New DES Platforms May Cut Thrombosis Risk

BY BRUCE JANCIN
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Snowmass, Colo. — Some of the most exciting of the drug-eluting stent platforms working through the developmental pipeline have the potential to curb the vexing problem of late stent thrombosis, Dr. Robert M. Bersin said at a conference sponsored by the Society for Cardiovascular Angiography and Interventions.

Furthest along of these is the BioMatrix stent system being developed by Biosensors International. It consists of a stainless-steel stent, a poly-L-lactide polymer as the drug-delivery vehicle, and the drug itself, a sirolimus analogue called Biolimus A9.

The technologic advantage of BioMatrix is that its drug-delivery polymer is the first to be fully bioabsorbable. That means there will be no residual polymer to flake off or promote inflammation.

"This polymer will disappear over time with no coating left behind, which is one of the issues we are currently evaluating as a potential factor in late stent thrombosis," explained Dr. Bersin, director of clinical research at the Washington Cardiovascular Research and Education Foundation, Seattle.

The sirolimus analogue is more lipophilic and elutes faster than the parent drug. It seems to be performing well, with an average in-stent late lumen loss at 6 months of only 0.26 mm, compared with 0.74 mm with a bare-metal stent (BMS). A trial to be reported later this year will give a good idea of how BioMatrix performs relative to drug-eluting stents (DESs) now on the market, he added.

A recent meta-analysis of all eight randomized prospective trials of the sirolimus-eluting Cypher stent and the paclitaxel-eluting Taxus paclitaxel stent clearly shows late stent thrombosis is a problem with both devices.

The BioMatrix stent's drug-delivery polymer is fully bioabsorbable, meaning there will be no residual polymer to flake off or promote inflammation.

Thrombosis rates with the two were superimposable upon those of BMSs out to about 18 months. Then the curves diverged. At 3 years, the stent thrombosis rate was 1.1% with Cypher and 1.3% with Taxus. Each rate was an absolute 0.5% more than with BMS comparators.

"Late stent thrombosis is a big issue today with drug elution," Dr. Bersin stressed. "This is a consistent issue with drug-eluting stents, regardless of brand."

A recent analysis showed that prior brachytherapy was the strongest predictor of stent thrombosis in patients with a DES. Renal failure was second, followed by anatomically difficult features, such as bifurcation lesions, and diabetes.

Numerous manufacturers are developing fully biodegradable DESs constructed of poly-L-lactide or other polymers. Because the materials lack the mechanical strength of traditional stainless steel or cobalt-chromium, sophisticated designs have been used to increase radial strength. These stents will not only eliminate the obstacles to repeat revascularization posed by permanent metal stents, but they could also solve the late thrombosis problem.

Berlin-based Biotronik AG is conducting clinical trials of a magnesium alloy–based DES that biodegrades through controlled corrosion. The appeal is that it may provide a temporary metal scaffolding with the same strength and performance characteristics as a permanent BMS, Dr. Bersin said.

A new paradigm for restenosis prevention is being developed by OrbusNeich. Its Genous stent, rather than locally delivering cytotoxic drugs to curb an overzealous vascular intimal healing response, is designed to enhance function of endogenous modulators to promote more efficient healing.

The Genous metallic stent is coated with a fragment of antibody to CD34 in order to capture circulating endothelial progenitor cells to accelerate endothelialization. In animal studies, the BMS still had bare struts 48 hours after implantation, while the Genous stent was completely coated with a monolayer of endothelial cells. Clinical trials are ongoing in Europe.

"This could offer a clear advantage in terms of stent thrombosis risk, especially in patients unable to take high-level antithrombotic agents for various reasons," the cardiologist said.

Another highly original stent platform design is a Conor DES containing nearly 600 laser-cut wells in the struts. These wells can be filled with two different drugs with a barrier layer in between—for example, an antiproliferative agent on the stent's intimal side and an antithrombotic drug on the luminal side. At least that's the plan; so far the wells have held only a single cytotoxic drug in trials. ■

Point/Counterpoint

Is carotid stenting safe for octogenarians?

Stent Older Patients With Care

The decision to place a carotid stent in a patient aged 80 years or older must be made cautiously, based on evidence that the outcomes of these patients are substantially worse than the outcomes of younger patients.

Although results from a randomized trial are not available, we reviewed the outcomes of 382 patients who received carotid stents during June 1996 and March 2004 at the University of Pittsburgh. About twice as many octogenarians died or had a stroke or myocardial infarction during the year after placement of a carotid stent compared with younger patients. During the first 30 days, there were nearly three times as many major adverse events among older patients. Neither symptom status nor use of embolic protection affected this finding.

Our series included patients who were entered into 1 of 10 different regulatory trials, but nearly a third were treated outside of a study. A variety of stent brands were used. Cerebral protection devices were used routinely starting in 2000; overall, protection devices were used in 62% of the older patients and in 52% of younger patients. The prevalence of asymptomatic carotid artery stenosis was 71% in patents aged 80 or older, and 74% in patients younger than 80.

During the first 30 days after the procedure, the incidence of death, stroke, or myocardial infarction was 9.2% in the octogenarian patients and 3.4% in younger patients.

One year post procedure, the combined rate for major adverse events was 25% among patients aged 80 or older compared with 13% among younger patients, (J. Vasc. Surg. 2006;43:297-304). Only 56% of patients were available for follow-up after 1 year. In a multivariate analysis that assessed 26 variables, the only factors significantly associated with major, adverse events at 30 days after treatment was octogenarian status, which raised risk 2.9-fold, and preprocedural treatment with aspirin, which cut risk by 77%.

Questions about the safety of carotid stenting in the elderly became more pressing with the results from the lead-in phase of the Carotid Revascularization Endarterectomy Versus Stent Trial (CREST), which in 2004 showed that in 749 patients the rate of death or stroke at 30-day follow-up was nearly threefold higher in older patients compared with those younger than 80. Future results from randomized studies will determine whether carotid stenting, endarterectomy, or medical management is the best option for patients aged 80 or older. ■

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Reconsider Your Medical Options

Increasingly, questions are being raised about the appropriateness of carotid artery stenting in patients aged 80 years or older who do not have symptoms of carotid artery disease.

Recent advances in carotid-disease medical management and an increased awareness of the dangers of stenting in elderly patients is leading to a paradigm shift in the way asymptomatic carotid disease is managed in octogenarians.

Medical management is now better than ever, with clopidogrel (Plavix) and statins joining aspirin as the cornerstones of therapy. Patients also can benefit from the many other drugs available.

And endarterectomy is still a viable option for selected patients. In fact, there is a growing realization that surgery may be a safer alternative than stenting for asymptomatic patients aged 80 or older.

Asymptomatic patients who are at low risk for a poor outcome from carotid stenting remain good candidates for the procedure. But recent experience has shown that higher-risk patients who are refused surgery because of their increased risk fare no better when they are instead treated with carotid stenting.

Additional evidence documenting the poor outcome of octogenarians comes from the Carotid Acculink/Accunet Postapproval Trial to Uncover Rare Events (CAPTURE), a postmarketing approval study sponsored by Guidant. Results from this study were recently reported by Dr. Jay S. Yadav of the Cleveland Clinic. About 25% of the 1,603 patients in CAPTURE were aged 80 or older.

Among the 1,224 patients aged younger than 80 in the study, the rate of death, stroke, or myocardial infarction during the first 30 days after carotid stenting was 4.3%, compared with a 7.7% rate among the 378 patients aged 80 or older.

Among the 1,446 (90%) of patients in the study who were asymptomatic, the rate of death, stroke, or myocardial infarction was 3.5% among the 1,116 patients who were aged younger than 80, and 6.4% among the 330 patients who were octogenarians.

Octogenarians also seem especially vulnerable to neurologic deficits that occur secondary to carotid stenting, even when an embolic filter is used. Microemboli that are too small to be caught by the distal filter flow from the carotid into the brain during stenting and may cause neurologic deficits, although this effect has not been measured in major studies. This may be why surgery is safer for these patients; endarterectomy does not seem to produce microemboli. ■

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