

# Use of Sirolimus-Eluting Coronary Stents in Routine Clinical Practice

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Restenosis has long remained the major limitation of intracoronary stenting, but several randomized trials have recently shown that the use of drug-eluting stents appear to reduce markedly the risk of recurrence following treatment of de novo lesions. To evaluate whether the results of randomized trials can be generalized to routine clinical practice, all patients receiving at least one sirolimus-eluting stent (SES) in two Swiss hospitals were entered into a prospective registry. Only target vessels with a reference diameter > 3.5 mm were excluded. Clinical follow-up was obtained after 6 months. A total of 183 patients were included. The procedural success was 97.8% and the incidence of in-hospital MACE was 2.2%. At  $7 \pm 2$  months, 95.6% of the patients were event-free, and target lesion revascularization was required in only three patients (1.6%). The excellent medium-term results obtained with the SES in randomized trials can be replicated in routine clinical practice. *Catheter Cardiovasc Interv* 2004;62:26–29. © 2004 Wiley-Liss, Inc.

**Key words:** percutaneous coronary interventions; drug-eluting stents; coronary angioplasty

## INTRODUCTION

The use of stents has significantly improved the outcome of percutaneous coronary interventions (PCIs) [1,2]. However, despite major advances in angioplasty and stenting, in-stent restenosis remains a major limitation. In the recently published ARTS and SOS trials [3,4], the incidence of additional revascularization 1 year after stenting with bare metal stents (BMSs) was 17% and 21%, respectively. In an earlier study [5] comparing BMS stenting with internal mammary grafting for isolated proximal LAD stenosis, we had also found a 24% occurrence of in-stent restenosis leading to a reintervention. Recently, drug-eluting stents have emerged as a very promising approach in preventing restenosis, and several different compounds have been shown to have a major impact on both the angiographic and the clinical outcome [6–9]. However, the overall experience still only concerns a relatively limited number of selected patients, specifically chosen for their simple or only moderately complex coronary anatomy. As for any new technological development, it is obvious that the results of such trials cannot be transposed to daily clinical practice without specific and systematic evaluation. We thus prospectively collected in consecutive patients treated in our institutions all data pertaining to the use of the sirolimus-eluting stent (SES), starting with the first patients who were treated when the device became commercially available in Switzerland.

## MATERIALS AND METHODS

Between April and September 2002, all patients requiring PCI were considered to receive an SES. Patients with vessels > 3.5 mm were excluded because the stent was available only up to 3.0 mm in diameter. There was no other restriction to the use of these stents except the preference of either the patient or the operator for a BMS.

The procedure was performed via the right femoral artery through a 6 Fr guiding catheter. The revascularization was nearly always done during the same session as the diagnostic angiography. Intravascular ultrasound was not used. All patients were pretreated with aspirin 100 mg/day, and a minority received clopidogrel 75 mg/day during 5–7 days prior to the procedure. Intravenous heparin (70 U/kg) was given at the beginning of the procedure. If not given earlier, a 300 mg loading dose of clopidogrel was administered at the end of the procedure. A successful procedure was defined as a residual steno-

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sis < 20% without a major cardiac event during the in-hospital stay.

CK, CK-MB, and/or troponin values were measured at least once on the morning of the day following the procedure. A diagnosis of non-Q-wave myocardial infarction was made if a value above twice the upper limit of normal was measured. A 12-lead ECG was recorded at the end of the procedure, and further tracings were obtained if indicated. Patients remained in hospital until the next day. Long-term aspirin 100 mg/day was prescribed at discharge, together with 2–12 months of clopidogrel 75 mg/day.

Quantitative coronary angiography evaluation was obtained in multiple views. For patients with angiographic follow-up, restenosis was defined as a 50% or more reduction of the luminal diameter occurring within the stented segment or the 5 mm proximal and distal to the stent.

Clinical follow-up was obtained at 1 and 6 months either by a visit or by telephone contact with the patient or the referring physician. Information was collected on vital status, occurrence of myocardial infarction, additional revascularization procedures, coronary angiography, clinical angina status, and current medication. Stress test or cardiac scintigraphy was performed in all patients at 6-month follow-up. As a rule, control angiography was performed only when clinically required (clinical or silent ischemia). Death, myocardial infarction, additional PCI or CABG to the target lesion, and documented target lesion occlusion were considered as major adverse cardiac events (MACE).

## RESULTS

### Patient Characteristics

One hundred and eighty-three patients were included in the registry. The baseline demographic and angiographic data are given in Tables I and II.

### Procedure

One hundred and sixty-seven (91.2%) patients underwent a single procedure and 16 (8.8%) a staged revascularization with two separate procedures to different vessels. Two hundred and fifty-six lesions were treated (1.4 lesions/patient) by implantation of one or several SESs in 223 lesions (87.1%), BMS in 25 lesions (9.8%), and balloon angioplasty only in 8 (3.1%). Overall, 308 SESs and 27 BMSs were implanted (1.8 stent/patient). Single-session multivessel angioplasty was performed in 17/167 patients (10.2%); overall, 33/183 patients (18%) had multivessel revascularization.

A platelet glycoprotein IIb/IIIa inhibitor was used in 12% of the patients. Major in-hospital cardiac events

**TABLE I. Demographic Data**

Number of patients	183
Female gender	38 (20.8%)
Mean age	62 ± 12 years
Hypertension	118 (64.5%)
Hypercholesterolemia	138 (75.4%)
Diabetes	41 (22.4%)
Family history	53 (29%)
Smoking	35 (19.1%)
Vessel disease	
One-vessel	56 (30.6%)
Two-vessel	65 (35.5%)
Three-vessel	62 (33.9%)
Previous MI	57 (31.1%)
Previous CABG	29 (15.8%)
Previous PCI	72 (39.3%)
Stable angina	138 (75.4%)
Silent ischemia	28 (15.3%)
Unstable angina	17 (9.3%)

**TABLE II. Angiographic Data (256 Treated Lesions)**

De novo lesion	220 (85.9%)
In-stent restenosis	36 (14.1%)
LAD	118 (46.1%)
RCA	52 (20.3%)
Circumflex	71 (27.7%)
Left main	7 (2.7%)
SVG	8 (3.1%)
Reference diameter (mm)	3.0 ± 0.1
MLD preprocedure (mm)	0.91 ± 0.1
MLD postprocedure (mm)	2.9 ± 0.1
% stenosis preprocedure	70 ± 12
% stenosis postprocedure	5 ± 10
Lesion length (mm)	15 ± 10
Lesion type	
A	31 (12.1%)
B	150 (58.6%)
C	66 (25.8%)
Chronic occlusion	10 (3.9%)
Number of stents	335 (1.8 stents/patient)
Lesions with multiple stents	61 (23.8%)
Multivessel stenting	33 (12.9%)
SES/BMS	308 (91.9%)/27 (8.1%)

occurred in four patients (2.2%). Three patients had a CPK rise (non-Q-wave acute MI), and one suffered a Q-wave myocardial infarction (occlusion of diagonal branch during an LAD procedure). There was no hospital death or need for emergent revascularization (Table III). Neither acute (< 24 hr) nor subacute (24 hr to 30 days) stent thrombosis was observed. Early procedure clinical success rate was thus 179/183 (97.8%). The median in-hospital stay was 1 day (range, 0–15).

### Follow-Up

A complete follow-up was obtained in all 183 patients (100%) after a mean period of 7 ± 2 months (Table IV). One hundred and forty-four patients (78.7%) were in

**TABLE III. In-Hospital Adverse Events**

Death	0
Myocardial infarction	4 (2.2%)
Q-wave	1 (0.6%)
Non-Q-wave	3 (1.6%)
CABG	0
Re-PCI	0
Cerebrovascular accident	0
Any events	4 (2.2%)

**TABLE IV. Cardiac Events During Follow-Up (In-Hospital Complications Included)**

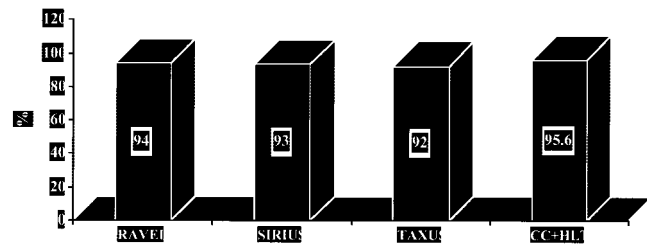
Death	0
Myocardial infarction	
Q-wave	1 (0.6%)
Non-Q-wave	3 (1.6%)
CABG	0
PCI (staged procedure excluded)	
TVR but not TLR	0
TLR	3 (1.6%)
Stent thrombosis	1 (0.6%)
MACE	8 (4.4%)
Angina class I	144 (78.7%)
Angina class II	37 (20.2%)
Angina class III	2 (1.1%)
Angina class IV	0 (0%)

angina class I, 37 (20.2%) in class II, 2 (1.1%) in class III, and none in class IV.

Twenty-five patients underwent control angiography because they were complaining of symptoms of typical or atypical angina pectoris. MACE, including the in-hospital events already described, occurred in eight patients (4.4%). There were no deaths, four myocardial infarctions (2.2%), and three (1.6%) additional target lesion revascularization procedures (three PCIs and no CABG). One patient was treated with a second SES for true in-stent restenosis within the SES, one was treated with a BMS for a proximal persistent lesion in a saphenous vein graft, and one patient with restenosis in a BMS was treated with further SES implantation. A fourth patient with recurrent angina 4 months after SES implantation was shown to have complete occlusion and was treated medically. Overall, 175 patients (95.6%) had an event-free survival at  $7 \pm 2$  months.

## DISCUSSION

To our knowledge, this is the first report on the routine clinical use of a coronary drug-eluting stent. It confirms the excellent safety profile of a sirolimus drug-eluting stent when applied in a broad variety of clinical and anatomical subsets. The rate of documented or suspected late thrombosis (during the first 6 months) was 0.6%, and the MACE-free survival at 6 months was 95.6%. These

**Fig. 1. MACE-free survival at 6-9 months in the randomized trials RAVEL, SIRIUS, TAXUS II, and in the present registry.**

main figures compare favorably with those observed in randomized trials with the same stent. In the first two randomized trials [6] with the sirolimus-eluting stent, the cumulative event-free survivals at 9-12 months were 94.1% and 92.9%, respectively (Fig. 1). The use of other drugs has also been tested, and paclitaxel has been associated with very promising results with MACE-free 6-month survivals around 90% [7,9].

Randomized controlled trials tend by necessity to be carried out in very selected populations of patients. As new devices and drugs in the field of interventional cardiology are increasingly, and appropriately, evaluated early by such trials, registries [10] are rapidly becoming an important element in the sequence leading from initial concept and experimentation to widespread clinical acceptance. This chain of evidence, which is likely to become a standard for many clinical innovations to come, should not be confused with the approach applied in the 1970s and 1980s. Registries concerning new devices were then often used as substitutes for the more demanding randomized trials. This was clearly not optimal, since if registries truly have the unique ability to reflect real-life practice, they cannot alone be seen as proof of the efficacy of any therapeutic modality.

To reach meaningful conclusions, registries must include all consecutive patients over a given period, use very broad inclusion criteria, have good follow-up information for all or nearly all patients, and not include compulsory investigation modalities (control coronary angiography, for instance) that deviate from usual practice.

The present registry meets all four of these prerequisites and suggests that the excellent results obtained in selected patient subsets could be replicated in more complex subgroups, such as those currently investigated in further ongoing randomized trial. For example, the MACE rate at 6 months for the 36 patients treated for in-stent restenosis in the present series was 5.6%, very similar to the 4.1% observed for the patients treated for de novo lesions only. Larger registries will be needed to help validate the use of drug-

eluting stents for a variety of different clinical and anatomical subsets.

The main limitation of the present study relates both to the duration and the type of follow-up that was obtained. While there are several theoretical reasons to fear a possible delayed restenotic process following SES implantation, such an occurrence has not been observed until now over periods extending up to 2 [8] or even 3 years. The 6-month time frame was chosen for convenience in the present series, because it has been an accepted standard for BMS. Our reliance on clinical rather than angiographic follow-up data means that unnecessary repeat procedures based solely on asymptomatic restenosis were avoided. It is possible, however, that we overestimated the true anatomical success rate of the procedure and this limits the validity of any direct comparison of our results with the drug-eluting arms of those randomized trials that used systematic angiographic follow-up.

Our data confirm that the excellent results obtained with the SES in randomized trials can be replicated in routine clinical practice, despite extending the indications to higher-risk patient subsets and more complex coronary lesions.

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