Paclitaxel-Eluting Stents Top Brachytherapy for Restenosis

BY MITCHEL L. ZOLER
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ATLANTA — Paclitaxel-eluting coronary stents were more effective for treating in-stent restenosis than was vascular brachytherapy in results from a study with almost 400 patients reported at the annual meeting of the American College of Cardiology.

The clear superiority of paclitaxel-eluting stents for this indication matched previously reported results for sirolimus-eluting stents, which were shown to be better than brachytherapy for in-stent restenosis in findings reported last November at the annual scientific sessions of the American Heart Association.

'The study is very definitive' for proving the superiority of paclitaxel-eluting stents.

DR. WAKSMAN

Vascular brachytherapy is currently the only treatment approved by the Food and Drug Administration for treating bare-metal stents that develop in-stent restenosis.

Both comparisons of drug-eluting stents with brachytherapy involved stenoses in bare-metal stents, but drug-eluting coronary stents also worked for treating restenosis in drug-eluting stents in a single-center series of 77 patients, which was reported in a poster at the meeting. The next challenge will be further study in finding the best way to treat restenosis in drug-eluting coronary stents.

The paclitaxel-eluting stent study was conducted at 37 centers in the United States and Canada during June 2003 to July 2004. All patients enrolled had a single, restenotic lesion in a bare-metal stent in a native coronary artery.

The patients were randomized to treatment with a paclitaxel-eluting stent or vascular brachytherapy using any Food and Drug Administration–approved, β-source radiation system.

The study was sponsored by Boston Scientific Corp., which markets the paclitaxel-eluting stent (Taxus) used in the study.

The primary end point was incidence of ischemia-driven target vessel revascularization 9 months after treatment. The rate of this event was 10.5% in 194 patients treated with the paclitaxel-eluting stent and 17.5% in patients treated with brachytherapy, a statistically significant difference in favor of the drug-eluting stent, reported Dr. Gregg W. Stone, professor of medicine and director of cardiovascular research and education at Columbia University in New York.

Dr. Stone also is a consultant to Boston Scientific.

The paclitaxel-eluting stent was superior to brachytherapy by several other efficacy measures assessed by angiography after 9 months. Compared with brachytherapy, stenting showed several advantages that contribute to improved long-term patency: greater initial acute gain owing to mechanical scaffolding by the stent, preservation of acute gain by limited late loss, and avoidance of the edge-effect produced by brachytherapy, Dr. Stone said.

Stenting was also at least as good as brachytherapy for both 30-day and 9-month measures of safety. The results were published simultaneously with Dr. Stone's report at the meeting (JAMA 2006;295:1253-63).

"The study is very definitive" for proving the superiority of paclitaxel-eluting stents over brachytherapy, commented Dr. Ron Waksman of the division of cardiology at the Washington (D.C.) Hospital Center, and a pioneer in the development of vascular brachytherapy.

Similar results were reported for sirolimus-eluting stents (Cypher), when compared with vascular brachytherapy for treating restenosis in bare-metal stents in a study by Dr. David R. Holmes Jr., professor of medicine at the Mayo Clinic in Rochester, Minn., and associates. The published report of those findings appeared in the same journal issue that contained Dr. Stone's paper (JAMA 2006;295:1264-73).

An editorial that commented on both studies noted that the data from the two studies were strong enough to move brachytherapy to a second-line choice for treating in-stent restenosis, although with a few exceptions. For the time being, brachytherapy remains the top option for treating restenosis in bifurcations; in vessels with excessive calcification, tortuosity, or angulation; or in other settings in which repeated stenting might risk procedure-related ischemic events, wrote Dr. Debabrata Mukherjee and Dr. David J. Moliterno of the University of Kentucky in Lexington (JAMA 2006;295:1307-9). The best treatment for in-stent restenosis in patients with renal dysfunction also is unclear, because those patients were excluded from both of the new studies.

Questions about how to treat in-stent restenosis will now shift to restenosis that occurs in drug-eluting stents, where brachytherapy is unlikely to have a role, Dr. Mukherjee and Dr. Moliterno wrote.

A step toward addressing this issue was made by cardiologists at the Prairie Heart Institute at Saint Johns Hospital in Springfield, Ill. They reported in a poster their experience with using a second drug-eluting stent to treat 86 lesions in 77 patients with restenosis that had occurred in a first drug-eluting stent. Their findings suggested that using the "opposite" drug-eluting stent the second time around might be the best approach. This seems to be the first report of using drug-eluting stents to treat stenoses that form in drug-eluting stents, said Dr. Marc E. Shelton, a cardiologist at the Prairie Heart Institute.

In this series, 64 of the lesions were treated using the same type of stent that had been used the first time (61 with sirolimus-eluting stents and 3 with paclitaxel-eluting stents), and 22 received the alternative stent type the second time around.

"It makes sense to change coatings if a patient didn't respond to a drug-eluting stent the first time," Dr. Shelton said in an interview.

After 1 year of follow-up, the patients who received a different type of drug coating the second time had an 18% rate of need for target lesion revascularization, compared with a 31% rate in patients who received the same type of drug coating the second time.

Also included in the series were 15 patients with 22 lesions that were treated with either balloon angioplasty, brachytherapy, or a bare-metal stent. In this group, the rate of target lesion revascularization after 1 year was 41%. The differences among the groups were not statistically significant. This was a series and not a randomized, controlled trial.

"It looks like using the opposite stent is no worse than using the same stent, and it may be better," Dr. Shelton said. ■

Absorbable Metal Stent Is Found Safe, Effective

BY CATHERINE HACKETT
Senior Editor

ATLANTA — A metal stent that provides scaffolding for a vessel wall for about 2 months before being absorbed was found safe and effective in a small, first-in-man trial in bioabsorbable stenting, Dr. Raimund Erbel reported at a conference sponsored by the American College of Cardiology.

"The absorbable metal stent is not just another stent. It represents a revolutionary leap forward in vascular interventional treatment," said Dr. Erbel, principal investigator of the Clinical Performance and Angiographic Results of the Multicenter, Nonrandomized Coronary Stenting With Absorbable Metal Stents (PROGRESS-AMS) study.

An absorbable stent reduces late stent thrombosis, a problem with drug-eluting stents.

DR. ERBEL

In PROGRESS-AMS, investigators at nine medical centers treated 63 patients with a de novo lesion in a single coronary artery. Of the patients, 70% were men and 18% had diabetes. The target lesion was in the left anterior descending artery in 22 patients, in the left circumflex artery in 18, and in the right coronary artery in 23; 24% had a prior percutaneous coronary intervention. Predilation was performed in all patients, and postdilation was performed in 67% of patients.

The primary efficacy end point was major adverse cardiovascular events—defined as cardiac death, nonfatal MI, or ischemia-driven target vessel revascularization (TVR)—of lower than 30% at 4 months. This end point was achieved: The rate was 24%, all accountable to ischemia-driven TVR. There were no occurrences of in-stent thrombosis, myocardial infarction, or death.

The stent used in the study, made by Berlin-based Biotronik GmbH, is made of a magnesium alloy and is indistinguishable from a standard bare-metal stent in appearance, Dr. Erbel said. Magnesium was chosen because it is an essential element for humans, who have a daily requirement of 350 mg. Furthermore, it is a calcium antagonist, has antiarrhythmic properties, and is not associated with allergies, he noted.

Among the clinical advantages of a bioabsorbable stent is that it clears the vessel of useless metal once it has been revascularized. Patients who have had in-stent restenosis may accumulate layers of metal in the affected vessel, making it increasingly difficult to treat, said Dr. Erbel, of Essen (Germany) University, at the conference, which was also sponsored by the Society of Cardiovascular Angiography and Interventions.

Dr. Erbel noted that late stent thrombosis, a problem with drug-eluting stents, is reduced with an absorbable stent, because as it degrades the endothelium becomes smooth, regains function, and undergoes positive remodeling. Such a stent is also an important development in pediatric cardiology. Permanent stents cannot be used in children because the vessels grow. Surgery is the only way to remove a stent that is outgrown.

Another advantage of the magnesium stent is its visualization options. When using MRI or CT, the stent is transparent. With MRI, "We saw no stent, but saw a nice open vessel," said Dr. Erbel, who is a consultant to Biotronik. However, with micro MRI, the struts can be seen because of higher resolution. And with intravascular ultrasound, one can "see the struts, nicely opposed to the vessel wall," he said. Imaging showed that the stent degradation process took 2-3 months. ■

VERBATIM

'This is a group of people that came here and did not see water marks on buildings and debris piled up in the street as a negative—they saw it as a positive.'

Dr. Ronald Amedee, on the physicians who filled Tulane University's residency slots, p. 64