Sirolimus-Eluting Stent Implantation in ST-Elevation Acute Myocardial Infarction

A Clinical and Angiographic Study

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Background—Sirolimus-eluting stents (SES) have recently been proven to reduce restenosis and reintervention compared with bare stents. Safety and effectiveness of SES in acute myocardial infarction remain unknown.

Methods and Results—Since April 16, 2002, a policy of routine SES implantation has been instituted in our hospital, with no clinical or anatomic restrictions, as part of the RESEARCH (Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital) registry. During 6 months of enrollment, 96 patients with ST-elevation acute myocardial infarction underwent percutaneous recanalization and SES implantation; these patients comprise the study population. The incidence of major adverse cardiac events (death, nonfatal myocardial infarction, reintervention) was evaluated. Six-month angiographic follow-up was scheduled per protocol. At baseline, diabetes mellitus was present in 12.5% and multivessel disease in 46.9%. Primary angioplasty was performed in 89 patients (92.7%). Infarct location was anterior in 41 (42.7%) of the cases, and 12 patients (12.5%) had cardiogenic shock. Postprocedural TIMI-3 flow was achieved in 93.3% of the cases. In-hospital mortality was 6.2%. One patient (1.1%) had reinfarction and target lesion reintervention the first day as a result of distal dissection and acute vessel occlusion. During follow-up (mean follow-up of 218±75 days), 1 patient died (1.1%), no patient had recurrent myocardial infarction, and there were no additional reinterventions. No early or late stent thromboses were documented. At angiographic follow-up (70%), late loss was −0.04±0.25, and no patient presented angiographic restenosis.

Conclusions—In this study, sirolimus-eluting stent implantation for patients with ST-elevation acute myocardial infarction was safe without documented angiographic restenosis at 6 months. (Circulation. 2003;108:1927-1929.)

Key Words: myocardial infarction • drugs • stents • restenosis

Routine stent implantation has been shown to have a better procedural success rate and clinical outcome than balloon angioplasty in patients presenting with acute myocardial infarction (AMI).1 However, in-stent restenosis and vessel reocclusion remain significant clinical problems limiting the long-term success of percutaneous treatment.1,2

Sirolimus-eluting stents (SES) have been proven to virtually abolish in-stent restenosis in elective patients with relatively simple lesions,3 with persistent neointimal growth inhibition up to 2 years.4 Recently, we have demonstrated that the 30-day outcomes of SES implantation for patients with acute coronary syndromes were similar to those of a control population treated with bare stents.5 Nevertheless, no specific information is presently available regarding the safety of these new devices in patients with AMI. Furthermore, the long-term clinical efficacy of SES for AMI is unknown. The rationale of the present study is therefore to evaluate the short- and midterm clinical and angiographic outcomes of SES implantation in a consecutive series of patients treated during the acute phase of AMI.

Methods

Patient Population

Since April 16, 2002, SES implantation (Cypher; Johnson & Johnson, Cordis Europa NV, Roden, the Netherlands) has been instituted as the default strategy for all percutaneous coronary interventions performed at our institution as part of the RESEARCH registry, which has been described elsewhere.6 All clinical situations and lesion morphologies were considered eligible. After 6 months of enrollment, 96 consecutive patients within 12 hours of an episode of AMI underwent mechanical reperfusion of the infarct-related artery...
with SES implantation; these patients comprise the present study population.

Procedure
Except for SES utilization, all procedures were performed according to standard techniques, and the final interventional strategy was left to the discretion of the operator. Weight-adjusted heparin was administered to achieve an activated clotting time of >300 seconds, or 200 to 250 seconds when platelet glycoprotein IIb/IIIa inhibitor was used. Postprocedural antiplatelet regimen consisted of lifelong aspirin use and 75 mg clopidogrel per day for 3 months. Prolonged clopidogrel prescription (6 months) was recommended for patients with at least one of the following characteristics: multiple SES (>3 stents), total stent length >36 mm, bifurcations, or in-stent restenosis. The local ethics committee approved the study protocol, and informed consent was obtained from all patients.

Definitions and Follow-Up
Patients were evaluated for the occurrence of death, reinfection (clinical symptoms or new electrocardiographic changes, associated with re-elevation of the creatine kinase and creatine kinase MB levels of >1.5 times the previous value if within 48 hours, >3 times the upper normal limit if after 48 hours),2 and target lesion revascularization (surgical or percutaneous reinervention motivated by a significant stenosis located within the stent or in the 5-mm segments proximal or distal to the stent). Information regarding repeat interventions was prospectively collected in the local database. Survival status was assessed by written inquiries to the Civil Registry. Questionnaires to assess clinical status were sent to all living patients. The patient, referring physician, and peripheral hospitals were directly approached whenever necessary for additional information.

To evaluate the incidence of restenosis after SES implantation for AMI, angiographic follow-up was scheduled at 6 months for all living patients. Binary restenosis was defined as a stenosis diameter >50% within the stent or in the 5-mm segments proximal or distal to the stent. Late loss was defined as the difference between the minimal luminal diameter immediately after the procedure and at follow-up.

Statistical Analysis
Continuous variables are expressed as mean±SD. Discrete variables are presented as count and percentages. Event-free survival curves were estimated according to the Kaplan-Meier method. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored.

Results
At baseline, mean age was 57±12 years. Twelve patients (12.5%) had diabetes mellitus, 10 (10.4%) had had a previous myocardial infarction, and 45 (46.9%) presented multivessel disease. Six patients (6.2%) had prior coronary angioplasty, and 1 (1%) had prior coronary bypass surgery. Mean creatine kinase level was 2685±2869 IU/L. Average time from the onset of symptoms to the beginning of the procedure was 3.6±2.9 hours. Primary angioplasty was performed in 89 patients (92.7%) and rescue angioplasty after failed thrombolysis in the remaining 7 (7.3%). Cardiogenic shock was diagnosed in 12 patients (12.5%). Periprocedural glycoprotein IIb/IIIa inhibitor (abciximab) was used in 45 patients (46.9%). Infarct location was anterior in 41 cases (42.7%). Overall, 104 culprit lesions were identified (in 8 patients, we found 2 different lesions anatomically and clinically related to the development of the AMI). The lesions were located in the left main in 2 cases (1.9%), the left anterior descending in 51 (49.0%), the left circumflex in 10 (9.6%), and the right coronary in 41 (39.4%). Before the procedure, TIMI flow 0 to 1 was present in 60.6% of the cases. Postprocedural TIMI-3 flow was achieved in 93.3%. Clopidogrel was prescribed for 3 months in 54% of patients and for 6 months in the remaining cases.

Complete follow-up was available for 99% of the patients at 218±75 days. A total of 6 deaths occurred during the index hospitalization (6.2%). In 1 case, death occurred as a result of brain death in a patient with prolonged out-of-hospital resuscitation. The other 5 cases were all admitted in cardiogenic shock; 3 of them died the same day of the procedure as a result of progressive hemodynamic deterioration. The other 2 patients died of overwhelming sepsis at days 23 and 86 after a prolonged, stormy course. One additional death (1.1%) resulting from heart failure occurred during follow-up, shortly after hospital discharge, in a 77-year-old patient with 3-vessel disease, who was admitted with a large inferior myocardial infarction and cardiogenic shock. In none of these cases, death occurred as an unexpected, sudden episode that could be attributable to stent thrombosis. Target lesion reintervention was necessary in 1 patient (1.1%) the same day as the procedure as a result of distal dissection, acute vessel occlusion, and reinfarction. There were no further cases of reinfarction or repeat intervention after discharge (Figure). Also, no early or late stent thromboses were documented.

Six-month angiographic follow-up was obtained in 62 patients (70%). The angiographic outcomes are shown in the Table. Late loss was −0.04±0.25 mm, and there were no cases of binary restenosis.

Discussion
The present study is the first report on SES implantation for patients with ST-elevation AMI. The main finding is that, in these patients, SES implantation appears highly effective in preventing neointimal proliferation and restenosis, with results similar to those observed in a randomized trial for relatively simple lesions.3

Primary percutaneous coronary intervention has been demonstrated to be more effective than thrombolytic therapy for the treatment of AMI.6 However, although consistently re-
produced by stent utilization, recurrent ischemia, restenosis, and reocclusion of the infarct-related artery occur in sizable proportions, increasing clinical events and healthcare costs. In the Stent PAMI (Stent Primary Angioplasty for Myocardial Infarction) trial, 6-month restenosis and target vessel revascularization rates were 20.3% and 7.7%, respectively. In the CADILLAC (Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications) trial, the corresponding values were 22.2% and 8.9%, and reocclusion of the infarct-related artery 5.7%. In this context, the absence of restenosis and reinterventions by SES as found in our study could further improve clinical outcomes, although this hypothesis should be tested in dedicated randomized trials.

Previous preclinical laboratory data suggested that sirolimus could decrease endothelial function in vitro, enhance agonist-induced platelet aggregation, and delay vascular healing. Altogether, these features can potentially increase the risk of thrombotic complications and adversely affect the outcome after SES implantation, especially in very susceptible patients such as those treated during the acute phase of myocardial infarction. However, the clinical significance of these preliminary findings remains elusive. Indeed, we recently demonstrated the safety of SES for patients with acute coronary syndromes, although AMI at presentation was still associated with a higher risk of adverse events at follow-up. The present study, with the very low event rate and the absence of episodes of acute and subacute thrombosis, confirms the safety of SES utilization, specifically in patients with AMI.

In this prospective, single-center registry of SES implantation in AMI, all the limitations inherent to this particular study design apply, and the patient number was relatively small. Notably, however, given the unrestricted inclusion criteria, this cohort of patients accurately reflects the daily practice in the “real world” of interventional cardiology, and therefore the results are extended to virtually all patients with AMI as a result of occlusion of native coronary vessels.

## Conclusions

Routine SES implantation during mechanical reperfusion of AMI is safe and associated with no evidence of late luminal loss and restenosis at 6 months. Larger studies are necessary to confirm these findings and to evaluate the impact of SES implantation on clinical events for patients with AMI.

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## References

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