Cost-Effectiveness of Drug-Eluting Stents Grows With Time

BY MITCHEL L. ZOLER
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WASHINGTON — By the first few months of this year, drug-eluting coronary stent had become more cost effective than ever before. Based on the price of drug-eluting stents, the average number of stents used per patient, and their efficacy at cutting the rate of restenosis, drug-eluting stents are now cost effective in any patient who would have a risk of restenosis of 10% or more if treated with bare-metal stents, David J. Cohen, M.D., said at a meeting sponsored by the Cardiovascular Research Institute of the Washington Hospital Center.

In contrast, based on last year’s averages, drug-eluting stents were cost effective whenever the restenosis rate with bare-metal stents was 12% or greater (CARDIOLOGY NEWS, March 2005, p. 7).

The upshot is that drug-eluting stents now make economic sense in wider coronary arteries and in vessels with shorter lesions. It is reasonable from an economic standpoint to use drug-eluting stents in most patients with coronary artery disease, Dr. Cohen, associate director of interventional cardiology at Beth Israel Deaconess Medical Center in Boston.

Drug-eluting stents add no incremental cost when used in patients with an expected restenosis rate with bare-metal stents of at least 10%.

In early 2003, the difference in cost of a drug-eluting coronary stent over a comparable bare-metal stent in most patients with coronary artery disease, Dr. Cohen, associate director of interventional cardiology at Beth Israel Deaconess Medical Center in Boston. At Dr. Cohen’s center, patients who had drug-eluting coronary stents placed in late 2004 received an average of 1.6 stents each. And the most current data from studies that compared drug-eluting stents with bare-metal stents showed that drug-eluting stents cut the need for target vessel revascularization by about 82%.

One additional issue for a cost-effectiveness calculation is that patients who receive drug-eluting stents require daily treatment with clopidogrel for several months, a regimen that costs about $120 per month.

Crunching all of these costs—adding a cost-savings number together yields the estimate that placement of a drug-eluting stent adds no incremental cost when used in patients with an expected restenosis rate with bare-metal stents of at least 10%.

Based on an analysis done by Dr. Cohen and his associates in the late 1990s, virtually all patients with diabetes have a restenosis rate of 10% or greater with bare-metal stents. The only exceptions are patients with lesions that are less than 30 mm in length that are in coronary arteries that are at least 4.0 mm in diameter. Among patients without diabetes, the risk is less than 10% with bare-metal stents occurs in all coronary arteries that are 4.0 mm in diameter or greater, regardless of lesion length, and in vessels that are 3.5 mm in diameter or greater if the lesion length is less than 25 mm.

When it comes to their clinical effect, “we know that most patients can accommodate a certain amount of stenosis before it overwhelmed their coronary flow reserve,” Dr. Cohen said. “So that target vessel revascularization rate is only 7% when late loss is 0.70 mm. A 0.62 mm late loss rate would not be expected to cause much target lesion revascularization,” he said.

“Late loss is significantly greater with the Endeavor stent than with other drug-eluting stents, but it is still low enough to produce excellent freedom from restenosis,” Dr. Stone concluded.

Another factor is that the ENDEAVOR II study mostly used patients with a low risk of drug-eluting stent restenosis. If the stent is tested in higher-risk patients or in higher-risk lesions, such as those in narrow coronary arteries, it’s possible that the higher rate of late loss will make a clinical difference, commented Lauri Mauri, M.D., a cardiologist at Brigham and Women’s Hospital in Boston.

Nonetheless, the Endeavor stent may have other attributes that make it an attractive option. The Driver bare-metal stent that’s the platform for the ABT-578-eluting stent was easy to use. Plus, the Endeavor stent uses a biocompatible phosphorylcholine coating that binds the drug layer to the metal stent. The sirolimus and paclitaxel-eluting stents use a polymer coating. The phosphorylcholine coating may explain why the rate of late thrombosis in the ENDEAVOR II study was so low, 0.7%. The polymer coats on the other drug-eluting stents may, in part, be why they have led to some problems with late thrombosis, Dr. Mauri said. But a study designed to definitively show whether these stents differ in their rate of late thrombosis would require several thousand patients.

New Stent Promising Despite High Late-Loss Rate

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ORLANDO, FLA. — A new type of drug-eluting coronary stent was safe and effective in its first phase III clinical trial, compared with a similar bare-metal stent in about 1,200 patients. But the trial raised novel issues on how effective drug-eluting stents must be at stopping the growth of coronary artery endothelium in order to prevent restenosis and the need for revascularization. That’s because the new stent, brand named Endeavor and coated with a sirolimus-like drug called ABT-578, was successful at capping the target-lesion revascularization rate at 4.6% after 9 months, despite allowing a surprisingly high average late lumen loss of 0.62 mm within stented coronary arteries.

The current paradigm is that inflating a balloon leads to a vascular response to injury that promotes intimal proliferation, restenosis, and (cardiac) events; but it didn’t work that way in this study, commented Lloyd W. Klein, M.D., at the annual meeting of the American College of Cardiology in Atlanta. The study was sponsored by Medtronic Inc., which makes both the Endeavor and Driver stents.

Two other studies, both funded by Medtronic and now in progress, are comparing the Endeavor stent with the two competing drug-eluting stents on the U.S. market. One study matches the Endeavor and sirolimus-eluting (Cypher) stents; the other matches the Endeavor and paclitaxel-eluting (Taxus) stents. Medtronic will not seek U.S. marketing approval for the Endeavor stent until results from these studies are in.

In the current study, the ABT-578-eluting stent also looked good by other clinical end points: the 4.6% rate of target-lesion revascularization with the drug-eluting stent, compared with a 12.1% rate with the bare-metal stent; and the 0.5% rate of stent thrombosis during 9 months with the drug-eluting stent, compared with 1.2% with the bare-metal stent.

But this drug-eluting stent was less successful by the angiographic measures that were collected in 89% of the first 600 patients enrolled in the study. Although the mean late loss of 0.62 mm in the drug-eluting stents improved on the 1.03-mm rate of late loss with the bare-metal stent, it’s a higher rate than has been seen in prior studies or with other types of drug-eluting stents. Similarly, the in-stent binary restenosis rate of 9.3% with Endeavor in this study improved on the 32.7% rate with bare-metal stents, and was a higher restenosis rate than in earlier studies with other brands of drug-eluting stents.

The late loss itself is a higher rate than has been seen in prior studies or with other types of drug-eluting stents. Similarly, the in-stent binary restenosis rate of 9.3% with Endeavor in this stent was much lower than the 33.9% rate with bare-metal stents, and was a higher rate than has been seen in prior studies or with other types of drug-eluting stents.

What explains this apparent paradox? “We know that most patients can accommodate a certain amount of stenosis before it overwhelmed their coronary flow reserve,” Dr. Cohen said. “So that target vessel revascularization rate is only 7% when late loss is 0.70 mm. A 0.62 mm late loss rate would not be expected to cause much target lesion revascularization,” he said.

“We go from a marked difference in biologic response to no difference in clinical results,” said Dr. Stone, although he also warned that these data were collected in three different studies, and comparisons across studies must be done cautiously.

He hypothesized that the difference in late-loss rates may stem from differences in drug-elution rates. “You wouldn’t expect such a difference in biologic responses based on any difference in the drugs.” But 73% of the sirolimus-eluting stent patients had late loss of 0.55 mm in the drug-eluting stent, whereas 80% of the paclitaxel-eluting stent patients had late loss of 2.05 mm in the drug-eluting stent. “It’s plausible that the difference in relation rates at least partially explains the difference in vascular effects between the two stents,” he said.

Patients don’t care about their intimal thickness; they care about whether they need to come back to the cath lab,” said Dr. Klein of Gottlieb Memorial Hospital in Melrose, Ill.

In the study, named ENDEAVOR II, 1,197 patients were enrolled at 72 centers in Europe, Asia, and Oceania. About 20% of patients had diabetes. The study’s primary end point was the composite incidence of cardiac death, non-fatal myocardial infarction, or need for target-vascular revascularization during 9 months of follow-up. The incidence of this composite end point was 8.1% in patients who received the drug-eluting stent and 15.4% in patients who received a comparable bare-metal stent (Driver), reported William Wijns, M.D., codirector of the Cardiovascular Centre at OLV Hospital in Aalst, Belgium. The study was sponsored by Medtronic Inc., which makes both the Endeavor and Driver stents.

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