Long-Term Clopidogrel After Stenting Improves Survival

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

WASHINGTON — Long-term clopidogrel use appears to improve outcomes—including all-cause mortality and recurrent myocardial infarction—after either bare-metal or drug-eluting stent placement for acute coronary syndrome, Dr. Michael Ho reported at a conference sponsored by the American Heart Association.

His retrospective study found a 60% reduced risk of death in stent patients who continued taking the drug for up to 2 years, compared with those who did not. There were also significantly reduced risks of hospitalization for acute myocardial infarction and the combined end point of death and acute MI, Dr. Ho said in an interview.

"These findings are hypothesis generating because of the observational nature of the study, and they suggest the urgent need for a randomized clinical trial to assess the efficacy of extended clopidogrel use among ACS patients receiving stents," said Dr. Ho, a cardiologist at the Denver Veterans Affairs Medical Center.

The findings are particularly intriguing "given the broader concerns of late events in drug-eluting stent patients," he said.

Data were extracted from a national sample of 1,455 acute coronary syndrome patients admitted to 127 VA medical centers during 2003-2004. The patients' mean age was 64 years. Twenty-one percent had previously experienced an MI; 19% had diabetes. Cerebrovascular disease was present in 5%, and 24% had reduced left ejection fraction.

All presented with acute MI or unstable angina and underwent percutaneous coronary intervention with the placement of a bare-metal or drug-eluting stent.

All of the patients were prescribed clopidogrel at discharge. Dr. Ho compared mortality and MI hospitalization rates between those who were still taking the drug and those who were not, using pharmacy records with a median follow-up of 18 months.

Overall, there was a 60% reduced risk of all-cause mortality in those who continued to take the drug, with both stent groups reaping a similar benefit (bare-metal stent, hazard ratio 0.36; drug-eluting stent, HR 0.48).

There was also a significantly reduced overall risk of another acute MI (HR 0.55) and the combined end point of all-cause mortality and acute MI (HR 0.51).

The magnitude of association between clopidogrel use and reduced mortality was consistent throughout the entire 18 months, Dr. Ho said. In the first 6 months, the reduced risk was 0.36; at 7-12 months, it was 0.43; and at 13-18 months, it was 0.37.

"This theory should be tested immediately in a randomized clinical trial," he said.

"Observational studies like this really raise the question of whether we should be giving these patients clopidogrel for longer periods than current guidelines recommend." ■

Endothelial Dysfunction Linked to Sirolimus Stents

BY JEFF EVANS
Senior Writer

WASHINGTON — Sirolimus-eluting stents may induce coronary endothelial cell dysfunction in arterial segments that are distal to their placement, unlike conventional percutaneous coronary interventions, according to the results of a small study.

The antiproliferative effect of sirolimus-eluting stents inhibits neointimal hyperplasia, but this effect also may impair endothelial cell proliferation in the area distal to the stent. This could "potentially lead to coronary endothelial dysfunction," said Dr. Kasai of the department of cardiology at Shinshu University, Matsumoto, Japan.

In a study that he presented at the annual meeting of the Society of Nuclear Medicine, Dr. Kasai and his colleagues included nine patients who underwent successful PCI for the treatment of stable angina or acute coronary syndrome after excluding patients with uncontrolled diabetes, symptoms of heart failure, or plasma brain natriuretic peptide levels greater than 100 pg/mL. Within 1 month after PCI, they quantitatively measured myocardial blood flow with ^{13}N-ammonia PET at rest and then 30 minutes later during a cold pressor test.

The patients were instructed not to take any drugs during the morning of the testing, but all took aspirin to prevent thrombotic events. The investigators defined the left anterior descending coronary artery as the area distal to the stent.

Dr. Kasai and his associates identified seven coronary artery segments that received conventional PCI (plain balloon angioplasty or bare metal stent), six segments that received sirolimus-eluting stents (SES), and normal control segments in each patient that had less than 75% stenosis.

At rest, there was no difference in myocardial blood flow between the normal control and reperfused segments that were distal to the SES. Normal control and reperfused stent-distal segments with conventional PCI also had similar myocardial blood flow at rest. During cold pressor testing, myocardial blood flow did not differ significantly between normal control and stent-distal segments that had been reperfused with either conventional PCI or SES. But the percentage increase in myocardial blood flow from rest to stress with the cold pressor test (representing coronary endothelial function) was significantly lower in reperfused areas distal to SES (28%) than in normal control segments (47%). This was not seen in comparisons between reperfused areas distal to conventional PCI (64%) and normal control segments (54%). ■

Endovascular Repair Superior for Thoracic Aortic Aneurysm

BY MITCHEL L. ZOLER
Philadelphia Bureau

BALTIMORE — An endovascular graft for repairing thoracic aortic aneurysms appeared to be superior to open surgical repair in preliminary results from the device's pivotal trial.

"Major morbidity, severe morbidity, and clinical utility" were better with TEVAR (thoracic endovascular aortic repair), and "there was similar overall and interim-term survival following TEVAR and open repair," Dr. Jon S. Matsumura said at the Vascular Annual Meeting.

"Most surgeons feel that TEVAR is the first-line treatment for patients with suitable anatomy, but we can't make any conclusions about superiority based on our current data," Dr. Matsumura said in an interview. The study was designed to assess outcomes at 1 year after treatment, but at the time of the report this duration of follow-up was not available for all patients in the study.

"We'll make a comparison when we have all the patients followed for 1 year, and the results are audited," said Dr. Matsumura, a vascular surgeon at Northwestern University, Chicago. Because of the limitations of the current data, statistically significant differences between the control and intervention groups have not yet been evaluated, he added.

The STARZ-TX2 (Study of Thoracic Aortic Aneurysm [TAA] Repair with the Zenith-TX2 TAA Endovascular Graft) was sponsored by Cook Medical Inc., which is developing the device. Dr. Matsumura is a consultant to Cook and receives research support from the company.

This was a nonrandomized study that enrolled 160 patients to treatment using the endovascular graft and 70 patients to conventional, open repair. Treatment was at 42 international centers in March 2004–July 2006. The patients who underwent endovascular repair were significantly younger, with an average age of 72 years, compared with an average age of 68 in the open-repair group. The open-repair patients also had significantly more comorbidities at the time of surgery.

Outcomes Following TEVAR and Open Thoracic Aortic Aneurysm Repair

Measure	Endovascular Repair (n = 160)	Open Repair (n = 70)
Average blood loss during repair	216 mL	2,538 mL
Average time spent in ICU	2.2 days	9.4 days
Average time spent in hospital	5.0 days	16.6 days
Average number of severe morbidities during first 30 days after repair	0.2	0.7
Percentage of patients having at least one severe morbidity during first 30 days after repair	9%	31%
Incidence of all-cause deaths during 1-year follow-up	8%	13%
Incidence of aneurysm-related deaths during 1-year follow-up	6%	10%
Incidence of strokes during 1-year follow-up	2.5%	8.6%

Source: Dr. Matsumura

At 1 year after surgery, the overall survival rate was 92% in patients who had endovascular repair, and 87% in the open-repair group. The endovascular-repair group also had better results for several measures, such as post-treatment morbidity scores, aneurysm-related deaths, and duration of hospitalization (see box).

The incidence of strokes during follow-up was 2.5% in the endovascular-repair group and 8.6% in the open-surgery group. Paraplegia appeared in 1.3% and 5.7%, respectively. Paraparesis occurred in 3.8% of the endovascular patients and in none of the control patients.

The patients who underwent endovascular repair had no stent fractures or barb separations. They did not need to undergo any conversion operations, and had no aneurysm ruptures. After 1 year, there was one type III endoleak. And at 1 year, only 7% of the aneurysms had grown, whereas 50% had become smaller, and 43% did not change in size. ■