Drug-Eluting Stents Favored in ST-Elevation MI

BY PATRICE WENDLING
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CHICAGO — The rate of major adverse cardiac events was roughly halved at 8 months by the use of sirolimus-eluting stents, compared with bare-metal stents in a randomized trial of 745 patients who underwent percutaneous coronary intervention for ST-segment elevation MI.

The Multicentre Evaluation of Single High-Dose Bolus Tirofiban vs. Abciximab with Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study (MULTISTRATEGY) also found that tirofiban was noninferior to abciximab in resolving ST elevation at 90 minutes.

"These findings may provide a robust scientific rationale for high-dose tirofiban as an alternative to abciximab in patients with STEMI," Dr. Marco Valgimigli said in a statement.

The open-label, 2-by-2 factorial trial showed that at 8 months, major adverse cardiac events (MACE) occurred in 29 of 372 patients (7.8%) treated with sirolimus-eluting stents and in 54 of 372 patients (14.5%) with bare-metal stents, Dr. Valgimigli reported on behalf of the MULTISTRATEGY investigators in a late-breaking clinical trial session at the Innovation and Intervention (i2) Summit. The difference was statistically significant.

The benefit was driven by a significant 69% relative risk reduction in target vessel vascularization from 10.2% to 3.2%.

Stent thrombosis was significantly lower in patients with sirolimus-eluting stents, regardless of which Academic Research Consortium definition was used, said Dr. Valgimigli, of the Cardiovascular Institute, University of Ferrara (Italy).

Results of the glycoprotein IIb/IIIa inhibitor arms of the study showed that tirofiban therapy was associated with a noninferior ST-segment resolution at 90 minutes following percutaneous coronary intervention when compared with abciximab.

In 722 patients with an interpretable ECG, at least 50% recovery from ST-elevation occurred in 308 of 361 (85.3%) patients in the tirofiban group and 302 of 361 (83.6%) patients in the abciximab group, according to Dr. Valgimigli's presentation and data published simultaneously online (doi:10.1001/jama.299.15.joc80026).

"Most importantly, these results proved to be consistent among multiple prespecified subgroups—including age, sex, diabetes, Killip class, stent type, number of diseased vessels, location of the infarction, time to treat the infarction—with no evidence of interaction between any of these groups and the study treatment," Dr. Valgimigli said at the meeting, cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Interventions.

Patient age was 64 years in the abciximab plus bare-metal stent (BMS) group, 63 years in the abciximab plus sirolimus-eluting stent (SES) group, 65 years in the tirofiban plus BMS group, and 63 years in the tirofiban plus SES group.

In the same trial, tirofiban was found noninferior to abciximab in resolving ST elevation at 90 minutes.

DR. VALGIMIGLI

At 30 days, the incidence of MACE, death, or MI, and definite or definite/probable stent thrombosis, did not differ significantly between the two groups. However, the incidence of thrombocytopenia was significantly more common with abciximab.

At 8 months, there also was no significant difference between patients treated with tirofiban or abciximab in the incidence of MACE (9.8% vs. 12.4%), death or MI (6.2% vs. 7.3%), and target vessel revascularization (6.2% vs. 7.3%), said Dr. Valgimigli, who reported receiving honoraria and research support from Merck USA. The study was partially supported by Merck.

Discussant Dr. E. Magnus Ohman, professor of cardiovascular medicine, Duke Clinical Research Institute, in Durham, N.C., pointed out that the 25-mcg/kg bolus of tirofiban used in the trial with a standard 0.15-mcg/kg per minute infusion is much higher than the approved bolus dose of 10 mcg/kg. Americans have limited experience with this higher dose and with the drug in general, as it is used in less than 4% of percutaneous coronary intervention cases in the United States, he said.

He also said that that the study was underpowered for the clinical end points and that the rate of transfusion was numerically higher in the tirofiban group, "leaving open the issue of how safe is this higher dose of tirofiban studied in this trial."

Dr. Ohman also questioned whether the 8-month follow-up on the stented patients was sufficient, given that late-stent thrombosis tends to occur after that period.

Regarding the tirofiban dose, Dr. Valgimigli said the investigators felt the 10-mcg bolus dosing was inadequate in patients with acute MI based on results of the TARGET trial, and that there is significant experience with the drug in Europe, where it is widely used. While bleeding is an important area of focus for practitioners, he said that very important data suggest that thrombocytopenia—which was significantly more common with abciximab than tirofiban—is an important clinical indicator as well.

Press briefing moderator Dr. William Knopf, chief operating officer at the Piedmont Heart Institute, Atlanta, said, "I think one of the most important things we learned from this trial is perhaps the correct dose of tirofiban that we can extrapolate into our patients." ■

Left-Main Barrier Broken?

Safe as CABG *from page 1*

plasty Versus Surgical Revascularization) registry.

This report "has tremendous implications because an unprotected left main artery was always thought absolutely not for the interventionalist, but that's changing," commented Dr. E. Murat Tuzcu, professor of medicine and director of interventional ultrasound at the Cleveland Clinic. Dr. Park's report "is very reassuring about safety from midterm results." Like several other experts, he cited the important role of results from a randomized study now in progress: the SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) study that is directly comparing PCI in the left main coronary with bypass surgery. Initial results from this study may be reported later this year.

"If SYNTAX shows similar results, then I think you'll see more and more of these interventions" in the United States," added Dr. Tuzcu. He estimated that currently about 20% of unprotected left main artery revascularization procedures performed in the United States involved PCI, with the vast majority done using CABG.

"In the early days of PCI, when procedural problems were common, manipulation of a left main coronary artery stent could be dangerous," commented Dr. Timothy J. Gardner, a cardiothoracic surgeon and medical director of the center for heart and vascular health at Christiana Hospital, Wilmington, Del. "There were medicolegal risks, and we got to a point of 'dogma' where any patient with left main disease would go for CABG, and failure to offer CABG was looked upon as bad medical judgment."

But over the past decade, "PCI techniques improved along with better stents, greater operator experience, and many fewer instances of procedural failure and patient death," Dr. Gardner said in an interview. "The MAIN-COMPARE results show that stenting of the left main coronary artery can be accomplished safely and successfully in many patients, including some with complex left main lesions."

In Korea, PCI for left main stenosis is a much more common procedure than in the United States, which allowed Dr. Park and his associates to perform this analysis. They reviewed 2,240 revascularizations of unprotected left main coronaries done during 2000-2006. During this period, 1,073 (97%) of the 1,102 patients who underwent PCI treatment had clinical and anatomical characteristics that made them eligible for treatment by either PCI or surgery. They had PCI because of either patient or physician preference. The remaining 29 (3%) had underlying conditions that made them poor surgical candidates.

During the first 3 years, the PCIs were done using bare-metal stents, and drug-eluting stents were mostly used starting in mid-2003. To account for this change, the researchers ran one analysis that compared PCI with bare-metal stents with surgeries done during the same period (January 2000–March 2003), and another analysis that compared PCIs with drug-eluting stents with coronary bypass done during May 2003–June 2006.

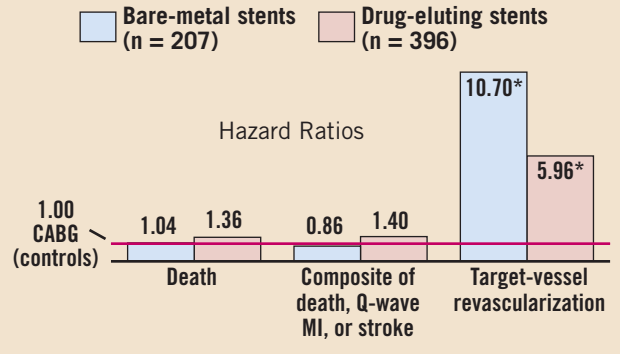
To adjust for baseline differences among patients, propensity-score matching was done. This produced 207 matched pairs of patients who had either PCI with a bare-metal stent or surgery, and 396 pairs of matched patients who had either PCI with a drug-eluting stent or surgery.

The incidence of both death and a combined end point of death, Q-wave MI, or stroke during an average follow-up of about 3 years showed no significant difference between the two sets of comparison pairs. (See box.) Simultaneously with Dr. Park's report at the meeting, these results were published online (N. Engl. J. Med. 2008 March 31 [Epub doi:10.1056/NEJMoa0801441]).

Not surprisingly, the analysis also showed that bypass surgery was substantially more effective than PCI for preventing the need for target vessel revascularization. Patients who received bare-metal stents were about 10-fold more likely to later need revascularization in their treated vessel, compared with the surgery patients. Among those treated with drug-eluting stents, the risk for having a second procedure in the same vessel was almost six-fold higher than the matched CABG patients, Dr. Park reported at the meeting, which was cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Intervention. The incidence of acute complications following PCI was 2.7%.

"Patient selection for stenting versus coronary artery bypass surgery should be based on the usual considerations, including the patient's coronary anatomy and overall clinical status, as well as the capability of the interventional cardiology team," said Dr. Gardner. ■

Outcomes of PCI Compared With CABG at 3 Years



*Statistically significant.
Note: Controls comprised matched pairs for both stent groups.
Source: New England Journal of Medicine

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