Sirolimus-Eluting Stents Edge Past Paclitaxel Stents

BY MITCHEL L. ZOLER
Philadelphia Bureau

ORLANDO, FLA. — Three more salvos were fired in the battle of competing drug-eluting coronary stents. When the smoke cleared and findings from the new head-to-head trials were reported at the annual meeting of the American College of Cardiology, the sirolimus-eluting stent, Cypher, had edged the paclitaxel stent, Taxus, in two studies, with the third and largest trial ending in a draw.

With the results from at least four head-to-head studies now reported (results from the fourth were reported last August at the annual meeting of the European Society of Cardiology), the sirolimus-eluting stent has shown some consistent advantages.

The biggest difference between the two types of coronary stents was seen in a study with 1,012 patients who were randomized to treatment with either sirolimus- or paclitaxel-eluting stents at two Swiss university hospitals, in Bern and Zurich. The randomized comparison of a sirolimus- with a paclitaxel-eluting stent for coronary revascularization, named SIRTAX, was funded by the hospitals and received no industry sponsorship, said Stephan Windecker, M.D., a cardiologist at the University Hospital in Bern.

The study randomized all comers who required coronary stenting. Slightly more than half of the patients had acute coronary syndrome, almost a quarter had triple-vessel disease, and about 20% had diabetes. About 8% of patients had ostial lesions, another 8% had lesions at bifurcations, 35% had calcified lesions, 37% had lesions of moderate or excessive tortuosity, and 2% of lesions were in saphenous vein grafts.

All patients were treated with 75 mg clopidogrel daily for a year following stenting, and all received 100 mg aspirin daily indefinitely.

The study's primary end point was the combined incidence of cardiac death, myocardial infarction, or ischemia-driven target lesion revascularization (TLR) within 9 months of treatment. The rate of this combined end point was 6.2% in the 503 patients who received sirolimus-eluting stents and 10.8% in the 509 patients who received paclitaxel-eluting stents, a statistically significant difference.

This outcome was driven largely by the difference in the need for TLR: 4.8% among patients who received sirolimus-eluting stents and 8.3% among those who got paclitaxel-eluting stents, also a statistically significant difference. All of the secondary end points also favored the sirolimus-eluting stent, although some of these were not statistically significant.

The advantage in the primary, combined end point for the sirolimus-eluting stents was especially dramatic in patients with diabetes. In this subgroup, sirolimus-eluting stents were associated with a better than threefold reduction in events, compared with the paclitaxel-eluting stents. The advantage was half as large in patients without diabetes. The two groups had identical rates of stent thrombosis.

Patients who received sirolimus-eluting stents also had significantly less angiographic restenosis than did those who got paclitaxel-eluting stents.

An even larger, higher-profile trial failed to show a clear advantage for either type of stent. The highly anticipated prospective randomized multicenter head-to-head comparison of the sirolimus-eluting stent (Cypher) and the paclitaxel-eluting stent (Taxus) trial, named REALITY, was done at 90 centers in Europe, Asia, South America, and Mexico (but not in the United States), enrolled 1,353 patients, and was sponsored by Cordis, the company that makes and markets the sirolimus-eluting, coronary stent.

This study involved a more highly selected group of patients, excluding those with ostial lesions, recent MIs, total occlusions, and certain other high-risk conditions. But 28% of patients had diabetes. After stenting, all patients received 100 mg of aspirin indefinitely. Daily treatment with a thienopyridine (clopidogrel or ticlopidine) was used for at least 2 months in all patients who received sirolimus-eluting stents and for at least 6 months in all patients who got paclitaxel-eluting stents.

The study's primary end point was the rate of in-lesion binary restenosis at 8 months after stenting, as measured by quantitative coronary angiography. This rate was 9.6% in the sirolimus-eluting stents and 11.1% in the paclitaxel-eluting stents, a difference that was not statistically significant, reported Marie-Claude Morice, M.D., a cardiologist at the Cardiovascular Institute in Paris.

Other important clinical end points also failed to show a statistically significant difference between the two stent types. The combined rate of major coronary end points—cardiac death, MI, and TLR, was 9.2% in the patients who received sirolimus-eluting stents and 10.6% in those who received paclitaxel-eluting stents. The difference in the revascularization rate only was even tighter: 5.0% in the sirolimus-eluting stent group and 5.4% in those who got paclitaxel-eluting stents.

The only major differences between stent types in this study were in late, in-stent lumen loss after 8 months, and in the rate of stent thrombosis during the first 30 days after treatment. Late loss averaged 0.1 mm with the sirolimus-eluting stents and 0.3 mm with the paclitaxel stents. Stent thrombosis occurred in 0.4% of patients who received sirolimus-eluting stents and in 1.8% of those who received paclitaxel-eluting stents. But the rate of stent thrombosis was not a prespecified end point for this study and a difference between the two stent types for this measure was unexpected. As a result, the clinical significance of this finding was unclear, Dr. Morice said.

The third set of study results presented at the meeting came from a single-center study with a total of 250 patients, all of whom had diabetes. Like the larger Swiss trial, this study had no commercial funding; the paclitaxel-eluting stent versus sirolimus-eluting stent for the prevention of restenosis in diabetic patients with coronary artery disease study, named ISAR-DIABETES, was sponsored solely by the German Heart Center in Munich.

This study had fewer exclusion criteria than the REALITY study. Exclusions were limited to patients with acute MI, left-main disease, in-stent restenosis, or an allergy to one of the study drugs.

The study's primary end point was the rate of in-segment, late lumen loss at 6-8 months after stenting, as measured by angiography. Follow-up angiography was done in 82% of patients. The average amount of late loss was 0.43 mm in patients who received sirolimus-eluting stents and 0.67 mm among those who got paclitaxel-eluting stents, a difference that was statistically significant, reported Adnan Kastrati, M.D., a professor of cardiology at the German Heart Center.

Patients who received sirolimus-eluting stents also had significantly less angiographic restenosis compared with those who got paclitaxel-eluting stents, 6.9% compared with 16.5%, respectively. But the results failed to show statistically significant differences in clinical end points. The rate of clinical restenosis was 6.4% in the patients who got sirolimus-eluting stents and 12.0% in those who received paclitaxel-eluting stents, a statistically nonsignificant difference. And the rates of death and MI at 9 months after stenting were similar in the two treatment groups.

Although the results from this third study showed differences only for angiographic end points but not for clinical end points, Dr. Kastrati said that he was convinced by the outcome. "The results will push us to select sirolimus-eluting stents for patients with diabetes," he said.

Last August, Dr. Kastrati reported the results from a fourth study that compared the two stent types, in 200 patients with in-stent restenosis. In that study, patients who received sirolimus-eluting stents had significantly less clinical restenosis than did patients who received paclitaxel-eluting stents. ■

Three Risk Factors Predict Stroke in Patients Undergoing CABG

BY DEBRA WOOD
Contributing Writer

ORLANDO, FLA. — Age greater than 70 years, abnormal preoperative neurologic status, and prior cardiac surgery are independent risk factors for stroke related to coronary artery bypass graft, Scott Woods, M.D., said at the annual meeting of the American Academy of Family Physicians.

"If you have a patient who needs CABG and has none of these three predictors, which are easy to determine by exam and history in the office, the risk of stroke is 1%," said Dr. Woods, director of epidemiology at the Bethesda Family Practice Residency Program, Cincinnati. "But if he has all three risk factors, the chance is one in three."

Cerebrovascular accidents (CVAs) are well-known adverse events associated with CABG surgery, occurring in about 3% of all cases, Dr. Woods said.

"If the predictors of this catastrophic event could be found, we could possibly avoid the events for those at greatest risk," he said. "That was the purpose of our project."

If your patient needs CABG and he has none of these three predictors, the risk of stroke is 1%, but if he has all three, the risk is 33%.

Dr. Woods conducted a nested case-control study to identify the risk factors. He used a 9-year, prospective cohort that included 6,245 patients who had CABG between October 1993 and June 2002.

Cases were matched to controls in a one-to-three ratio: There were 171 patients who had a stroke and 513 controls. The CVA rate at the facility was 2.7%, very close to the national average. The study population was primarily white, with few Hispanic and Asian patients.

Dr. Woods considered 38 variables, including medical history and operative factors, such as pump time and perfusion time. Regression analysis uncovered three independent predictors of stroke.

Age older than 70 years was associated with a 4.6-fold increase in risk. Abnormal neurologic findings such as slurred speech or hemiparesis prior to surgery upped the chance of a stroke by a factor of 4.24, and previous cardiac surgery was associated with a 1.75-fold increase in risk.

The research also indicated that if the patient had one of the two stronger predictors—age over 70 or abnormal neurologic findings—the risk was 1 in 25 (4%) that he or she would suffer a CVA associated with the surgery. A patient aged 70 years or older who also had an abnormal neurologic finding during the preoperative exam had a one in five (20%) risk of suffering a CVA. If all three risk factors were present, the chance of suffering a CVA was one in three (33%).

If the patient's risk of stroke is 20% or 33%, "you certainly need to counsel them on it," Dr. Woods said. The patient may find the risk to be too high. "Obviously, it's a judgment call." ■