Original articles

Angiographic follow-up after coronary implantation of the Multilink™ stent: a prospective observation

Paolo Russo, Giuseppe Steffenino, Antonio Dellavalle, Flavio Ribichini, Valeria Ferrero, Antonello Vado, Eugenio Uslenghi

Catheterization Laboratory, Division of Cardiology, Hospital S. Croce e Carle , Cuneo, Italy

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Coronary stent; Restenosis.

Background. **A growing variety of coronary stents is becoming available on the market. Results of randomized trials may be difficult to apply to less selected patients, and experience with every device cannot be obtained in every center. Detailed information about the immediate and long-term results achieved with one device can be a helpful reference for interventional cardiologists. The aim of this study was to test the applicability and the clinical and angiographic results, both immediate and at 6 months, of the Multilink™ coronary stent in a cohort of unselected patients undergoing coronary angioplasty.**

Methods. **From March 1997 to June 1998 coronary angioplasty was performed in 391 patients in our center, with the use of stents in 339 patients.**

Results. **Three hundred and seventeen Multilink™ stents were successfully implanted in 295 lesions in 277 patients; an acute coronary syndrome was present in 209 cases (75%), and lesion types B2 and C accounted for 30% of lesions. In 7 cases (2.4%) the Multilink™ stent did not cross the lesion, and another device was implanted. Subacute stent occlusion occurred in 1 patient (0.36%) after primary angioplasty. After 6 months from the procedure, clinical follow-up data were available for 252 out of 254 patients: none had died, and angina or myocardial ischemia occurred in 25 patients (9.9%). A control angiogram was performed in 239 out of 254 patients (94%) at 178 – 34 days. Restenosis occurred in 44/239 patients (18.4%) and in 48/247 lesions (19.4%). In patients with vs without restenosis the original lesion was longer (p = 0.009), and diabetes mellitus was more frequent (p = 0.002), as was the use of multiple stents (p = 0.005). In single 15, 25 and 35 mm long stents restenosis occurred in 13.9, 15.5 and 46.2% of cases, respectively (p = NS).**

Conclusions. **The Multilink™ stent showed a low rate of subacute occlusion (0.36%) and could be used safely also in patients with acute coronary syndromes. The use of a single, 15 or 25 mm long Multilink™ stent was associated with a low angiographic recurrence rate (14-16%).**

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Address:

Dr. Giuseppe Steffenino

Laboratorio di Emodinamica
Azienda Ospedaliera S. Croce e Carle
Via Coppino, 26
12100 Cuneo
E-mail: steffenino.g@scroce.sanitacn.it

Introduction

Stents are being widely used in percutaneous coronary interventions in the United States[1] and also in Italy[2] both to treat or to prevent acute/subacute coronary occlusion after balloon angioplasty, and to reduce the risk of restenosis[3,4]. A growing number of stent designs are available on the European market, but direct experience with every device cannot be accumulated in each center performing coronary interventions. Data about the acute and long-term performance of one device in a non-selected cohort of patients can be helpfully shared among interventional cardiologists. This is the aim of the present report.

Methods

The device. The Multilink™ stent (Advanced Cardiovascular Systems Inc., Temecula, CA, USA) is a laser-cut slotted-tube stent made from 316L stainless steel, with a thickness of about 0.06 mm. The vessel surface covered by metal changes between 15 and 7% for a range of final stent diameters. The use of this device is recommended for vessels of 3 to 4.5 mm in diameter. Stents used in this study were pre-mounted on rapid exchange, compliant delivery balloons with a diameter of 3, 3.5 or 4 mm; available lengths were 15, 25 and 35 mm. Although the stent itself was only faintly radio-opaque, the delivery balloons were provided with a ra-

dio-opaque marker at both ends. During the study period, a new, less compliant delivery balloon (HP) became available in certain sizes and lengths, and was used in some of our patients.

Patient selection. Consecutive male and female patients undergoing percutaneous coronary angioplasty in our center were considered for inclusion in this study. Criteria used in patient selection, due to the absence of surgical back-up in our center, have been published[5]. All *de novo* lesions in vessels with an initial quantitative coronary angiography reference diameter of > 2.5 mm were considered for implantation of a Multilink™ stent; the final decision, however, whether any or which stent should be used, was the operator s choice.

Treatment protocol. Coronary interventions were performed through the percutaneous femoral or brachial access using 8 or 6 F guiding catheters. All lesions were first dilated with a compliant balloon (balloon/artery ratio 1); all stents were dilated at 12 atm with the original balloon carrying the pre-mounted stent (the nominal pressure of deployment was between 6 and 8 atm), post-dilation with a non-compliant balloon of the same diameter or bigger was the operator s choice, without exceeding a 1.1 balloon/artery ratio. Treatment with ticlopidine 250 mg bid was started at least 2 days before the procedure in most patients, and continued for 1 month afterwards in all. Abciximab was not used, nor was intracoronary thrombolysis. Heparin 10 000 IU was routinely administered at the beginning of the procedure or, in the presence of a running intravenous heparin drip, in a dose sufficient to achieve an activated clotting time of about 300 s, which was measured 30 min after heparin bolus administration and maintained throughout the procedure. Heparin infusion was continued for 48 hours after primary angioplasty, and for 12 hours in few other selected cases at the operator s discretion.

Assessment of results and definitions. All measurements of the lesions were performed in two orthogonal projections by use of on-line quantitative coronary angiography (Philips DCI, Eindhoven, The Netherlands), after intracoronary nitroglycerin administration.

Immediate angiographic success was defined as successful deployment of the stent, with a residual stenosis < 30% of luminal diameter and a Thrombolysis in Myocardial Infarction[6] grade 3 flow at the end of the procedure. Acute and subacute stent occlusions were defined as the occlusion of the stented vessel, as detected by whatever means, within 6 hours and within 30 days, respectively, after completion of the procedure. Clinical recurrence was defined as the appearance of angina or signs of ischemia or new myocardial infarction following the procedure. Peri- or post-procedural myocardial infarction was defined as either the appearance of new Q waves on the electrocardiogram, or an elevation > 3 times normal (or re-elevation) of cardiac enzymes. Angiographic restenosis was defined as a stenosis 50% of luminal diameter of the stented lesion at control coronary angiography; the latter was scheduled at 6 months after the procedure, but was performed earlier in case of clinical recurrence.

Statistical analysis. Statistical analysis was performed using the SPSS software (release 5.01 for Windows). Student s t-test and one-way ANOVA with Bonferroni s correction for pairwise comparison were used to test differences between mean values of continuous variables. The χ^2 test was used for nominal variables, and the Yates correction was applied when indicated. Potential association among clinical and angiographic variables, and restenosis was tested by univariate methods. The null hypothesis was rejected for $p < 0.05$.

Results

From March 1997 to June 1998, 391 patients were treated with coronary angioplasty in our center. Stents were used in 339 patients; in 277 of these 317 Multilink™ stents were successfully implanted in 295 lesions. In 7 additional cases (2.4%) the Multilink™ stent could not cross the lesion: the Multilink™ stent was retrieved without difficulty, and another stent was implanted. In the remaining 55 patients who underwent coronary stent implantation during the study period a different type of device was preferred mostly a coil stent due to a small (< 2.5 mm) reference diameter of the vessel. Males were 74%, mean age was 62 – 9 years, 24% had had a previous myocardial infarction, and 2.5% had had previous coronary bypass surgery; mean left ventricular ejection fraction was 0.56 (Tables I and II).

Three hundred and seventeen Multilink™ stents were implanted in 295 *de novo* lesions (Table III): 201 stents were 15 mm, 82 were 25 mm, 34 were 35 mm; 22 lesions were treated with 2 stents (due to the length of the lesion or to residual dissection after stent implantation). The mean percent diameter stenosis before coro-

Table I. Baseline clinical characteristics of the patients with successful implantation of a Multilink™ stent.

No. patients	277
Male	205 (74%)
Age (years)	62 – 9
Coronary risk factors	
Smoke	178 (64%)
Arterial hypertension	132 (48%)
Diabetes	28 (10%)
Hypercholesterolemia	78 (28%)
History of myocardial infarction	66 (24%)
Previous coronary bypass surgery	7 (2.5%)
Previous coronary angioplasty (other lesion)	8 (2.9%)
Clinical presentation	
Acute myocardial infarction	52 (19%)
Unstable angina	157 (56%)
Stable angina/silent ischemia	68 (25%)

Table II. Baseline angiographic characteristics of the 277 patients with successful implantation of the Multilink™ stent.

Multivessel disease	94 (34%)
Left ventricular ejection fraction	0.56 – 0.1
Treated lesions	295
Lesion distribution	
Left main stem	2 (0.6%)
Left anterior descending	81 (27.5%)
Left circumflex	36 (12.2%)
Right coronary artery	153 (51.7%)
Diagonal/obtuse marginal branch	18 (6.2%)
Saphenous vein graft	5 (1.8%)
Lesion morphology (ACC/AHA)	
Type A	47 (16%)
Type B1	160 (54%)
Type B2	59 (20%)
Type C	29 (10%)

Table III. Procedural characteristics of the 277 patients with successful implantation of the Multilink™ stent.

Lesions	295
Lesions treated with 1 stent	273 (92.5%)
Lesions treated with 2 stents	22
Stents implanted	317
15 mm	201
25 mm	82
35 mm	34
Lesion QCA before PTCA	
Percent diameter stenosis	73 – 18
MLD (mm)	0.7 – 0.4
Reference diameter (mm)	2.6 – 1.1
Lesion length (mm)	17 – 8
Lesion QCA after stenting	
Percent diameter stenosis	5 – 5
MLD (mm)	2.9 – 0.5
Reference diameter (mm)	3.0 – 1.2
Net gain (mm)	2.2 – 0.3

MLD = minimum luminal diameter; PTCA = coronary angioplasty; QCA = quantitative coronary angiography.

nary angioplasty was 73 – 18%, the initial quantitative coronary angiography reference diameter was 2.6 – 1.1 mm, and the mean lesion length was 17 – 8 mm. After stenting the mean percent diameter stenosis was 5 – 5%, and the final reference diameter was 3.0 – 1.2 mm with a net gain of 2.2 – 0.3 mm.

Subacute occlusion occurred in 1 patient (0.36%) 20 hours after implantation of a 15 mm Multilink™ expanded at a diameter of 3.0 mm during primary angioplasty; upon immediate control angiography in-stent thrombosis appeared to be the cause, and repeat balloon dilation to 3.5 mm was performed with success.

Clinical follow-up at 6 months was available in 252 out of 254 eligible patients (99%); 2 patients were lost at follow-up. For the remaining 23 patients the 6-month follow-up interval had not expired. There was no death. Myocardial infarction had occurred in 1 patient without symptoms; new Q waves were observed on the electrocardiogram at the time of the protocol angiographic control. Angina and ischemia without symptoms recurred in 15 and in 9 patients, respectively. Overall clinical recurrence was present in 25 patients (9.9%). Clinical recurrence in the subgroup of 159 patients in our cohort who were treated with a single 15 mm Multilink™ stent was observed in 16 (10%).

Angiographic follow-up (Table IV) at 178 – 34 days was available in 239 of 254 patients (94%); control coronary angiography in 2 patients was performed in another center, and quantitative angiographic data are not available. All of the remaining 13 patients who were located at clinical follow-up but did not undergo control coronary angiography had neither angina nor ischemia; one and two Multilink™ stents had been implanted in 12 and in 1 of them, respectively.

Table IV. Follow-up angiographic data after successful implantation of a Multilink™ stent.

Time to control angiogram (days)	178 – 34 (range 80-190)
Patients re-examined/eligible	239/254 (94.1%)
Lesions re-examined/eligible	247/263 (93.9%)
Lesion QCA at follow-up*	
Percent diameter stenosis	27 – 25
MLD (mm)	2.08 – 0.92
Reference diameter (mm)	2.89 – 1.0
Late loss (mm)	0.77 – 0.74
Overall restenosis per patient	44/239 (18.4%)
With multiple stents	8/17 (47%)
With single stent	36/222 (16.2%)
15 mm	21/151 (13.9%)
25 mm	9/58 (15.5%)
35 mm	6/13 (46.2%)
Overall restenosis per lesion	48/247 (19.4%)

Abbreviations as in table III. * available for 245 lesions and 237 patients only.

Restenosis was observed in 44/239 patients (18.4%) and in 48/247 lesions (19.4%) (Table IV). Restenosis was present in 21 (13.9%) out of 151 patients treated with a single 15 mm Multilink™ stent who had follow-up coronary angiography.

Among clinical and angiographic factors currently implicated in recurrence of stenosis after stenting[7] (Table V), only diabetes mellitus, lesion length, and the use of multiple stents were significantly associated with restenosis in our patient cohort. The use of longer stents was associated with a higher, albeit not significant, restenosis rate.

Discussion

In our patients acute stent thrombosis was not observed, and subacute stent occlusion occurred in 1 patient (0.36%). Subacute occlusion has recently been report-

Table V. Clinical and angiographic characteristics of patients with and without angiographic restenosis.

Variable	No restenosis (n=195)	Restenosis (n=44)	p =
Smoke	120 (61.5%)	27 (61.4%)	NS
Hypertension	92 (47.1%)	23 (52.2%)	NS
Diabetes mellitus	13 (6%)	11 (25%)	0.002
Acute coronary syndrome*	148 (75.8%)	32 (72.7%)	NS
Stenting in bailout (vessel occlusion)	40 (20.5%)	9 (20.4%)	NS
Lesion length (mm)	16.7 – 7	22.8 – 10	0.009
Reference diameter before stenting (mm)	2.65 – 0.88	2.67 – 0.5	NS
MLD before stenting (mm)	0.7 – 0.5	0.69 – 0.7	NS
MLD post-stenting (mm)	2.99 – 0.5	2.85 – 0.9	NS
Use of multiple stents	9 (4.6%)	8 (18%)	0.005

MLD = minimum luminal diameter. * includes acute myocardial infarction and unstable angina.

ed to occur in 1.8% of 218 patients after implantation of the Multilink™ stent[8]; although the distribution of vessel diameter and lesion morphology, and the incidence of elective stent use in that study were similar to ours, none of those patients had primary angioplasty for evolving myocardial infarction, only 25% had unstable angina and all were treated with aspirin alone. A multicenter experience with the use of the 15 mm Multilink™ stent in 126 unselected patients, mostly treated with ticlopidine, has recently been published[9]. Unstable angina was present in 37% of patients, no primary angioplasty was performed, mean vessel reference diameter before angioplasty was 3 mm, lesion types B2 or C accounted for 32% of cases, and stents were used in bailout conditions in 1% of patients. Subacute occlusion occurred in 1.6% of patients; peri-procedural myocardial infarction, however, occurred in 4.8% of patients, with the need for repeat angioplasty or coronary bypass surgery in 3.1% of cases.

Clinical and angiographic recurrence was observed in 9.9 and 18.4%, respectively, of our whole cohort, and in 10 and 13.9% of the patients treated with a single 15 mm Multilink™ stent; 35 mm long and multiple stents were used in a minority of cases and underwent angiographic control less often than shorter and single stents (Tables III and IV). Although comparison of recurrence rates among different patient series is not straightforward, reference should be made to three recent large follow-up studies with the use of a single 15 mm Multilink™ stent. One hundred and two patients with effort angina were included in WEST-1[10]; clinical and angiographic recurrence at 6 months (follow-up was 95% complete) was observed in 15 and 17% of patients, respectively. Patients with Braunwald class 3 unstable angina and evolving myocardial infarction were not included in WEST-2[11], and stent implantation was guided by intravascular ultrasound assessment; control coronary angiography was performed in 90% of 165 eligible patients and showed restenosis in 12.8%, with major adverse cardiac events in 9.1% of cases. One thousand patients with focal *de novo* lesions in native coronary vessels were randomized to the elective implantation of a 15 mm Multilink™ or a Palmaz-Schatz stent in the ASCENT study[12]. Angiographic follow-up at 6 months was 75% complete and showed restenosis in 16% of Multilink™ stents.

WEST-2[11] and ASCENT[12] studies showed an overall restenosis rate concordant with the low restenosis rate of our series for the 15 mm stent. The difference (12.8% in WEST-2 and 16% in ASCENT) can be explained by lesion selection, ultrasound guidance and lower rate of angiographic follow-up in ASCENT (the lower the rate of angiographic follow-up, the higher the restenosis rate, because only symptomatic patients re-undergo angiography).

In our cohort restenosis was found to have a statistically significant association with diabetes mellitus, lesion length, and the use of multiple stents. This is consistent with previous observations[13-15]. An acute coronary syndrome at presentation was very frequent in our patients (75%) and bailout stent implantation accounted for 15.5% of cases; neither of these variables was significantly associated with restenosis in our cohort.

This study, albeit prospective, has some limitations which should be considered. In fact, due to the absence of surgical back-up in our center, about 15% of potential candidates to elective balloon coronary angioplasty are currently referred to other institutions, due to either a perceived high risk of severe complications in case vessel occlusion should occur, or patient preference. Although lesion morphology in itself, as a predictor of the probability that an occlusive complication may occur, was not considered in the selection of our candidates this potential selection bias should be acknowledged. Furthermore, all angiographic analyses were performed on-line by the operators and X-ray technicians involved in the procedures, and not by an independent laboratory.

Since, however, the patients in this study were consecutive and included a substantial percentage with acute coronary syndromes, and no exclusion criteria were used with the exception of a vessel reference di-

ameter of < 2.5 mm, our cohort may be representative of the everyday patient encountered in clinical practice. Our data show that in such patients the use of the Multilink™ stent, with high pressure expansion and ticlopidine treatment, is associated with a high percentage of immediate success, a low incidence of subacute thrombosis (0.36%), and a low angiographic recurrence rate (14-16%) when single 15 and 25 mm stents are implanted.

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