

Multivessel coronary stenting: predictors of early and late outcome

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**Coronary angioplasty;
Multivessel disease;
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Background. At present, only few data are available on the early and late outcome following multivessel coronary stenting. Of note, in these studies, the left anterior descending (LAD) artery was treated in less than 40% of cases. These patients may not fully represent the population commonly referred for surgical revascularization.

Methods. In-hospital and long-term (18 ± 4 months) events were evaluated in 272 consecutive patients who had multivessel stent implantation including the LAD artery in each case. All clinical, angiographic, and procedural variables were analyzed to identify the predictors of acute and long-term major adverse coronary events.

Results. Eighteen patients (6.6%) had in-hospital major adverse coronary events (death 0.7%, coronary artery bypass grafting 0.4%, and myocardial infarction 6.3%). Acute and subacute stent thrombosis rates were 1.5 and 1.1%, respectively. At 18 ± 4 months, event-free survival was 71%. Target lesion revascularization was performed in 54 (20%) patients (42 coronary angioplasty and 12 coronary artery bypass grafting). The jeopardy score was the predictor of in-hospital major adverse coronary events ($p = 0.016$, odds ratio 1.34, 95% confidence interval 1.05-1.69), and diabetes mellitus was the predictor of long-term major adverse coronary events ($p = 0.027$, odds ratio 2.80, 95% confidence interval 1.12-6.96).

Conclusions. Multivessel coronary stent implantation with treatment of the LAD artery in all instances is a safe procedure with low acute and long-term major adverse coronary events. The risk-benefit ratio must be assessed carefully for each patient, particularly taking into account the jeopardy score and the presence of diabetes mellitus.

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Introduction

Randomized comparison between coronary angioplasty and coronary artery bypass grafting in patients with multivessel disease suitable for both approaches¹ showed that these two techniques have a similar effect on mortality and myocardial infarction rates during follow-up, and that patients who undergo coronary angioplasty required more repeat interventions (mainly due to restenosis). However, these published randomized trials were conducted before stents were available to improve angioplasty results and reduce late restenosis.

At present, pending the final results of some ongoing coronary-stent vs bypass surgery trials²⁻⁴, only few data are available on the early and late outcome following multivessel coronary stenting^{5,6}. Of note, in these studies, the left anterior descending (LAD) artery was treated in less than 40% of cases. Certainly, this is not the population

that we face every day in the operating room. In our opinion, this fact represents an important limitation weakening the conclusions of these studies on the advantages of stent implantation in multivessel coronary angioplasty.

In the present study, we assessed the early and late outcome of patients who underwent multivessel coronary stent implantation invariably involving the LAD artery.

Methods

Patient population. From March 1993 to June 1998, 520 consecutive patients underwent multivessel coronary stenting during a single intervention session in our Institution. The decision to treat with a percutaneous approach patients with multivessel disease potentially good candidates for surgery was taken based on the following elements: 1) technical suitability for percutaneous revas-

cularization with the knowledge that this approach would not have jeopardized any future surgical option, 2) patient's and/or referring physician's preference. From this population, we selected the 272 patients (with 670 lesions) who had stent implantation in the LAD artery and in at least another vessel (i.e. right coronary artery, circumflex artery, major diagonal and obtuse marginal branch, and descending posterior artery). Some patients have been previously included in another study⁵. Multivessel coronary disease was defined as $\geq 70\%$ stenosis by visual estimate in two or more coronary arteries.

Angiographic analysis. Angiographic measurements were performed with an automated computer-based system (QCA-CMS version 3.0, MEDIS, Leiden, The Netherlands). Lesions were characterized according to the modified American College of Cardiology/American Heart Association classification⁷.

Jeopardy score. The degree of multivessel coronary artery disease was defined by applying a jeopardy score (i.e. a measure of potentially ischemic myocardium) according to Califf et al.⁸. With this scoring system the coronary tree is divided into six segments of almost equal myocardial perfusion (e.g., LAD artery, major diagonal branch, circumflex coronary artery, major obtuse marginal branch, right coronary artery, and posterior descending artery). By applying a point score of 2 for each significant lesion and additional 2 points for each vessel distal to that lesion, a total maximal score of 12 can be achieved.

Stent implantation procedure. Intracoronary stenting was performed by using techniques previously described⁹. All patients received aspirin 325 mg before stent deployment, and 10 000 U intra-arterial bolus of unfractionated heparin at the beginning of the procedure. Angiographic success was defined as a final angiographic residual stenosis of $< 20\%$ by visual estimate.

Post-procedure management and follow-up. After successful stent implantation was achieved, no further heparin was administered, and sheaths were removed in 4 to 6 hours. One hundred and thirty-nine patients (51%) had aspirin alone (325 mg/day), 18 patients (6%) received only ticlopidine (250 mg bid for 1 month), whereas the combination of aspirin and ticlopidine was used in the remaining 115 patients (43%). Follow-up was performed in all patients by an interview or a telephone conversation. Any major adverse coronary events (i.e. Q wave and non-Q wave myocardial infarction, bypass surgery, coronary angioplasty, and death) were considered. Indications for repeat revascularization in the follow-up were 1) recurrent angina, and/or 2) angiographic restenosis.

Statistical analysis. In order to include in the analysis all the angiographic and procedural variables, we con-

verted some continuous variables into categorical variables.

Reference vessel diameter. For the purpose of statistical analysis, in a single patient, we gave a score of 0 in case all vessels were large (≥ 3.0 mm), a score of 1 in case only 1 vessel was small (< 3.0 mm), and a score of 2 when ≥ 2 vessels were small.

Lesion length. In a given patient, we gave a score of 0 in case all lesions were short (≤ 10 mm), a score of 1 when only 1 lesion was long (> 10 mm), and a score of 2 when ≥ 2 lesions were long.

Type of lesion. We gave a score of 0 in case of a non-complex (A, B1) lesion, a score of 1 when, in a given patient, only 1 lesion was complex (B2, C) and a score of 2 when ≥ 2 lesions were complex.

Total occlusion. We gave a score of 0 in case of absence of total occlusion, a score of 1 in case only 1 total occlusion was present in a given patient and a score of 2 in case ≥ 2 total occlusions were present.

Stent length score. We gave a score of 1 in case the stent length was ≤ 15 mm, a score of 2 in case the stent length was 16-29 mm, a score of 3 in case the stent length was 30-59 mm and a score of 4 in case the stent length was ≥ 60 mm. The sum of the single stent scores gives the stent length score in a single patient.

Stent length index. Stent length score normalized to the total number of stents in the single patient.

Residual stenosis. We gave a score of 1 in case the residual stenosis post-stent implantation was $< 20\%$, and a score of 2 in case at least one residual stenosis $\geq 20\%$. Continuous variables are presented as mean \pm 1 SD. Differences between groups were assessed by χ^2 analysis for categorical variables and Student's t-test for continuous variables. The contribution of all clinical, angiographic, and procedural variables to the early and late outcome was evaluated with multivariate logistic regression analysis. Event-free survival curves were calculated using the Kaplan-Meier method; differences between the groups were tested with the log-rank test statistic. Probability values < 0.05 were considered statistically significant. Data were analyzed with SPSS 7.5.0 for Windows.

Results

Procedural results. Clinical, angiographic and procedural characteristics of the population are summarized in tables I and II. Angiographic success was 99%. Proximal LAD artery treatment was performed in 149 patients (55%), whereas 98.5% of patients (268/272) had a stent

Table I. Clinical characteristics of the 272 patients.

Age (years)	59 ± 10
Male	243 (89%)
Previous myocardial infarction	151 (55.5%)
Left ventricular ejection fraction (%)	59 ± 12
Symptoms	
Silent ischemia	9 (5%)
Stable angina	100 (36.8%)
Unstable angina	163 (58.2%)
Diabetes mellitus	28 (10.3%)
Hypertension	137 (50.4%)
Current smoker	62 (22.8%)
Former smoker	109 (40.1%)
Hypercholesterolemia	155 (57%)
Coronary artery disease	
Double vessels	164 (60.3%)
Triple vessels	108 (39.7%)

Table II. Angiographic and procedural characteristics of the 272 patients.

Jeopardy score	6.8 ± 2.3 (4-12)
Reference diameter (mm)	3.13 ± 0.47
Lesion site	
Ostial	18 (6.6%)
Proximal	123 (45.2%)
Mid	114 (41.9%)
Distal	17 (6.3%)
Lesion type*	
Non complex (A/B1)	31 (11%)
Complex (B2/C)	241 (89%)
Lesion length (mm)	13 ± 9
Total occlusion	92 (33.8%)
Thrombus	11 (4%)
MLD (mm)	
Pre	0.80 ± 0.34
Post	2.98 ± 0.56
Diameter stenosis (%)	
Pre	74 ± 18
Post	5 ± 13
Dilated vessel	
LAD + RCA	92 (33.8%)
LAD + LCx	87 (32%)
LAD + others	44 (16.2%)
LAD + RCA + LCx	11 (4%)
LAD + RCA + LCx + other	38 (14%)
Stent type (%)	
PS	20
NIR	17.8
ACS MultiLink	9.6
PURA	7.4
AVE GFX	4.8
Crown	4.4
Wiktor	3.7
GR Flexstent	3.3
Dart	3
CrossFlex	2.6
BeStent	1.9
Wallstent	1.5
Combination	8.9
Other	11.1
Stent length (mm)	22 ± 13

LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; MLD = minimal lumen diameter; RCA = right coronary artery. * modified American Heart Association/American College of Cardiology criteria.

implantation in the proximal and/or mid-LAD artery. The vessels treated were 2.2 ± 0.5 per patient. The lesions treated were 2.9 ± 1.0 per patient. Intra-aortic balloon counterpulsation support was used before starting the procedure in 26 patients (9.6%). Abciximab was administered in 16 patients (5.9%). Prior to stent deployment, debulking therapy (directional or rotational atherectomy) was performed in 58 patients (21.4%). The stents implanted are summarized in table II.

In-hospital major adverse coronary events. Eighteen patients (6.6%) suffered in-hospital major adverse coronary events (Table III). There were 2 deaths (0.7%), one elective bypass surgery (0.4%), and 17 acute myocardial infarctions (6.3%) (4 Q wave, and 13 non-Q wave). Acute stent thrombosis occurred in 4 patients (1.5% patient, 0.6% of lesion), and subacute stent thrombosis in 3 patients (1.1 and 0.5% lesion). By logistic regression analysis, the number of stent per patient was the only predictor of stent thrombosis ($p = 0.04$, odds ratio-OR 3.96, 95% confidence interval-CI 1.02-49.3). The jeopardy score was the only predictor of in-hospital major adverse coronary events ($p = 0.016$, OR 1.34, 95% CI 1.05-1.69). In particular the mean value of the jeopardy score was 6.7 ± 2.2 in the group without in-hospital major adverse coronary events vs 7.9 ± 2.3 in the group with in-hospital major adverse coronary events ($p = 0.033$). A jeopardy score ≥ 10 well differentiated patients with from those without in-hospital complications ($p = 0.01$, RR 3.29, 95% CI 1.20-8.99; Fig. 1).

Long-term outcomes. Event-free survival was 71%. Recurrent angina occurred in 16% of patients. Seventy-nine patients (29%) suffered long-term major adverse coronary events. There were 6 deaths (2.2%), 54 (20%) target lesion revascularization (12 bypass surgery, 42 repeat coronary angioplasty), 16 new coronary angioplasty (5.9%), and 5 acute myocardial infarctions (1.8%). The rate of any repeat revascularization was 24.4%. In particular, 12 patients (4.4%) had only one target lesion or

Table III. In-hospital and long-term major adverse coronary events in the global population.

In-hospital follow-up	
Acute myocardial infarction	17 (6.3%)
Non-Q wave	13 (4.8%)
Q wave	4 (1.5%)
Bypass surgery	1 (0.4%)
Re-angioplasty	0
Death	2 (0.7%)
Long-term follow-up	
Acute myocardial infarction	5 (1.8%)
Target lesion revascularization	54 (20%)
Bypass surgery	12 (4.4%)
Coronary angioplasty	42 (15.6%)
New coronary angioplasty	16 (5.8%)
Death	5 (1.8%)
Global events	79 (29%)

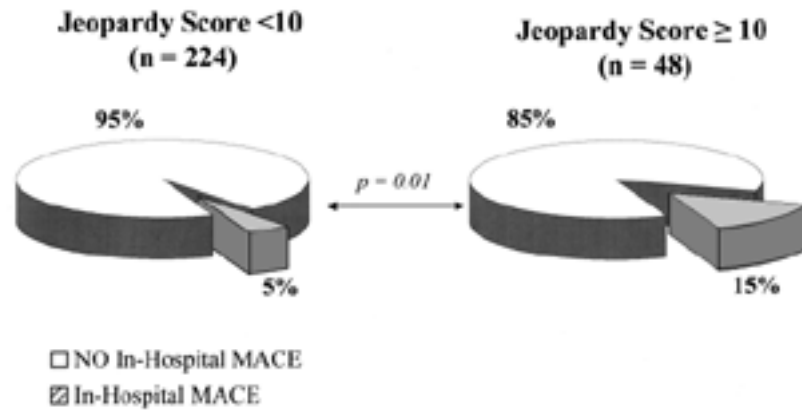


Figure 1. Occurrence of in-hospital major adverse coronary events (MACE) in patients with jeopardy score < 10 and ≥ 10.

vessel revascularization, and 42 patients (15.6%) had ≥ 2 target lesion or vessel revascularization. By logistic regression analysis, the stent length score was the only predictor of target lesion revascularization ($p = 0.019$, OR 1.27, 95% CI 1.04/1.56). Furthermore, there was a trend toward a lower event-free survival in patients with unstable vs stable angina (Fig. 2). Diabetes mellitus was the only predictor of long-term major adverse coronary events ($p = 0.027$, OR 2.80, 95% CI 1.12-6.96; Fig. 3).

Diabetic vs non-diabetic patients. There were 28 (10.3%) diabetic patients: 6 of them were insulin-dependent. Diabetic patients were often women (7/28 vs 26/244, $p = 0.027$), with triple-vessel disease, higher jeopardy score and angiographic evidence of thrombus (Tables IV and V). The number of lesions treated per patient was similar, although diabetics more often had ≥ 3 vessels treated than non-diabetics (35.6 vs 26%, $p < 0.05$). The 55% of diabetic patients experienced long-term major adverse coronary events vs the 29% of the non-diabetic patients ($p = 0.01$, Table VI). The occurrence of death and of new coronary angioplasty was significantly higher in diabetic patients. The following variables were more frequent in diabetic patients with long-term

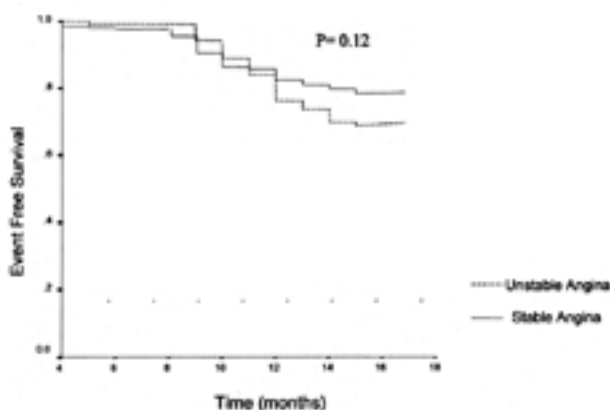


Figure 2. Kaplan-Meier curves of probability of survival and freedom from myocardial infarction, bypass, and repeat coronary angioplasty during the

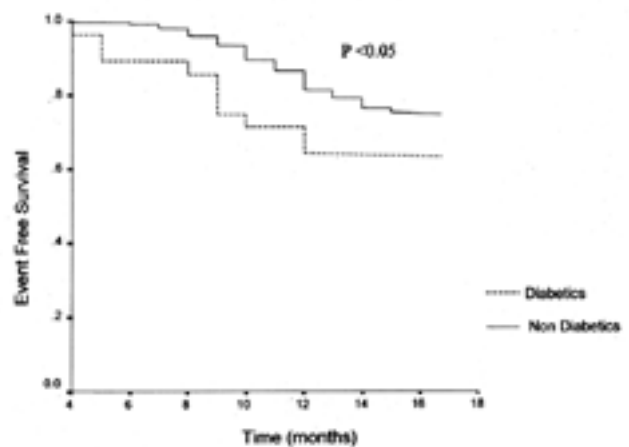


Figure 3. Kaplan-Meier curves of probability of survival and freedom from myocardial infarction, bypass, and repeat coronary angioplasty during the

Table IV. Clinical characteristics of the diabetic and non-diabetic patients.

	Diabetics (n = 28)	Non-diabetics (n = 244)
Age (years)	61 ± 9	59 ± 11
Male	21 (75%)*	218 (91%)s
Previous myocardial infarction	17 (60.7%)	134 (54.9%)
Left ventricular ejection fraction (%)	60 ± 12	60 ± 12
Unstable angina	10 (35.7%)	90 (36.9%)
Hypertension	16 (57.2%)	121 (49.6%)
Current smoker	6 (21.4%)	56 (22.9%)
Former smoker	9 (32.1%)	100 (40.9%)
Hypercholesterolemia	16 (57%)	136 (57%)
Coronary artery disease		
Double vessels	10 (35.3%)*	154 (63.1%)
Triple vessels	18 (64.3%)*	90 (36.9%)

* $p < 0.05$.

major adverse coronary events: bifurcation stenting (1/9 vs 7/11, $p = 0.005$, OR 11.6), incomplete revascularization (0/11 vs 7/10, $p = 0.003$, OR 2.4), and presence of three-vessel disease (1/14 vs 5/8, $p = 0.006$, OR 22.4).

Table V. Angiographic characteristics of the diabetic and non-diabetic patients.

	Diabetics (n = 28)	Non-diabetics (n = 244)
Jeopardy score	7.6 ± 2.2 (4-12)*	6.7 ± 2.3 (4-12)
Reference diameter	3.04 ± 0.47	3.10 ± 0.50
Lesion site		
Ostial	2 (7.1%)	16 (6.5%)
Proximal	12 (42.8%)	111 (45.5%)
Mid	12 (42.8%)	102 (41.8%)
Distal	2 (7.1%)	15 (6.1%)
Lesion type**		
Non complex (A/B1)	2 (11.1%)	29 (11.9%)
Complex (B2/C)	26 (92.9%)	215 (88.1%)
Lesion length (mm)	14 ± 8	13 ± 9
Total occlusion	9 (32.1%)	83 (26.1%)
Thrombus	3 (10.7)*	8 (3.3%)
MLD (mm)		
Pre	0.81 ± 0.34	0.85 ± 0.34
Post	2.98 ± 0.60	3.01 ± 0.56
Diameter stenosis (%)		
Pre	77 ± 14	75 ± 16
Post	8 ± 13	4 ± 13
Dilated vessel		
LAD + RCA	11 (39.3%)	81 (33.2%)
LAD + LCx	5 (17.8%)	82 (33.6%)
LAD + others	2 (11.1%)	42 (17.2%)
LAD + RCA + LCx	5 (17.8%)*	6 (2.5%)
LAD + RCA + LCx + other	5 (17.8%)	33 (13.5%)
Vessel treated/patient	2.3 ± 0.5	2.3 ± 0.5
Lesion treated/patient	3.0 ± 1.0	2.9 ± 1.0
Stents/patients	3.0 ± 1.0	3.1 ± 1.3
• 2	10 (35.7%)	112 (45.9%)
3-5	17 (60.7%)	116 (47.5%)
> 5	1 (3.6%)	16 (6.6%)
Stent length (mm)	23 ± 13	22 ± 14
Bifurcation stenting	7 (25%)	61 (25%)
Final balloon size (mm)	3.5 ± 0.5	3.5 ± 0.5
Balloon-artery ratio	1.2 ± 0.2	1.2 ± 0.1
Maximal inflation pressure (atm)	15 ± 3	15 ± 3

Abbreviations as in table II. * p < 0.05; ** modified American Heart Association/American College of Cardiology criteria.

Discussion

Feasibility and safety of multivessel stenting procedures. In the present study we found that multivessel stenting in patients with coronary artery disease involving the LAD artery is a safe procedure. It is inter-

esting that the only determinant of stent thrombosis was the number of stents per patient, although 51% of patients had only aspirin as post-stent antiplatelet therapy (due to the fact that many patients were a part of a randomized trial comparing aspirin vs aspirin plus ticlopidine). Aspirin as the only post-stent antiplatelet therapy did not reach statistical significance probably because of the small sample size.

Predictors of in-hospital outcome. The jeopardy score was the only predictor of in-hospital outcome of patients with multivessel stent implantation. It has been demonstrated that, in addition to the number of diseased vessels, the location of the obstructions and the status of the left ventricle influence the prognosis of patients with coronary artery disease^{10,11}. As originally described⁸, the coronary circulation is made of six arterial segments and a higher weight is given to stenosis with a proximal location. This score, therefore, is a simple method of estimating the risk of in-hospital complications when reviewing the coronary angiograms prior to multivessel coronary angioplasty.

Predictors of long-term outcome. Total stent length in a given patient was the only predictor of target lesion revascularization. Stent length has been demonstrated to be an important predictor of in-stent restenosis¹². In this context, the innovative concepts of "provisional" and "spot" stenting may have a new outlet for their evolution¹³.

Diabetes mellitus was the only predictor of occurrence of long-term major adverse coronary events (Fig. 2). In particular, diabetic patients had higher incidence of death and new coronary angioplasty than non-diabetics did. The choice of the best coronary revascularization strategy for diabetic patients with multivessel coronary disease has always been complex¹⁴. High restenosis rates, inability to fully revascularize all ischemic territories and progression of atherosclerosis¹⁵ are generally cited as the major problems that limit the effectiveness of percutaneous coronary revascularization in diabetic patients. Stenting could still maintain a significant advantage over coronary angioplasty but only when applied to diabetic patients without three-vessel coronary artery disease¹⁶.

Table VI. Occurrence of long-term major adverse coronary events in diabetic and non-diabetic patients.

	Diabetics (n = 28)	Non-diabetics (n = 244)	p	RR
Acute myocardial infarction	0	5 (2.1%)	0.44	
Death	4 (14.3%)	2 (0.8%)	< 0.0001	13.38 (95% CI 2.82-63.37)
Bypass surgery	1 (3.6%)	12 (4.9%)	0.75	
Repeat coronary angioplasty	4 (14.3%)	38 (15.7%)	0.68	
New coronary angioplasty	5 (17.8%)	11 (4.5%)	0.02	3.56 (95% CI 1.92-10.51)

CI = confidence interval.

Study limitation. The principal limitation is that this is a retrospective study; as such, our patient cohort does not include patients with multivessel disease who (a priori) were considered to be better candidates for bypass surgery. We should, however, note that the results of the present study referred to a population who were "potential" candidates for bypass surgery. In fact we included in the present analysis only those patients with multivessel coronary disease involving the LAD artery. The methodology to transform continuous data into categorical variables may be open to criticism; still it was essential to perform an appropriate statistical analysis. In-hospital major adverse coronary events is relatively low; routine creatine kinase levels were not obtained and major adverse coronary events may be far higher in this study than has been reported. Glycoprotein IIb/IIIa receptor antagonists were used in a small percentage of cases. It has been demonstrated that these drugs may lower the rate of complications in unstable patients and also in diabetic patients. Furthermore, follow-up by telephone conversation might have underestimated the recurrence of silent ischemia.

In conclusion, although multivessel stent implantation is a safe procedure, a careful assessment of the jeopardy score is still crucial to identify patients with high risk of acute complications. Despite improvement in procedural success and a decrease in restenosis rate with stent implantation compared to standard coronary angioplasty as reported in most randomized trials, diabetic patients continue to maintain a high incidence of events when treated percutaneously. While awaiting more conclusive results from randomized trials, our results suggest some caution in applying stenting to diabetics with multivessel disease and involvement of the LAD artery.

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