SIROLIMUS-ELUTING STENT IS EFFICACIOUS IN TREATING COMPLEX IN-STENT RESTENOSIS*

The placement of a coronary stent is the main treatment for coronary stenosis; therefore, in-stent restenosis is the most common form of restenosis today. The sirolimus-eluting stent (SES) has demonstrated a 0% restenosis rate in de novo lesions, but data were lacking in more complex lesions. A small observational study evaluated the efficacy of the SES in 16 patients with recurrent severe in-stent restenosis in a native coronary artery and objective evidence of ischemia. Patients with vessel diameters of >2.5 mm and <3.5 mm were allowed to participate and all were treated with a stent loaded with 140 µg sirolimus/cm² to be slowly released (>28 days). Aspirin 325 mg/day was to be given indefinitely as well as clopidogrel 300 mg loading dose followed by 75 mg/day for 2 to 4 months. Serial coronary angiography was conducted at baseline and at 4 months.

In total, 26 SES were implanted: 9 patients received single stents, 6 patients received 2 stents for long lesions, and 1 patient received 5 stents due to a totally occluded vessel. Quantitative coronary angiography was satisfactory in 15 (93.8%) patients. After 9 months of follow-up, 2 patients had died and 1 patient experienced a myocardial infarction. Neointimal hyperplasia was observed in an area not completely covered by 2 sirolimus-eluting stents in 1 patient. Patients who had undergone brachytherapy in the past can have prolonged endothelial dysfunction and represent a particular therapeutic challenge; such patients were responsible for one third of all adverse events in this study. The authors proposed that clopidogrel should be administered for an extended time period in patients who are to receive >1 sirolimus-eluting stent for the treatment of in-stent restenosis, especially if the patient has a history of failed brachytherapy, total vessel occlusion, or poorly deployed stents. The promising results with the sirolimus-eluting stent in complex lesions reported should be confirmed in a randomized multicenter study.


CATCH-UP RESTENOSIS NOT FOUND 2 YEARS AFTER SIROLIMUS-ELUTING STENT PLACEMENT*

Although efficacy and safety of sirolimus-eluting stents (SES) has been established at 1 year after placement, longer-term results were lacking until recently. Thirty of the first patients treated with SES were evaluated for clinical, angiographic, and intravascular ultrasound outcomes 2 years after the initial procedure. Patients were treated with the fast-release (FR) formulation (<15 days; n=15) or the slow-release (SR) formulation (>28 days; n=15).

Most of the patients experienced <0.5 mm in-lesion and in-stent late lumen loss (71% of FR and 85% of SR patients). No differences between treatment groups were observed for in-lesion lumen loss; however, the SR treatment group experienced statistically lower in-stent lumen loss (-0.09 ± 0.24 mm) compared with the FR group (0.28 ± 0.41 mm; P=.007). In the SR treatment group, no patient had a
>0.2 mm in-stent lumen loss. Between years 1 and 2, no changes in in-lesion minimal lumen diameter were observed in the FR group, but increases were demonstrated in the SR group (P = .001 for minimal lumen diameter at 1 year vs 2 years). None of the patients developed in-stent restenosis (≥50% diameter stenosis) and none died.

Long-term safety and efficacy of the sirolimus-eluting stent was demonstrated in this study as in-lesion restenosis developed in only 1 patient; in-stent restenosis was not observed in any patient; freedom from repeat target vessel revascularization was achieved in 90% of patients; and neointimal proliferation remained minimal.


**SLOW-RELEASE PACLITAXEL POLYMER-COATED STENT FOR THE TREATMENT OF IN-STENT RESTENOSIS**

Based upon the positive results of the Paclitaxel-eluting Stent for Prevention of In-Stent Restenosis (TAXUS) I feasibility trial, the paclitaxel-coated stent has been evaluated in more complex patient populations, namely those with in-stent restenosis. The TAXUS III study was a single-arm study conducted in 28 patients enrolled from 2 centers. In order to participate, patients had to have in-stent restenosis of a native coronary artery with evidence of ischemia. Candidate vessels had a diameter between 3.0 and 3.5 mm. The TAXUS stent had a total load of 1.0 µg/mm² paclitaxel that was slowly released via a copolymer carrier system that allowed for initial drug release over the first 48 hours followed by slow release over the next 10 days. Patients were also treated with aspirin ≥ 75 mg and clopidogrel 300 mg loading dose followed by 75 mg/day for 6 months. Angiography and intravascular ultrasound (IVUS) were conducted 6 months after stent placement while clinical follow-up was conducted at 6 and 12 months postprocedure. Death, myocardial infarction, target vessel repeat percutaneous coronary intervention, and coronary artery bypass grafting made up the major adverse cardiac events (MACE).

Of the 25 patients who underwent 6-month angiography, 4 (16%) had binary angiographic restenosis. The minimal luminal diameter was 2.40 mm after the procedure and was significantly lower at 6-month follow-up at 1.84 mm. A diameter stenosis of 30.8% was observed at follow-up with an average in-stent late loss of 0.54 mm. Late loss at the proximal edges of the stents was 0.20 mm and was 0.11 mm at the distal edges. No evidence of positive or negative vessel remodeling or late acquired incomplete stent apposition was observed via IVUS. Angiographic restenosis was observed in the gap between 2 paclitaxel-eluting stents. After 12 months of follow-up, no subacute stent thrombosis or deaths occurred. The MACE rate at 30 days was 4% and at 6 months was 29%. No additional MACE was reported between 6- and 12-month follow-up.

Results of this small open-label study demonstrated that the use of the polymer-based paclitaxel-eluting stent is safe and potentially effective for the treatment of in-stent restenosis. Longer-term follow-up is ongoing in an effort to provide further insight into the efficacy of the paclitaxel-coated stent in this patient population.


**HEALTH CARE ADMINISTRATORS SHOULD BE PREPARED FOR DRUG-ELUTING STENTS TO HIT THE US MARKET**

Once drug-eluting stents become available in the United States, members of the US healthcare management team should find high demand by patients and physicians for this innovative therapy likely. It is estimated that initial costs for these types of stents may be up to $3000, a price that is 3 times as expensive as current bare-metal stents. Currently the worldwide coronary stent market is $2 billion and may climb to $5.8 billion by the end of this year.

Competition in the marketplace may serve to moderate the price of drug-eluting stents. Six different companies are currently involved in the clinical development these stents. The approval of the first drug-eluting stent is bound to have dramatic effects on
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cardiovascular healthcare as alluded to by the fact that the Centers for Medicare and Medicaid Services approved a diagnosis-related group in August 2002. The average payment for drug-eluting stent placement will be $11,805; the payment will be $14,522 for patients presenting with a heart attack.

The use of drug-eluting stents is anticipated to be cost effective in the long run while the short-term impact may be negative. Contracts for groups or hospital systems will not offer any protection for costs associated with the drug-eluting stents at this time as none are currently approved, and it is expected that demand will surpass supply for the first year after approval. Careful monitoring of bare-stent inventory is advised as an additional means for controlling costs when drug-eluting stents are approved because the demand for the bare stent will most likely plummet. Fortunately, stiff competition in the drug-eluting stent arena should allow for greater choice with lower costs in the future. In order to prepare for the drug-eluting stent revolution, the development of guidelines for their use should be a top priority for hospital administrators. These healthcare officials are encouraged to cooperate with physicians and insurance companies in setting up a cost management plan to prepare for the economic impact sure to be associated with this new technology.


STENT SUMMIT PRODUCES A GRANT-SUPPORTED RESEARCH/EDUCATIONAL TOOL FOR CARDIOVASCULAR CARE MANAGERS*

Cardiovascular administrators will be challenged in the near future by the need to meet demands of physicians and patients while remaining fiscally accountable in the era of the drug-eluting stent. In December 2002, a Stent Summit was convened to address the financial impact the drug-eluting stent may have on US hospitals. Members of the summit consisted of physicians, administrators, managed care experts, and financial specialists and these advisors reviewed a research database of 200,000 coronary artery bypass graft (CABG) and percutaneous transluminal coronary angioplasty (PTCA) patient cases from the following 7 states: Virginia, California, Florida, New Jersey, New York, Washington, and Wisconsin. The output from this meeting was an educational piece in a format for audio- or video-conferencing including individual workbooks with CD-ROM/video. This tool includes background on drug-eluting stent utilization, a research patient-based financial model, an economic model with software to estimate hospital budgets, and recommendations and action steps for hospital management.

One of the first duties of the panel of experts was to develop a case cost analysis and a comprehensive 3-year financial forecast. Cardiac service's current financial contributions at hospitals were estimated using Medicare cost reports from 1999 and projected gains/losses were tabulated. Although there are some differences in physician choice and patient procedures at various institutions, decisions on the projections of patient volumes, expenses, and revenues will require a multidisciplinary team. This team should include physicians in active practice from surgery and medicine, clinical staff familiar with drug-eluting stents, financial staff able to utilize financial modeling, and managed care staff to negotiate adjustments to payments. Drug-eluting stents may double the budget for cardiac services; however, a decrease in readmission rates for redo procedures will likely contribute considerable savings. Additionally, a potential increase in patients eligible for PTCA in conjunction with a drug-eluting stent should be considered. The net budgetary impact of drug-eluting stents may actually be neutral given the savings provided by a reduction in CABG procedures and fewer readmissions.

The model developed by the Stent Summit was designed to assist cardiac care administrators with tools to respond to revenue and expense implications of the drug-eluting stent. The important clinical benefits of the drug-eluting stent are exciting for the medical community and senior administrators should have strategies in place for this new technology such that nominal impacts are made on the cardiovascular budget.
