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Treatment of Multivessel Coronary Artery Disease With Sirolimus-Eluting Stent Implantation: Immediate and Mid-Term Results

Dejan Orlic, MD,* Erminio Bonizzoni, PHD,‡ Goran Stankovic, MD,* Flavio Airoldi, MD,† Alaide Chieffo, MD,† Nicola Corvaja, MD,* Giuseppe Sangiorgi, MD,* Massimo Ferraro, RN,* Carlo Briguori, MD,† Matteo Montorfano, MD,† Mauro Carlino, MD,† Antonio Colombo, MD, FACC*†

Milan, Italy

OBJECTIVES This study evaluated clinical outcome after multivessel stenting with sirolimus-eluting stents (SES) in unselected lesions.

BACKGROUND Safety and effectiveness of multivessel SES implantation is currently unknown.

METHODS Major adverse cardiac events (MACE) (death, myocardial infarction [MI], and repeat revascularization) were analyzed at 30 days and at 6 months after multivessel SES implantation.

RESULTS In 155 consecutive patients, 573 SES were implanted in 3.3 ± 1.3 lesions per patient. At 30 days, the cumulative MACE rate was 10.3%: 7.1% patients developed a non–Q-wave MI, 1.9% developed a Q-wave MI, 0.6% died for non-cardiac reasons, and 0.6% had a repeat revascularization. Clinical follow-up was obtained in all 112 eligible patients treated for 359 lesions at a mean time of 6.5 ± 2.2 months. The cumulative MACE rate was 22.3%: 3 (2.7%) deaths (1 for cardiac reasons), 4 (3.6%) MIs, target lesion revascularization (TLR) in 16 (14.3%) patients with 24 (6.7%) lesions. Target vessel revascularization was required in 18 (16.1%) patients due to TLR of lesions treated with SES or to disease progression (1.8% of patients). Cox regression analysis revealed total stent length per patient as the most powerful independent predictor of MACE. Overall stent thrombosis occurred in three (1.9%) patients.

CONCLUSIONS Multivessel SES implantation can be safely performed on patients with complex coronary artery disease. The need for revascularization increases because of the cumulative effect of TLR on patients with multiple lesions. (J Am Coll Cardiol 2004;43:1154–60) © 2004 by the American College of Cardiology Foundation

Observational and randomized studies comparing outcome between stented and surgically treated patients with multivessel disease reported higher restenosis and repeat revascularization rates in patients treated with bare metal stents (BMS) than in those after surgical treatment (1–5). In reported randomized studies, treatment of stenotic lesions in native coronary arteries by implantation of the sirolimus-eluting stent (SES) (Cypher, Cordis, a J&J, Warren, New Jersey) (6,7) or the paclitaxel-eluting stent (Taxus, Boston Scientific, Natick, Minnesota) (8) showed a low percent of angiographic restenosis and additional revascularization. However, in the Randomized Study with the Sirolimus-Coated Bx Velocity Balloon-Expandable Stent in the Treatment of Patients with de Novo Native Coronary Artery Lesions (RAVEL) trial, only patients with a single lesion in one vessel were included (6). In the U.S. Multicenter, Randomized, Double-Blind Study of the Sirolimus-Eluting Stent in De Novo Native Coronary Lesions (SIRIUS) trial, 25.3% of the patients had two-vessel disease, and 15.4% had three-vessel disease in the sirolimus arm, but only one lesion per patient was treated with the SES (7). In the recently published study, A Paclitaxel-Eluting Stent for the Prevention of Coronary Restenosis (ASPECT), in the arm with high dose of paclitaxel, 33% of the patients had two-vessel disease, 13% had three-vessel disease, and 7% had complex lesions (9).

No study was specifically dedicated to evaluate the effectiveness of drug-eluting stents in patients with multivessel disease. We report safety and clinical effectiveness of multiple SES implantations in patients with multivessel coronary artery disease.

METHODS

Patients and lesions. For this analysis, all consecutive patients who were referred to our center between April 16, 2002, and March 5, 2003, and underwent elective percutaneous coronary intervention (PCI) with multivessel stenting using SES were selected. Patients included in this study had either stable or unstable angina, or silent ischemia and at least two lesions located in different vessels treated with SES. Different vessels were defined as involvement of two major epicardial vessels (right, left anterior descending, circumflex, or left main coronary arteries) (10) or one major epicardial vessel and a branch (≥2.5 mm in diameter)

From *EMO, Centro Cuore Columbus Hospital, Milan, Italy; †San Raffaele Hospital, Milan, Italy; and ‡Institute of Medical Statistics and Biometry, University of Milan, Milan, Italy.

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Abbreviations and Acronyms

BMS = bare metal stent
CABG = coronary artery bypass grafting
CK = creatine kinase
MACE = major adverse cardiac events
MI = myocardial infarction
PCI = percutaneous coronary intervention
PTCA = percutaneous transluminal coronary angioplasty
SES = sirolimus-eluting stent
SIRIUS = U.S. Multicenter, Randomized, Double-Blind Study of the Sirolimus- Eluting Stent in De Novo Native Coronary Lesions
TLR = target lesion revascularization
TVR = target vessel revascularization

originating from another major epicardial vessel. Occasionally, conventional percutaneous coronary angioplasty (PTCA) was performed without stent implantation in vessels 1.5 to 2.5 mm. Stenting procedures were performed in the usual fashion (11). All stents were implanted with high pressure (>12 atm) final stent dilation with an attempt to fully cover the angiographic lesion with the stent. For lesions located at the bifurcation site, the T or the Crushing stenting techniques (12,13) were utilized to treat the main branch and the side branch. Intravascular ultrasound was used only according to the decision of the operator.

End points and definitions. The aim of our study was to determine procedural success, composite 30-day and six-month major adverse cardiac events (MACE) after multivessel SES implantation. Procedural success was defined as angiographic success without death, non–Q-wave or Q-wave myocardial infarction (MI), emergency coronary artery bypass grafting (CABG), or repeat PCI of the target vessel before discharge. Angiographic success was defined as a final diameter stenosis of <30% with a Thrombolysis In Myocardial Infarction (TIMI) flow rate of grade 3 according to TIMI trial. Composite 30-day MACE reflects the safety of the procedure, and was defined as death, non–Q-wave or Q-wave MI, or target lesion revascularization (TLR) (CABG or repeat PCI). Six-month rate of MACE reflects clinical effectiveness of the procedures and was defined as death, MI, or target vessel revascularization (TVR). Non–Q-wave MI was defined according to World Health Organization definition: increase of total creatine kinase (CK) two times or more the upper limit of normal range with an elevated MB isoform level (mass analysis) without development of new Q waves (more than 0.04 s in 2 or more contiguous leads). A Q-wave MI was present when, in addition to CK elevation, there were new Q waves in at least two leads. In all patients, CK and CK-MB were evaluated every 6 h three times after the procedure or until normalization if they were elevated.

Complete revascularization was defined as restoration of TIMI 3 flow with residual stenosis <30% to all myocardial territories. Complex lesions were defined as type B2 or C according to modified American College of Cardiology/American Heart Association classification (14).

Stent thrombosis was defined as occlusion or filling defect at the stent site documented by angiography or chest pain with electrocardiographic changes suggestive of MI in the territory of the stented vessel or occurrence of sudden death.

Medical therapy. Antiplatelet therapy with aspirin (100 to 325 mg every day) and thienopyridines (ticlopidine 250 mg twice a day or clopidogrel 75 mg every day) was started at least three days before the procedure. A loading dose of 300 mg of clopidogrel was given in all other cases. Intravenous heparin (70 to 100 IU/kg) and additional boluses, if required to maintain activated coagulation time >250 s, were administered after a sheath insertion. Use of glycoprotein IIb/IIIa receptor inhibitors was left to the decision of the operator. Aspirin and clopidogrel were continued for at least three months or up to six months to one year when more than two stents were implanted or a vessel was stented over a segment longer than 33 mm.

Quantitative angiographic analysis. Angiograms suitable for quantitative analysis were obtained both before and after stent implantation using the same angiographic view that had revealed the greatest stenosis in the stented segment. The analysis was done with a computer-assisted system using an automated edge detection algorithm (CMS version 5.0 and 5.2, MEDIS, Leiden, the Netherlands). The outer diameter of the contrast-filled catheter was used for calibration. Regarding the angiographic pattern of restenosis, focal lesion was defined as lesion length <10 mm, multifocal as >1 focal lesion in the same stented segment with normal segment in between, and diffuse restenosis as lesion length ≥10 mm. Relative gain was defined as ratio between acute gain and reference vessel diameter.

Follow-up. Clinical follow-up was obtained by direct telephone interview with the patient at one and at six months. Angiographic follow-up was suggested between 8 and 12 months after stenting unless clinically indicated at an earlier time.

Statistical analysis. Descriptive statistical analysis was performed by using continuous variables expressed as mean value ± 1 standard deviation and by using categorical variables presented as percent frequency. For comparison between groups with categorical data, chi-square testing was used. The Cox proportional-hazards regression model was used to determine independent predictors of MACE. The Wald test was used to determine the importance of the individual coefficient. A p value lower than 0.05 was required for statistical significance. Kaplan-Meier event-free survival curves were constructed. Statistical analysis was performed with commercially available software (SPSS 11 for Windows, SPSS Inc., Chicago, Illinois).

RESULTS

A total of 511 lesions were treated with 573 SES in 155 patients. A mean of 3.6 ± 1.5 lesions per patient underwent

Table 1. Baseline Clinical Characteristics

	SES (n = 155 Patients)
Age, yrs	61.2 ± 10.6
Men, %	146 (94.2%)
Current smoker, %	18 (11.6%)
Hypercholesterolemia, %	104 (67.1%)
Systemic hypertension, %	88 (56.8%)
Diabetes mellitus, %	37 (23.9%)
Prior CABG, %	31 (20.0%)
Prior MI, %	74 (47.7%)
Unstable angina, %	32 (20.6%)
Two-vessel disease, %	67 (43.2%)
Three-vessel disease, %	88 (56.8%)
Left ventricular ejection fraction, %	53.1 ± 8.6
Three-vessel stenting, %	27 (17.4%)
Patients with bifurcation lesions, %	71 (45.8%)
Patients with CTO, %	28 (18.1)

Values are mean ± SD or numbers and percentage of patients.
CABG = coronary artery bypass grafting; CTO = chronic total occlusion; MI = myocardial infarction; SES = sirolimus-eluting stent.

stent implantation (SES or bare-metal stent [BMS]) or PTCA, and in 3.3 ± 1.3 lesions, SES were implanted (87% of the treated lesions). A total of 37 BMS were implanted in proximal parts of large vessels. Plain balloon angioplasties were performed without stent implantation in small vessels: distal vessel segments or small side branches of bifurcation lesions (40 lesions). Complete revascularization was achieved in 109 (70.3%) patients.

Procedure. Sirolimus-eluting stents were successfully deployed to all the lesions with final angiographic success in 508 (99.4%) lesions. In one case (lesion located at distal vessel segment), abrupt closure of the vessel segment distal to the implanted SES occurred and was left untreated; in the other two lesions, final diameter stenosis was more than 30%.

Patients and lesion characteristics. Patient characteristics are reported in Table 1. A total of 74 (47.7%) patients had previous MI. Low ejection fraction of the left ventricle (≤35%) was found in 8 (5.2%) patients. Two-vessel disease was found in 67 (43.2%) patients, and three-vessel disease in 88 (56.8%) patients. Two-vessel SES implantation was performed in 128 patients (400 lesions), and three-vessel SES in 27 patients (111 lesions). The qualitative angiographic results are reported in Table 2. Lesions were located in the left anterior descending coronary artery (40.1%) predominantly in proximal or mid-segments of the treated vessel (66.2%). Eighty-one (15.8%) lesions were located in ostial/proximal segments of the left anterior descending coronary artery. There was a high percentage (81.4%) of complex lesions. Unprotected left mains were treated in seven patients. A relatively high proportion of 200 (39.1%) lesions were located in small vessels (reference vessel diameter ≤2.5 mm). Among 87 bifurcation lesions, both branches were treated with the SES deployment in 76 (87.4%) lesions.

Quantitative angiographic results. Table 3 reports the quantitative angiographic results. The reference vessel diameter was 2.64 ± 0.57 mm. Residual stenosis was 12.7 ± 7.8%. The mean lesion length at baseline was 16.7 ± 10.8 mm, and 163 (31.9%) lesions were long (>20 mm). Mean length of stented segment was 27.5 ± 13.5 mm. After final stent dilation, the acute gain was 1.74 ± 0.60 mm and relative gain 0.65 ± 0.23.

Table 2. Baseline Lesion and Procedural Characteristics

	SES (n = 511 Lesions)
Target vessel, %	
LM	15 (2.9%)
LAD	205 (40.1%)
LCx	164 (32.1%)
RCA	121 (23.7%)
LIMA	6 (1.2)
Location in vessel, %	
Ostial	90 (17.6%)
Proximal	192 (37.6%)
Mid	146 (28.6%)
Distal	83 (16.2%)
ACC/AHA lesion type,* %	
A	10 (2.0%)
B1	85 (16.6%)
B2	245 (47.9%)
C	171 (33.5%)
Bifurcation, %	168 (32.9%)
In-stent restenosis, %	51 (10.0%)
Calcium (moderate to severe), %	22 (4.3%)
Eccentric, %	406 (79.4%)
Total occlusion, %	44 (8.6%)
Pretreatment, %	
Plain balloon, %	368 (72.0%)
Atherectomy, %	11 (2.1%)
Number of SES per lesion	1.12 ± 0.38
Number of SES per patient	3.29 ± 1.27
Stented segment length, mm	27.5 ± 13.5
Maximum balloon diameter, mm	2.92 ± 0.41
Maximum balloon pressure, atm	16.2 ± 3.1
Usage of IIb/IIIa inhibitor, % of patients	92 (59.3%)
IABP, % of patients	3 (1.9%)
Usage of IVUS, % of lesions	61 (11.9%)

Values are mean ± SD and percentage of lesions. Percentages of patients are indicated. *Modified American College of Cardiology/American Heart Association (ACC/AHA) lesion classification.
IABP = intra-aortic balloon pump; IVUS = intravascular ultrasound; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LIMA = left internal mammary artery; LM = left main coronary artery; RCA = right coronary artery; SES = sirolimus-eluting stent; SVG = saphenous vein graft.

Table 3. Quantitative Coronary Angiographic Results

	SES (n = 511 Lesions)
Baseline	
Reference vessel diameter, mm	2.64 ± 0.57
MLD, mm	0.89 ± 0.49
Diameter stenosis, %	66.2 ± 17.2
Lesion length, mm	16.7 ± 10.8
Final	
MLD, mm	2.62 ± 0.49
Diameter stenosis, %	12.7 ± 7.8
Acute gain, mm	1.74 ± 0.60
Relative gain	0.65 ± 0.23

Values are mean ± SD of lesions.
MLD = in-lesion minimum lumen diameter; SES = sirolimus-eluting stent.

Table 4. Procedural Success and Complications

	SES (n = 511 Lesions)
Angiographic success, %	99.4
Procedural success, %	91.3
Abrupt vessel closure, %	1 (0.6%)
Acute thrombosis, %	1 (0.6%)
Any procedural complication, %	2 (1.2%)

Values are percentage of lesions.
SES = sirolimus-eluting stent.

Procedural complications and 30-day outcomes. Procedural complications and 30-day outcome are reported in Tables 4 and 5. One patient had abrupt closure of a vessel segment distal to the SES. One patient had Q-wave MI due to acute, periprocedural thrombosis after stent deployment in a bifurcation lesion. After mechanical aspiration of thrombus and adjunctive therapy with glycoprotein IIb/IIIa receptor inhibitor, final TIMI 3 flow was restored. In one patient, urgent PCI was performed 2 h after the procedure because of chest pain associated with ST-segment elevation. Critical stenosis due to dissection at the distal margin of the SES was successfully treated by additional stent implantation. No patient died while in the hospital, and no patient required emergent surgical revascularization.

A total of 11 (7.1%) patients developed a non–Q-wave MI, and two patients (1.2%) had a Q-wave MI. Rise of CK-MB ≥3 times the upper normal range was found in 26 (16.8%) patients after the procedure. Increase in CK-MB ≥3 times the upper normal limit occurred in 17 (12.8%) patients with two-vessel SES implantation and in 9 (32.1%) patients ($p = 0.025$) with three-vessel SES implantation.

No patient developed major hematoma requiring transfusion, pseudoaneurysm, or need for vascular repair at the access site.

After the discharge, within 30-day clinical follow-up, one patient died because of intracranial bleeding. One patient had a Q-wave MI 10 days after discontinuation of clopidogrel because of urgent abdominal operation. In this period, no repeat revascularization was required.

Six-month clinical outcome. A total of 112 patients (359 lesions) eligible for 6-month clinical follow-up completed a mean follow-up time of 6.5 ± 2.2 months (range, 1.8 to 13.2 months). Table 6 reports the specific adverse events that occurred during this follow-up. Two patients died: one patient two months after the index procedure because of acute MI at 10 days after unplanned suspension of clopidogrel; the other patient died three months after the procedure because of vascular complications after surgical repair of abdominal aortic aneurysm. One patient had MI 5.7 months after the index procedure. Target lesion revascularization was required in 24 (6.7%) lesions in 16 (14.3%) patients. Target vessel revascularization, including non-target sites, was required in 18 (16.1%) patients. It is important to mention that all revascularization events were due to TLR of lesions treated with SES or to disease progression. No revascularization was required in segments treated by PTCA or BMS. Cumulative MACE occurred in 25 (22.3%) patients. The different clinical outcomes are illustrated by the Kaplan-Meier estimates of event-free survival among patients who reached 250-day follow-up without TLR (Fig. 1A), without TVR (Fig. 1B), or without MACE (Fig. 1C).

Cox regression analysis was used to identify independent predictors for cardiac events. Independent predictors of occurrence of TLR were reference vessel diameter (hazard ratio = 0.346, $p = 0.0280$) and final minimum lumen diameter (hazard ratio = 0.359, $p = 0.0058$). Predictors of TVR were: final minimum lumen diameter (hazard ratio = 0.228, $p = 0.04$), total stent length per patient (hazard ratio = 1.010, $p = 0.02$), and maximum stent length per vessel

Table 6. Six-Month Clinical Outcome

End Point	SES n = 112 Patients 359 Lesions
Death, % of patients	3 (2.7%)
Myocardial infarction Q-wave, % of patients	4 (3.6%)
Cerebrovascular accidents, % of patients	0
TLR, % of lesions	24 (6.7%)
PCI, %	20 (5.6%)
CABG, %	4 (1.1%)
TLR, % of patients	16 (14.3%)
TVR, % of patients	18 (16.1%)
Cumulative MACE*, % of patients	25 (22.3%)

Values are numbers and percentages of patients or lesions when indicated.
CABG = coronary artery bypass grafting; MACE = major adverse cardiac events (death, myocardial infarction, or target vessel revascularization); PCI = percutaneous coronary intervention; SES = sirolimus-eluting stent; TLR = target lesion revascularization; TVR = target vessel revascularization.

Table 5. In-Hospital and 30-Day Outcome

	In-Hospital MACE* (n = 155 Patients)	30-Day MACE (n = 155 Patients)	Composite 30-Day MACE (n = 155 Patients)
Death, %	0	1 (0.6%)	1 (0.6%)
Q-wave MI, %	2 (1.2%)	1 (0.6%)†	3 (1.9%)
Non–Q-wave MI, %	11 (7.1%)	0	11 (7.1%)
Repeat PCI, %	1 (0.6%)	0	1 (0.6%)
Emergent CABG, %	0	0	0
Total MACE, %	14 (9.0%)	2 (1.3%)	16 (10.3%)

Values are numbers and percentages of patients. *MACE included death, Q-wave and non–Q-wave myocardial infarction, and target vessel revascularization; †subacute thrombosis.
CABG = coronary artery bypass grafting; MACE = major adverse cardiac events; MI = myocardial infarction; PCI = percutaneous coronary intervention; UNL = upper normal limit.

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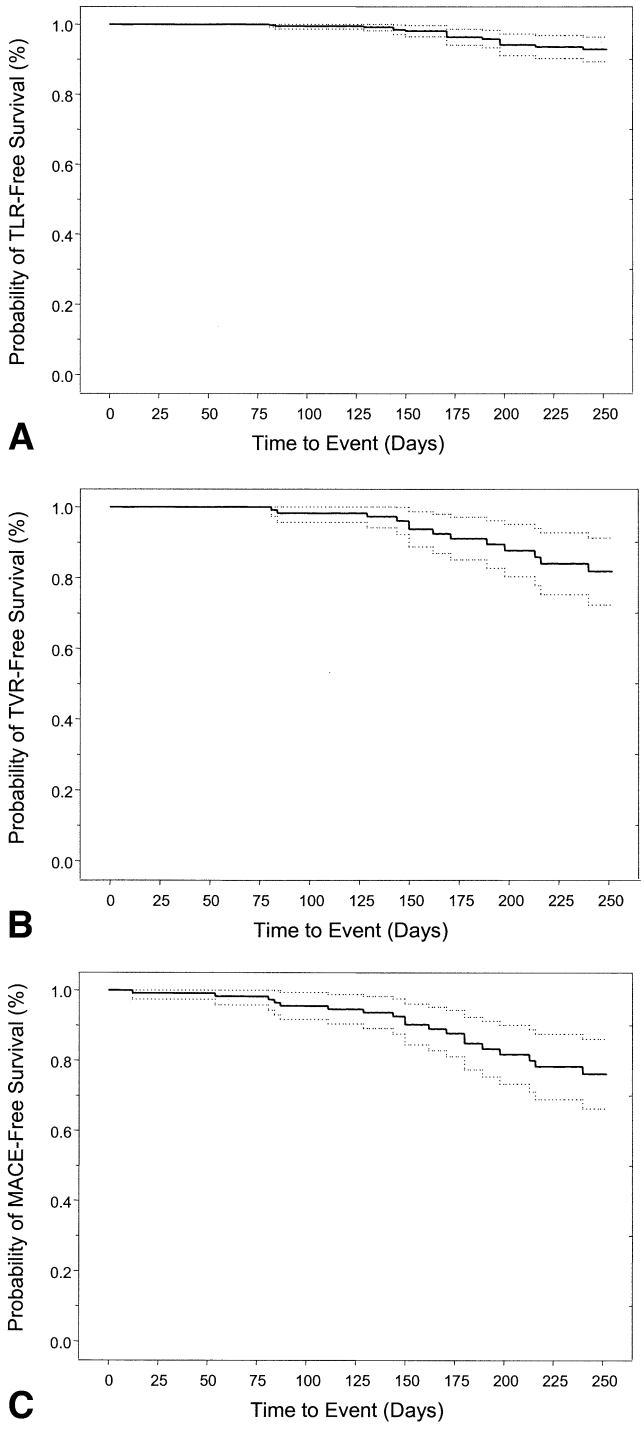

Figure 1. Kaplan-Meier estimates of the probability of survival without target lesion revascularization (TLR) **(A)**, without target vessel revascularization (TVR) **(B)**, and without cumulative total major adverse cardiac events (MACE) **(C)**.

(hazard ratio = 1.013, p = 0.04). Predictors of MACE were: diabetes (hazard ratio = 2.406, p =0.04), total stent length per patient (hazard ratio = 1.009, p = 0.02), and maximum stent length per vessel (hazard ratio = 1.012, p = 0.03) (Table 7). Variables included in this model were: unstable angina, diabetes, complex lesions (type C according to modified American College of Cardiology/American Heart Association classification), reference vessel diameter, lesion length, three-vessel stenting, final minimum lumen diameter, stent length per lesion, and total stent length per patient as potential predictors of TLR, and additionally, maximum stent length per vessel for TVR and MACE.

Angiographic follow-up was performed in 27 patients (93 lesions). Clinically driven follow-up angiography was performed in 11 patients, and routine control follow-up angiography in 16 patients. Total occlusion of the stented vessel was found in two patients: one asymptomatic and one with effort angina. In the other 25 patients (86 lesions), restenosis (≥50% of diameter stenosis) was found in 14 patients (24 lesions). Pattern of restenosis was focal in 23 lesions and diffuse in one lesion. Among focal lesions, four were multifocal. All restenotic lesions occurred in the stented segment. Revascularization of the restenostic lesions was performed in all 24 lesions, while the two total occlusions were not revascularized. There were no patients with revascularization of the non-target vessel alone.

Incidence of stent thrombosis. Of 155 patients treated with SES, a total of two documented thrombotic events and one possible thrombosis occurred. One of them was acute and intraprocedural, one subacute (28 days) associated with MI and stent occlusion, and one possible late thrombosis (54 days) was associated with sudden death. In the last two patients, clopidogrel was discontinued seven to 10 days before the events.

DISCUSSION

The major findings of this study evaluating the outcome of patients after multivessel SES implantation are: the MACE rates at 30 days appear low and comparable to other studies evaluating a less complex population (4,13); at a mean follow-up of 6.5 months, the 22.3% MACE rate is mainly driven by a 16% need for revascularizations; despite the fact that TLR remains low (6.7%), the increase in need for revascularization per patient occurs due to treatment of multiple lesions.

A mean of 3.3 ± 1.3 lesions per patient were treated with SES implantation, more than in major trials: 2.7 lesions in the Stent Or Surgery (SOS) trial and 2.6 lesions in the Arterial Revascularization Therapies Study (ARTS). Angiographic success of 99.4% is comparable with the range from 97% to 100% achieved with bare metal multivessel stenting in observational (4,5,15,16) and randomized (1,2) studies. Complete revascularization was achieved in 70.3% patients, as in one major randomized trial (17). The lesions treated with SES implantation in this report are characterized by high percentages of complex lesions (81%), long lesions (32%), and lesion site in vessels ≤2.5 mm (39%). The rate of MI was acceptable: 7.1% for a non–Q-wave MI and 1.2% for a Q-wave MI.

When we look at all post-procedural rises of CK-MB ≥3 times the upper normal range, this complication was found

Table 7. Predictors of TLR, TVR, and MACE by Cox Regression Analysis

Variables	Hazard Ratio	95% Lower Confidence Limit	95% Upper Confidence Limit	p Value
TLR				
Reference vessel diameter	0.346	0.134	0.892	0.028
Final minimum lumen diameter	0.359	0.174	0.744	0.006
TVR				
Final minimum lumen diameter	0.228	0.054	0.969	0.045
Total stent length per patient	1.010	1.001	1.020	0.024
Maximum stent length per vessel	1.013	1.001	1.026	0.037
Total MACE				
Diabetes	2.406	1.037	5.583	0.041
Total stent length per patient	1.009	1.001	1.017	0.022
Maximum stent length per vessel	1.012	1.001	1.023	0.027

MACE = major adverse cardiac events; MLD = in-lesion minimal lumen diameter; TLR = target lesion revascularization; TVR = target vessel revascularization.

in 26 (16.8%) of our patients. In the ARTS study, the abnormal level of CK-MB was observed in 31% of patients in the stenting arm (1). This difference may be explained by the more liberal use of glycoprotein IIb/IIIa receptor inhibitors in our study (59.3%), compared with the 8% in the SOS trial (2) and almost no usage in the ARTS trial. More frequent rises in CK-MB ≥3 times the upper normal range were found among patients with three-vessel SES implantation compared with those in whom two-vessel SES deployment was performed (32.1% vs. 12.8%, p = 0.025). This finding may imply a need for a more liberal elective use of glycoprotein IIb/IIIa receptor inhibitors when three-vessel SES implantation is planned.

The fact that the early outcome remained similar to that in previous reports dealing with less complex patient cohorts (1,2,5) testifies to the overall improvement in the safety and success of PCI procedures over the past years.

MACE at six months. The 22.3% MACE rate at an average follow-up time of 6.5 months may appear high in light of the expectations after the introduction of drug-eluting stents. The fact that the main determinant of late events was the need for new revascularization points to three considerations: 1) when the operator has a device available such as a drug-eluting stent that is supposed to deliver a very low restenosis rate, the tendency to treat more lesions increases; 2) when these stents are implanted in complex lesions, their performance is inferior to the performance reported in randomized trials; and 3) the relatively low restenosis rate per lesion reported in randomized trials adds up when multiple lesions are treated in the same patient.

When restenosis was detected, its pattern was focal in most of the lesions, a situation that should make re-intervention easier. The fact that all restenoses occurred inside the stents was probably due to our strategy to use longer stents and to pay attention to fully cover the diseased segment. A prior study from our laboratory evaluating BMS implantation in multivessel disease reported a 30% six-month need for re-interventions on target vessels (5) compared with 16% in the present study.

Regression analysis revealed that reference vessel size and final minimum lumen diameter were associated with increased risk for TLR. The higher risk of restenosis in small vessels was also reported in a subanalysis of the SIRIUS trial (7). As far as the total stent length per patient and the maximum stent length per vessel being predictors of TVR, we believe that these two parameters reflect the lesion complexity and the extension of the disease burden at risk for restenosis and re-intervention. Among the clinical variables, the fact that diabetes mellitus was a predictor of total MACE confirms the importance of this risk factor. Concerns may arise about the conservative use of glycoprotein IIb/IIIa inhibitors in these patients in our study (23 of 37, 62.2%).

Thrombotic events. Considering the complex patient population treated, there was a low incidence of thrombotic events. In particular, all subacute thrombosis occurred in two patients who stopped clopidogrel before the date prescribed. There were two late SES occlusions detected at follow-up angiography, which were not associated with any acute event, and we cannot determine if thrombosis occurred.

Study limitations. Important limitations of this report are the limited number of patients available for clinical follow-up and the low number of elective angiographic follow-ups performed. Despite these shortcomings, the initial observations are important because they help to place the SES in the appropriate perspective when they are used in patients who are potentially surgical candidates.

Conclusions. Use of the SES allows safe treatment of patients with complex coronary artery disease. The persistence of new revascularization procedures during the follow-up suggests the need for a better understanding of the reasons for the failure to further improve the percutaneous approach in most patients with multivessel coronary artery disease.

Reprint requests and correspondence: Dr. Antonio Colombo, EMO Centro Cuore Columbus, Via Buonarroti 48, Milan, Italy. E-mail: info@emocolumbus.it.

REFERENCES

1. Serruys PW, Unger F, Sousa JE, et al. Comparison of coronary artery bypass surgery and stenting for the treatment of multivessel disease. N Engl J Med 2001;344:1117–24.
2. SoS Investigators. Coronary artery bypass surgery versus percutaneous coronary intervention with stent implantation in patients with multivessel coronary artery disease (the Stent or Surgery trial): a randomised controlled trial. Lancet 2002;360:965–70.
3. Rodriguez A, Bernardi V, Navia J, et al. Argentine randomized study: Coronary Angioplasty with Stenting versus Coronary Bypass Surgery in Patients with Multiple-Vessel Disease (ERACI II): 30-day and one-year follow-up results. ERACI II investigators. J Am Coll Cardiol 2001;37:51–8.
4. Kornowski R, Mehran R, Satler LF, et al. Procedural results and late clinical outcomes following multivessel coronary stenting. J Am Coll Cardiol 1999;33:420–6.
5. Moussa I, Reimers B, Moses J, et al. Long-term angiographic and clinical outcome of patients undergoing multivessel coronary stenting. Circulation 1997;96:3873–9.
6. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med 2002;346:1773–80.
7. Leon MB, Moses JW, Popma JJ, et al. A multicenter randomized clinical study of the sirolimus-eluting stent in native coronary lesions: angiographic results. Circulation 2002;106:II393.
8. Colombo A, Drzewiecki J, Banning A, et al. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions. Circulation 2003; 108:788–94.
9. Park SJ, Shim WH, Ho DS, et al. A paclitaxel-eluting stent for the prevention of coronary restenosis. N Engl J Med 2003;348:1537–45.
10. King SB 3rd. The Emory Angioplasty vs. Surgery Trial (EAST). Semin Interv Cardiol 1999;4:185–90.
11. Leon MB, Baim DS, Popma JJ, et al. A clinical trial comparing three antithrombotic-drug regimens after coronary artery stenting: Stent Anticoagulation Restenosis study investigators. N Engl J Med 1998; 339:1665–71.
12. Kobayashi Y, Colombo A, Akiyama T, Reimers B, Martini G, di Mario C. Modified "T" stenting: a technique for kissing stents in bifurcational coronary lesion. Cathet Cardiovasc Diagn 1998;43: 323–6.
13. Colombo A, Stankovic G, Orlic D, et al. The modified "T" stenting technique with "crushing" for bifurcation lesions: immediate results and 30-day outcome. Cathet Cardiovasc Intervent 2003;60:145–51.
14. Ryan TJ, Faxon DP, Gunnar RM, et al. Guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart Association Task Force on Assessment of Diagnostic and Therapeutic Cardiovascular Procedures (Subcommittee on Percutaneous Transluminal Coronary Angioplasty). Circulation 1988;78:486–502.
15. Laham RJ, Ho KK, Baim DS, Kuntz RE, Cohen DJ, Carrozza JP Jr. Multivessel Palmaz-Schatz stenting: early results and one-year outcome. J Am Coll Cardiol 1997;30:180–5.
16. Mathew V, Garratt KN, Holmes DR Jr. Clinical outcome after multivessel coronary stent implantation. Am Heart J 1999;138:1105–10.
17. van den Brand MJ, Rensing BJ, Morel MA, et al. The effect of completeness of revascularization on event-free survival at one year in the ARTS trial. J Am Coll Cardiol 2002;39:559–64.