Sirolimus-Eluting Stent Bests Rivals for Efficacy

BY MITCHEL L. ZOLER

ORLANDO — The largest comparison to date of the three drug-eluting coronary stents on the U.S. market showed that the sirolimus-eluting stent was significantly more effective and at least as safe as were the other two models, on the basis of results from a Korean study with more than 2,600 patients.

The most notable difference among the sirolimus-, zotarolimus-, and paclitaxel-eluting coronary stents compared in the study was the 12-month rate of ischemia-driven target-lesion revascularization (TLR), which occurred at a rate of 1.4% in 878 patients who received one or more sirolimus-eluting coronary stents (SES), Dr. Seung-Jung Park said at the annual meeting of the American College of Cardiology.

This rate was significantly below the 4.9% TLR rate among the 883 patients who received the zotarolimus-eluting stents (ZES), and significantly less than the 7.6% rate among the 884 patients who received paclitaxel-eluting stents (PES).

Despite the clear efficacy advantage of SES in this study, "the definitive answer" regarding the relative long-term safety of the three stent types will not be available until results are reported from a controlled study now underway with more than three times as many patients, said Dr. Stephan Windecker, head of interventional cardiology at the Swiss Cardiovascular Center in Bern.

Dr. Windecker summarized the findings of three studies, including the new report, that compared ZES and SES, and concluded that SES were "more effective with a similar safety profile as ZES."

He also summarized findings from two studies, including the new report, that compared ZES and PES and concluded that ZES "were at least as effective with a better safety profile than PES."

The better safety profile of ZES compared with PES was based on the rate of MIs in a combined analysis of the ZEST results and findings from the ENDEAVOR IV study, which compared ZES and PES in about 1,500 patients. The combined results showed that ZES reduced the rate of MIs by 30% compared with the rate in PES recipients, a statistically significant difference, said Dr. Windecker.

He disclosed that he has received consulting fees from Cordis Corp., a Johnson & Johnson company that markets the SES (Cypher); from Boston Scientific, the company that markets the PES (Taxus Liberte); and from Medtronic, the company that markets the ZES (Endeavor).

The Zotarolimus-Eluting Stent Versus Sirolimus-Eluting Stent and Paclitaxel-Eluting Stent for Coronary Lesions (ZEST) trial was done at 19 centers in South Korea. It enrolled unselected patients who required coronary stenting to treat silent ischemia, stable angina, unstable angina, or non–ST-elevation myocardial infarction. The study excluded patients with ST-elevation MI, left main disease, in-stent restenosis, severe left ventricular dysfunction, or cardiogenic shock.

The study was sponsored in part by Medtronic. Dr. Park said that he and all of his associates had no other financial relationships to disclose.

The average patient age was 62, and two-thirds were men. A quarter of the patients had diabetes. The most common indication for stenting was unstable angina, in 47%, followed by stable angina, in 39%. An average of 1.6 stents were placed in each patient. The total lesion length stented was more than 20 mm in 55% of patients, and 10-20 mm in 40%.

The study's primary end point was the combined rate after 12 months of death from any cause, MI, and ischemia-driven target-vessel revascularization. The combined rate was 8.3% in the SES patients, 10.1% in the ZES patients, and 14.2% in those treated with PES, reported Dr. Park, director of interventional cardiology at the Asian Medical Center in Seoul, South Korea. The difference in rates between the ZES and PES patients was statistically significant; the difference between the ZES and SES groups was not significant.

The significant efficacy differences among the three groups was confined to differences in the rates of target-vessel revascularization and TLR. The rates of death and MI were similar in the three groups.

The rate of definite or probable stent thrombosis was significantly lower in the SES group, with no stent thrombosis at all, compared with the ZES patients (a 0.7% rate) and the PES patients (0.8%). The overall low rate of stent thromboses makes the risk estimates "imprecise," Dr. Windecker said. ■

Drug-Eluting Stent Safety Concerns Are 'Laid to Rest'

BY BRUCE JANCIN

ORLANDO — The largest study of coronary stenting ever conducted has documented significantly better clinical outcomes with drug-eluting than with bare-metal stents.

The observational study involving 262,700 Medicare patients with 30-month follow-up found a 25% decrease in deaths and a 23% reduction in myocardial infarctions in drug-eluting stent (DES) recipients after adjustment for 102 potential confounding variables.

Moreover, there was no hint of a late increase in stent thrombosis in the 83% of patients who received DES, contrary to the findings in a number of earlier, far smaller randomized trials.

"The concerns about the safety and effectiveness of these devices, I think, have been laid to rest," Dr. Pamela S. Douglas said in presenting the study findings at the annual meeting of the American College of Cardiology.

"We feel that our sample size of over a quarter-million patients makes our data much more robust than what's been out there, and we can now say with some confidence that drug-eluting stents are not killing people," added Dr. Douglas, professor of research in cardiovascular medicine at Duke University, Durham, N.C., and director of the cardiovascular imaging program at the Duke Clinical Research Institute.

The most remarkable feature about this study, according to many observers, was its unique design. The study was carried out by linking data from the ACC–National Cardiovascular Data Registry to Medicare claims data without using patient names or other individual identifiers. This was accomplished through sophisticated statistical techniques involving a weighted probability matching process.

Adjusted rates of revascularization and bleeding were 9% lower in patients who received drug-eluting stents than in those who received bare metal stents. Rates of late stent thrombosis could not be looked at directly, so the investigators analyzed the incidence of ST-elevation myocardial infarction as a marker. They found no late excess in DES recipients.

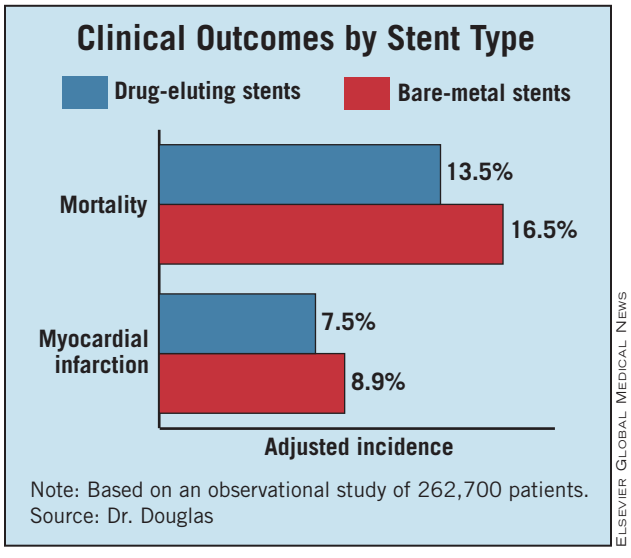
'Our sample size of over a quarter-million patients makes our data much more robust than what's been out there.'

DR. DOUGLAS

Small randomized trials have shown no significant reduction in rates of death or MI but a large decrease in coronary revascularization with DES—just the opposite of the findings in this huge real-world study. Because of this discrepancy, Dr. Douglas and coworkers did a subanalysis limited to the less than 20% of patients in their study population who fit the eligibility criteria for the major stenting randomized trials. The results were "exactly the same" as in the full study, according to the cardiologist.

Although the huge patient numbers involved in the new study were dazzling, not everyone found the results compelling.

"I didn't see anything terribly illuminating here. In every registry the people who get the drug-eluting stents do better. But why do they do better? That's the real question," Dr. Spencer B. King III said in an interview.



Note: Based on an observational study of 262,700 patients.
Source: Dr. Douglas

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The answer, he added, almost certainly lies in unmeasured confounding variables that simply cannot be controlled for in an observational study, no matter how big.

For example, the study database did not contain information on long-term use of dual antiplatelet therapy including clopidogrel (Plavix), but the use of such therapy was surely greater in DES recipients, which could explain their lower rates of mortality and MI.

And selection bias was likely at work, too; some patients are probably selected for bare metal stents because they're sicker, unable to afford costlier DES, or deemed unlikely to comply with dual antiplatelet therapy, according to Dr. King, executive director for academic affairs at Saint Joseph's Health System in Atlanta.

Discussant Donald E. Cutlip of Beth Israel Deaconess Medical Center, Boston, also cited confounding issues as a study limitation, but said that the study nonetheless carries an important message: "It's not that drug-eluting stents should now be used in all patients because of their improved safety, but that with appropriate device selection, using bare metal stents in the right patients, we can still treat a large proportion of patients with drug-eluting stents safely, including possibly with reductions in death and MI," Dr. Cutlip said.

The study was published simultaneously with Dr. Douglas's presentation (J. Am. Coll. Cardiol. 2009;53:1629-41).

The study was sponsored by the Agency for Healthcare Quality and Research. Dr. Douglas reported having no financial conflicts of interest. ■