Stenting, CABG Compared in Multivessel Disease

ARTICLES BY
MITCHEL L. ZOLER
Philadelphia Bureau

ORLANDO, FLA. — Stenting may have finally edged past coronary bypass surgery for treating multivessel coronary disease, according to the results from an uncontrolled series of 607 patients who underwent revascularization using drug-eluting stents.

One year after patients underwent multivessel revascularization with sirolimus-eluting (Cypher) coronary stents, their rate of major adverse events was better than the rate in a similar series of patients who underwent coronary bypass graft (CABG) surgery in the late 1990s, Patrick Serruys, M.D., said at the annual meeting of the American College of Cardiology.

"This study is a breakthrough," commented Valentin Fuster, M.D., director of the cardiovascular institute at Mount Sinai Medical Center in New York. "Even though this was not a prospective, randomized, controlled study, I'm convinced that for patients with multivessel disease, drug-eluting stents may have more of an impact today on the rate of death and myocardial infarction than coronary artery bypass grafting."

The biggest question remaining is whether surgery or drug-eluting–stent placement is the best treatment for such patients with diabetes. In the new study, 26% of enrolled patients had diabetes, so the applicability of the results to patients with diabetes remains unclear.

In this multicenter series, 54% of patients had triple-vessel disease, and 46% had two-vessel disease. All patients were treated with percutaneous coronary intervention using sirolimus-eluting coronary stents. The Arterial Revascularization Therapies Study Part II (ARTS II) was designed to test whether multivessel stenting was not inferior to CABG.

The study's primary end point was the combined rate of death, MI, stroke or transient ischemic attack, and need for revascularization 1 year after treatment. This combined rate was 10.4%, reported Dr. Serruys, chief of interventional cardiology at the thorax center of Erasmus University in Rotterdam, the Netherlands.

This rate was compared with the 11.7% rate in a very similar series of 605 patients who underwent CABG during the late 1990s in ARTS I, said Dr. Serruys.

In ARTS II, the incidence of death was 1.0%, the rate of cerebrovascular events was 0.8%, the rate of MI was 1.2%, and the rate of clinically necessary revascularization procedures was 7.4%. (See box.)

In the historic series of CABG patients, the 1-year rate of death was 2.7%, the rate of cerebrovascular events was 1.8%, the rate of MI was 3.5%, and the rate of clinically necessary revascularization was 3.7%.

Comparison of the combined adverse events showed that stenting was not inferior to CABG. The results further showed that stenting was statistically superior to bypass surgery after 1 year of follow-up, said Dr. Serruys.

After adjustment for baseline differences in the patients enrolled in both studies, the combined rate of major adverse events was 8.1% in the patients who underwent stenting and 13.1% among the patients who had bypass surgery.

The superiority of stenting with sirolimus-eluting stents in ARTS II contrasted with the results of the bare-metal–stent arm of ARTS I. In that series of 600 patients, done concurrently with the coronary bypass arm, the combined rate of major adverse events was 26.5% after 1 year, primarily because the rate of clinically necessary revascularization was 17.0%.

The difference in revascularization rates between ARTS I, with bare-metal stents, and ARTS II, with drug-eluting stents, "shows the difference that drug-eluting stents make," commented Fayez Shamoon, M.D., a cardiologist at St. Michael's Medical Center in Newark, N.J. Based on the new results, "most interventional cardiologists would be willing to treat triple-vessel disease with a drug-eluting stent," except in patients with diabetes, left main disease, or a left ventricular ejection fraction of 35% or less, he told this newspaper. ■

Major Adverse Event Rates After 1 Year

	Drug-Eluting Stent ARTS II (n = 607)	CABG ARTS I (n = 605)	Bare-Metal Stent ARTS I (n = 600)
Revascularization	7.4%	3.7%	17.0%
Myocardial Infarctions	1.2%	3.5%	5.0%
Deaths	1.0%	2.7%	2.7%
Cerebrovascular Events	0.8%	1.8%	1.8%

Source: Dr. Serruys

High Loading Dose of Clopidogrel Cuts Occurrence of MIs During Intervention

ORLANDO, FLA. — A 600-mg loading dose of clopidogrel was safe and more effective than the standard 300-mg dose prior to percutaneous coronary intervention in a study with 255 patients.

"Pretreatment with a 600-mg loading dose of clopidogrel given 6 hours before a percutaneous revascularization procedure reduced periprocedural myocardial infarctions and improved short-term prognosis," Germano Di Sciascio, M.D., said at the annual meeting of the American College of Cardiology.

"This is the first study to compare a 600-mg loading dose of clopidogrel with any other dose based on clinical outcomes, and the results are sufficient to change clinical practice," commented Peter Berger, M.D., director of interventional catheterization at Duke University Medical Center, Durham, N.C.

Many physicians already use a 600-mg loading dose, especially for high-risk patients, because it produces quicker and more complete inhibition of platelet activity, noted Dr. Di Sciascio, professor of medicine and chairman of the department of cardiology at the University of Rome. But until now, the safety and efficacy of this dose had not been proven in a clinical study, and official guidelines had continued to endorse a 300-mg loading dose.

The Antiplatelet Therapy for Reduction of Myocardial Damage During Angioplasty (ARMYDA-2) study enrolled patients with effort angina and a positive stress test result or a recent ST-segment elevation acute MI who were scheduled to undergo coronary angiography. All patients underwent catheterization at either of two Italian hospitals: the Campus Bio-Medico of the University of Rome, or the Vito Fazzi Hospital in Lecce. The study received no external funding. Of 329 patients who had angiography, 255 had significant coronary artery disease and went on to have a percutaneous intervention.

An average of 6 hours before revascularization, patients were treated with either a 300-mg or 600-mg dose of clopidogrel. All patients also received aspirin and a weight-adjusted regimen of intravenous heparin. Treatment with a glycoprotein IIb/IIIa receptor antagonist could also be used at the operator's discretion. Following each procedure, all patients continued to receive a standard, daily regimen of aspirin and clopidogrel.

The study's primary end point was the combined rate of death, MI, and target-vessel revascularization at 30 days after the procedure. MI was defined as a postprocedural elevation of serum creatine kinase-MB (CK-MB) to more than three times the upper limit of normal.

This end point was reached in 4% of patients who received a 600-mg loading dose, compared with 12% of patients who received a 300-mg loading dose, a statistically significant difference. There were no deaths. One patient who received the 600-mg dose required revascularization, and five patients in the 600-mg group had an MI. A total of 15 patients in the 300-mg group had an MI.

Several secondary end points also favored the higher loading dose, including any rise in CK-MB above the upper limit of normal, and an increase in troponin I levels.

No patient in the study had a major bleed or needed a transfusion following revascularization.

In a multivariable analysis that controlled for possible confounding factors such as stent length, use of a IIb/IIIa inhibitor, and use of a statin starting before the procedure, treatment with the higher clopidogrel loading dose cut the incidence of periprocedural MI by 52%. Pretreatment with a statin was also associated with a significant 72% reduction in MIs. The effect of statin pretreatment and the 600-mg loading dose was additive: Patients who received both had an 80% reduced risk of a periprocedural MI, Dr. Di Sciascio said. ■

Patients Need Not Stop Clopidogrel for Surgery

WASHINGTON — Patients on long-term clopidogrel treatment don't need to stop the drug before surgery, Richard E. Kuntz, M.D., said at a meeting sponsored by the Cardiovascular Research Institute at Washington Hospital Center.

"There is growing experience that it's safe to perform surgery on a patient taking clopidogrel. At our institution, surgeons will operate on these patients. There is no significant difference in morbidity and mortality" during surgery, said Dr. Kuntz, a cardiologist at Brigham and Women's Hospital in Boston.

This approach to dealing with patients on long-term treatment with the antiplatelet clopidogrel (Plavix) was endorsed also by Ron Waksman, M.D., of the division of cardiology at Washington Hospital Center. "If we push our surgeons, they'll do surgery without waiting to stop clopidogrel," said Dr. Waksman, who chaired the meeting.

The issue of when to stop clopidogrel recently became critical for patients who take the drug after they have received drug-eluting coronary stents. A report last year detailed four anecdotal cases of patients who developed clinically significant coronary thrombosis within a drug-eluting stent after their clopidogrel and aspirin regimens were stopped (Lancet 2004;364:1519-21). In three of these cases, patients had stopped their antiplatelet medications before surgery.

These reports have made experts wary about stopping aspirin and clopidogrel in their patients.

Although standard practice when placing drug-eluting coronary stents is to treat patients with clopidogrel for 2-3 months (for sirolimus-eluting stents) or 6 months (for paclitaxel-eluting stents), Dr. Kuntz recommended continuing the drug even longer.

To prevent stent thrombosis, patients with a drug-eluting stent should continue clopidogrel "as long as possible, as long as they can afford it," he said. ■