction below 40%, or a left anterior descending coronary occlusion. Time from MI to randomization didn't affect outcome, either.

The rate of nonfatal reinfarction was 6.9% in the PCI group and 5.0% with medical management, a trend that did not reach statistical significance, but that is "worrisome," said Dr. Hochman.

He stressed that late PCI remains clearly indicated in the highest-risk post-MI patients deliberately excluded from OAT, including those with angina at rest, severe heart failure, or triple-vessel disease.

OAT included a mechanistic substudy called the second Total Occlusion Study of CAnada (TOSCA-2) involving 332 subjects who underwent repeat angiography at 1 year. TOSCA-2 lead investigator Dr. Vladimir Dzavik reported that the 1-year infarct artery patency rate was 83% in the late PCI group, compared with 25% with medical therapy alone. There was also less left ventricular dilation in the PCI arm. Nonetheless, ejection fraction at 1 year improved by a similar amount—roughly 4%—in the two groups.

It seems likely that late PCI in stable patients has two competing effects: It reduces left ventricular enlargement, while also increasing the risk of MI. The net effect is no benefit, said Dr. Dzavik, the Brompton Group Professor in Interventional Cardiology at the University of Toronto.

Observers hailed OAT as a major, practice-changing study. Current AHA/American College of Cardiology guidelines on acute MI management give late PCI in patients with a blocked artery a class IIb recommendation with a C level of evidence. That means it's not an unreasonable thing to do and is supported only by expert opinion. Class IIb/level C is the weakest endorsement the guidelines panel bestows. Dr. Sidney C. Smith Jr. predicted in an interview that the guidelines committee will soon revisit that recommendation in response to the OAT trial.

"OAT looks like a very good study to me, a very carefully done study by good investigators on an important problem. The preliminary results are very persuasive," said Dr. Smith, professor of medicine and director of the Center for Cardiovascular Science and Medicine at the University of North Carolina, Chapel Hill.

OAT discussant Dr. Robert M. Califf, noting that fewer than 500 OAT participants came from the United States, castigated many of his fellow American cardiologists for failing to keep an open mind in the face of scientific uncertainty, particularly when, as in this case, the stance suited their economic self-interest. Many of the nation's top medical centers declined to participate in the randomized trial on the grounds that their cardiologists felt they couldn't ethically leave an infarct-related artery closed. They already "knew" it was wrong despite an absence of quality evidence.

It's enough to make one ask whether a spirit of scientific inquiry—the ability to admit uncertainty—ought to be adopted as a health care quality performance measure, added Dr. Califf, professor of medicine and vice chancellor for clinical research at Duke University, Durham, N.C.

Simultaneously with Dr. Hochman's presentation, the OAT results were published online (N. Engl. J. Med. 2006 Dec. 7 [Epub doi:10.1056/NEJMoa066139]). ■

Less Bleeding With Bivalirudin in PCI

BY ALICIA AULT
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WASHINGTON — The direct thrombin inhibitor bivalirudin seems to be more effective than heparin in reducing major bleeding episodes in patients undergoing percutaneous coronary intervention, according to a study presented at a symposium sponsored by the Cardiovascular Research Foundation.

The study, ACUITY-PCI, is a substudy of the Acute Catheterization and Urgent Intervention Triage Strategy trial. ACUITY was presented at the American College of Cardiology meeting in March; the ACUITY-PCI results were presented at a symposium sponsored by the Cardiovascular Research Foundation (CRF).

In ACUITY-PCI, 7,789 patients who underwent catheterization were randomized to one of three arms: unfractionated heparin or enoxaparin (Lovenox), depending on local hospital practice, combined with a glycoprotein IIb/IIIa inhibitor; bivalirudin (Angiomax) with a glycoprotein IIb/IIIa inhibitor; or bivalirudin alone. These were high-risk patients: 65% in each arm—about 1,690 patients in each group—had elevated troponin levels at baseline. Patients underwent PCI within 20 hours of admission. There was a mean of 1.5 lesions attempted per patient.

The majority of patients in each arm had a stent implanted, with 60% getting a drug-eluting stent, said Dr. Gregg Stone, CRF vice-chairman and a professor of medicine at Columbia University, New York.

The study measured three primary end points at 30 days postcatheterization: a composite net clinical benefit, an ischemic composite, and major bleeding. Major bleeding was defined as noncoronary artery bypass–related bleeding, intracranial hemorrhage, intraocular bleeding, retroperitoneal bleeding, reoperation for bleeding, and major transfusion.

Overall, bivalirudin alone reduced major bleeding by 48%. There was a 50% reduction in the need for transfusions, said Dr. Stone.

At 30 days, 7% of patients in the heparin plus glycoprotein IIb/IIIa inhibitor, 8% of patients receiving bivalirudin plus a glycoprotein IIb/IIIa inhibitor, and 4% of patients receiving bivalirudin alone had major non–coronary artery bypass graft bleeding.

Bivalirudin alone reduced major bleeding by 48% and cut the need for transfusions by 50%.

DR. STONE

There was no difference among the three arms in the components of the composite end point of ischemia: death, myocardial infraction, or unplanned revascularization for ischemia, said Dr. Stone.

In addition, there was no difference among the arms in patients who had elevated troponin levels in net clinical outcomes, ischemic composite, or major bleeding.

The study authors also examined patients who had exposure to a thienopyridine—usually clopidogrel (Plavix). Again, there was a major reduction in bleeding with bivalirudin alone, whether patients had taken a thienopyridine or not, said Dr. Harvey White, of Green Lane Hospital in Auckland, New Zealand, who briefed reporters on the results.

The study authors concluded that in patients with moderate and high-risk acute coronary syndrome undergoing contemporary PCI, replacing the standard of heparin and a glycoprotein IIb/IIIa inhibitor with bivalirudin alone results in similar rates of ischemia and a 50% reduction in bleeding, said Dr. White.

The study also helped assuage concerns about using bivalirudin in troponin-positive patients.

And, he added, the findings are consistent with the results seen in Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE-2), in which there was a 41% reduction in major bleeding with bivalirudin alone.

Dr. Stone noted that ACUITY-PCI did have some limitations, including that it is not technically a randomized trial and that it was underpowered for noninferiority testing and subgroup analysis. It should be considered a hypothesis-generating study, he said.

In discussing the ACUITY-PCI, Dr. Eric Topol, chairman of the department of cardiovascular medicine at Case Western Reserve University, Cleveland, said that the subgroups were still interesting to examine, especially the impressive results in patients with troponin elevations.

One interesting note—despite large amounts of antiplatelet therapy, there was still a stent thrombosis rate of about 1.4% at 30 days, said Dr. Topol.

Overall, "There is a trade-off with a slight increase in MI, which is small, but it's compared with a significant, greater than 50% reduction in bleeding," said Dr. Topol.

He also agreed that the replication of the REPLACE-2 results give "key validation" to bivalirudin's utility.

Dr. Topol had no conflicts to report. Dr. White served briefly as a consultant to the Medicines Company, which makes bivalirudin. Dr. Stone is on the speaker's bureau for the Medicines Company and also receives significant research support. ■

Low-Permeability Stent Reduces AAA Volume, Diameter at One Year

WASHINGTON — The low-permeability version of the Gore Excluder stent graft appears to reduce the volume and diameter of abdominal aortic aneurysms at 1 year significantly more than did the older, more permeable version of the stent, according to the results of a prospective study comparing the two models.

The high rate of failure with the original Gore Excluder stent graft, in which the mean maximum abdominal aortic aneurysm (AAA) diameter increased by at least 5 mm in 36% of patients after 5 years, prompted the stent's manufacturer, W.L. Gore & Associates Inc., to add a new low-permeability layer between the device's expanded polytetrafluoroethylene layer and its reinforcing membrane, Dr. Manish Mehta said at the annual meeting of the Eastern Vascular Society.

The Food and Drug Administration approved the new device in July 2004.

In a series of 428 patients who received either the new or the old Excluder for AAA treatment during 2001-2005 at the Institute for Vascular Health and Disease at Albany (N.Y.) Medical College, Dr. Mehta and his colleagues compared the outcomes of 214 patients who had CT angiography imaging results available 1 year after the procedure.

The CT angiograms revealed that 114 consecutive patients with the low-permeability stent had significantly greater declines in mean AAA volume than 100 consecutive patients with the original type of stent (163 mL to 141 mL vs. 156 mL to 160 mL). The percentage of patients with more than a 5% drop in AAA volume also was significantly greater in patients with the new stent (52%) than in those with the old stent (6%), reported Dr. Mehta, a vascular surgeon at the institute.

Compared with recipients of the old stent graft, significantly fewer patients with the new device had more than a 5% increase in AAA volume (12% vs. 2.6%).

A significantly greater percentage of patients with the low-permeability stent had at least a 5-mm decrease in maximum AAA diameter (25% vs. 8%). The mean preoperative maximum AAA diameter was similar among the patients with the new (5.4 cm) or old (5.3 cm) Excluder.

—Jeff Evans