# **Original article**

# Long-term outcomes following drug-eluting stent implantation in unprotected left main bifurcation lesions

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**Background** The safety and efficacy of drug-eluting stents (DES) implantation in unprotected left main (LM) bifurcation lesions has yet to be determined. The aim of the present report was to evaluate the long-term outcome following implantation of DES in unprotected LM bifurcation lesions.

**Methods** We identified 70 consecutive patients treated with DES in unprotected LM bifurcation lesions from April 2003 to January 2005. Of them, 42 patients were treated with sirolimus-eluting stent (SES) and 28 patients were treated with paclitaxel-eluting stent (PES).

**Results** Stents to the left anterior descending and to the circumflex were implanted in 62 patients. During 1-year follow-up, 3 (4.3%) patients died of cardiac causes. One of them had myocardial infarction and adjudicated as possibly due to stent thrombosis. Angiographic follow-up was available in 80% of patients. The per lesion restenosis rate was 13.4% in the entire cohort, of which 10.7% occurred in lesions treated with SES and 16.1% in those treated with PES (P=0.58). All restenosis was focal and occurred in the lesions treated with a stent with stent size to post-procedural reference vessel diameter ratio <1.0 (17.6% vs 0, P=0.04). The per patient target lesion revascularization rate at 1 year was 17.1%. One year survival free from major adverse cardiac events was 77.1%.

**Conclusions** Treatment of LM bifurcation lesions using DES is a safe and feasible way with a low one-year mortality. The need for revascularization in 17% of patients demands for improvement.

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**S** everal studies of bare metal stents (BMS) have shown the safety and feasibility of percutaneous treatment for left main (LM) disease.<sup>1-3</sup> Yet, the restenosis rate with BMS was as high as 19% to 31%,<sup>1,4-6</sup> particularly when the distal bifurcation is involved. Recently, sirolimuseluting stent (SES)(Cypher<sup>TM</sup>, Cordis/Johnson & Johnson, Warren, NJ, USA) has remarkably decreased the restenosis rate in bifurcations with exclusion of LM lesions.<sup>7</sup> The purpose of this study was to evaluate the long-term clinical and angiographic results following drug-eluting stents (DES) implantation, either SES or paclitaxel eluting stent (PES)(Taxus<sup>TM</sup>, Boston Scientific, Natick, MA, USA) in unprotected LM bifurcation lesions.

# METHODS

#### **Study population**

Demographic and procedural data regarding all patients undergoing angioplasty at our centers are prospectively entered into a dedicated database. All consecutive patients treated with DES, either SES or PES in unprotected LM bifurcation lesions between April 2003 and January 2005 were identified. LM bifurcation was defined as distal LM disease (diameter stenosis  $\geq$  50%) with or involving the ostium of left anterior descending artery (LAD) and/or the ostium of left circumflex artery (LCX). The stenosis at the ostium of LAD or at the ostium of LCX in some cases occurred following pre-dilatation of the most diseased branch and the lesion was then treated as a bifurcational stenosis by intention to treat. Patients with acute myocardial infarction (AMI) were not included in the present report.

Percutaneous treatment rather than surgery was considered in any of the following situations: (1) suitable anatomy and lesion characteristics for stenting with contraindication to surgery on the basis of comorbidity; (2) suitable anatomy and lesion characteristics for stenting and patient preference with the agreement of the referring physician for a percutaneous approach, both of them being aware of the procedural risks.<sup>2,5,8,9</sup> European system for cardiac operative risk evaluation (EuroSCORE) was used in order to stratify the risk of death in cardiac surgical patients. The score is calculated as the sum of predefined numerical values assigned to clinical risk factors. A score value  $\geq 6$  was considered as high risk for surgery.<sup>10</sup>

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# Procedures and post-intervention medications

All procedures were performed with standard interventional techniques. One of the 5 stenting techniques was used: "Crush", "V", "T" or modified "T", provisional "T" and occasionally "Culotte" stenting.<sup>11-15</sup> The selection of a specific strategy was at the operators' discretion. The decision to use two stents was based on the presence of at least one of the following criteria: (1) lesions involving the ostium of both branches; (2) the angle between both branches was less than 45 degree and significant plaque shift could be expected; (3) either branch showed residual stenosis or a dissection following placement of a stent in one branch and balloon dilatation in the other.

Kissing balloon post-dilatation was encouraged to achieve optimal stent placement. The use of intravascular ultrasound (IVUS) and debulking were left to the operators' discretion. An intra-aortic balloon pump was used in selected patients with impaired systolic function.

Anti-platelet therapy and peri-procedural anti-coagulation followed our standard protocol.<sup>7</sup> Post-procedure creatine kinase (CK) was routinely measured in all patients following the index procedure. All patients were on maintenance aspirin therapy and thienopyridine was administered for at least 6 months following DES implantation.

## Clinical definition and follow-up

Clinical follow-up was performed by telephone contact or office visit throughout the entire follow-up period. Angiographic follow-up was recommended between 6 and 8 months post procedure unless clinically indicated earlier.

All deaths were considered as cardiac unless otherwise documented. A non-Q-wave AMI was defined as elevation of CK levels >2 times the upper limit of the normal value with an elevated CK-MB level in the absence of pathological Q-waves. Target lesion revascularization (TLR) was defined as a repeat revascularization with a stenosis  $\geq$  50% in the treated lesions. Target vessel revascularization (TVR) was defined as repeat revascularization within the treated vessels. In order to identify a new procedure performed on the target vessel but in an area clearly far away from the target lesion (after the first septal perforator in the LAD and/or after the first obtuse marginal branch in LCX), we introduce the term "remote TVR". Any remote TVR was not considered major adverse cardiac events (MACE). For the purposes of this study, MACE were defined as cardiac death, AMI and TLR. Cumulative MACE were considered as the cumulative occurrence of MACE in-hospital and during 1-year follow-up.

Stent thrombosis was defined as an acute coronary syndrome with angiographic documentation of either vessel occlusion or thrombus within or adjacent to a previously successfully stented vessel or, in the absence of angiographic confirmation, either AMI in the distribution of the treated vessel or death not clearly attributable to other causes.<sup>16</sup> According to the timing of the events, stent thrombosis was categorized into: intra-procedural, subacute (after the end of the procedure to 30 days) and late stent thrombosis (>30 days).

# Quantitative coronary angiographic (QCA) analysis

Cineangiograms were analyzed with a validated edge detection system (CMS, version 5.2, MEDIS, Leiden, the Netherlands) at baseline, after the procedure and at follow-up. All angiographic data were obtained from the single "worst" in the least foreshortened view. The type of bifurcation lesions was categorized by Lefevre's classification.<sup>17</sup> Angiographic restenosis was defined as diameter stenosis  $\geq$  50% within a previously treated segment.

# Statistical analysis

Continuous variables were presented as mean±standard deviation (SD) or median with interquartile ranges and compared using independent sample t test or the Mann-Whitney U test. Categorical variables were presented as frequencies (%) and compared with chi-square statistics or Fisher exact test. The influence of clinical, angiographic and procedural variables on restenosis was evaluated by univariate and stepwise Logistic regression analyses. All variables with a P value < 0.10 in the univariate analysis (bifurcation location, lesion length and stent size to post-procedural RVD ratio<1) were entered into the multivariate model to test for independent effects. The results were presented as adjusted odds ratios (OR)with 95% confident interval (CI). The rates of survival free of MACE and TLR were graphically represented with the Kaplan-Meier method. The influences of baseline variables on the 1 year TLR were evaluated with Cox proportional hazards regression analysis. Only those variables with a P value <0.10 in the univariate analysis (bifurcation location, lesion length and stent size to post-procedural RVD ratio <1) were entered into the multivariable model. The results are presented as adjusted hazard ratios (HR) with 95% CI. All tests were 2-tailed and P value <0.05 was considered statistically significant. Statistical analysis was performed with SPSS 11.5 (SPSS Inc., Chicago, IL, USA).

#### RESULTS

#### **Baseline and procedural characteristics**

A total of 70 consecutive patients were enrolled in this study, of them, 42 patients were treated with SES (SES group) and 28 patients with PES (PES group). Thirty-two (45.7%) patients had other lesions treated in the index procedure. EuroSCORE  $\geq 6$  was present in 14 (20.0%) patients (Table 1). Baseline lesion and procedural characteristics are shown in Tables 2 and 3. The "Crush" and "V" stenting techniques were the most frequently used (70.0%).

Table 1. Baseline clinical characteristics				
	Entire cohort ( <i>n</i> =70)	SES Group (n=42)	PES Group $(n = 28)$	P value*
Age (years)	63 ± 11	$62 \pm 12$	$65 \pm 9$	0.20
Male ( <i>n</i> (%))	60 (85.7)	37 (88.1)	23 (82.1)	0.51
Current or ex-smoker $(n (\%))$	37 (52.9)	23 (54.8)	14 (50.0)	0.81
Hypercholesterolemia (n (%))	49 (70.0)	29 (69.0)	20 (71.4)	1.0
Hypertension (n (%))	45 (64.3)	25 (59.5)	20 (71.4)	0.45
Diabetes mellitus (n (%))	18 (25.7)	11 (26.2)	7 (25.0)	1.0
Prior MI ( <i>n</i> (%))	32 (45.7)	18 (42.9)	14 (50.0)	0.63
Unstable angina (n (%))	18 (25.7)	13 (31.0)	5 (17.9)	0.34
LVEF (%)	$50.8 \pm 11.1$	$50.2\pm9.6$	$51.8 \pm 13.2$	0.57
EuroSCORE (n (%))				0.31
EuroSCORE 1-2	19 (27.1)	13 (31.0)	6 (21.4)	
EuroSCORE 3-5	37 (52.9)	23 (54.8)	14 (50.0)	
EuroSCORE 6 plus	14 (20.0)	6 (14.3)	8 (28.6)	
Other lesions treated in the index procedure $(n (\%))$	32 (45.7)	21 (50.0)	11 (39.3)	0.47
Glycoprotein IIb/IIIa inhibitors (n (%))	23 (32.9)	16 (38.1)	7 (25.0)	0.31

Values are presented as number (%) or mean ± SD. \*SES group vs PES group. LVEF: left ventricular ejection fraction; MI: myocardial infarction.

Table 2.	Baseline	lesion	characteristics
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	Entire cohort	SES Group	PES Group	
	( <i>n</i> =70)	(n=42)	( <i>n</i> =28)	P value*
Total occlusion $(n (\%))$				
LM-LAD	1 (1.4)	1 (2.4)	0	1.0
LCX	6 (8.6)	4 (9.5)	2 (7.1)	1.0
Restenotic lesions (n (%))				
LM-LAD	11 (15.7)	9 (21.4)	2 (7.1)	0.20
LCX	10 (14.3)	9 (21.4)	1 (3.6)	0.20
Guidance of IVUS (n (%))				
LM-LAD	16 (22.9)	9 (21.4)	7 (25.0)	0.78
LCX	14 (20.0)	7 (16.7)	7 (25.0)	0.54
Adjunctive Debulking (n (%))				
LM-LAD	5 (7.1)	3 (7.1)	2 (7.1)	1.0
LCX	3 (4.3)	2 (4.8)	1 (3.6)	1.0
Bifurcation type ( <i>n</i> (%))				0.84
Type 1	17 (24.3)	9 (21.4)	8 (28.6)	
Туре 2	27 (38.6)	17 (40.5)	10 (35.7)	
Type 3	4 (5.7)	3 (7.1)	1 (3.6)	
Type 4	22 (31.4)	13 (31.0)	9 (32.1)	

Values are presented as number (%) or mean±SD. \*SES group vs PES group. IVUS: intravascular ultrasound. LAD: left anterior descending artery. LCX: left circumflex artery. LM: left main.

#### QCA analysis

QCA analysis results are shown in Tables 4 and 5. Angiographic follow-up was available in 56 (80.0%) patients, of them 34 (81.0%) patients in SES group and 22 (78.6%) in PES group at median period of 6.7 months after the index procedure (interquartile ranges: 5.4 to 8.7 months). The per lesion restenosis rate was 13.4% (15/112) of which 11.8% (8/68) occurred in the SES group and 15.9% (7/44) in the PES group (P=0.73). There were no significant differences regarding late lumen loss and restenosis rates between LM-LAD and LCX (late lumen loss:  $(0.29 \pm 0.31)$  mm vs  $(0.30 \pm 0.35)$  mm, P=0.87; restenosis rate: 10.7% vs 16.1%, P=0.58). All cases of restenosis were focal ( $\leq 10$  mm in length). Of these restenotic lesions, 3 located only in the LM-LAD, 6 in LCX and 6 in both branches. Per patient restenosis rate was 21.4% (12/56) of which 20.6% (7/34) occurred in the SES group and 22.7% (5/22) in the PES group (P=1.0). By Logistic regression analysis, lesion length (OR: 1.13, 95%CI 1.03 to 1.23, P=0.009) was identified as the predictive factor of restenosis.

#### **Clinical outcomes**

In-hospital results and clinical follow-up outcomes are shown in Table 5. One patient in the PES group suffered an intra-procedural stent thrombosis and developed non-Q-wave AMI. Clinical follow-up was available in all patients at a median period of 12.3 months after the index procedure (interquartile ranges: 7.0 to 17.3 months). Cardiac death occurred in 3 (4.3%) patients: the first patient (treated with SES) died of a Q-wave AMI 7 days after premature discontinuation of antiplatelet therapy because of acute pancreatitis (55 days after the index procedure and was adjudicated as late stent thrombosis), the second patient died of pulmonary edema (118 days after the procedure, this patient had severe aortic and mitral regurgitation), the third patient died of complications related to elective bypass surgery. One patient in PES group developed a non-Q-wave AMI 103 days after the index procedure and was adjudicated as a late stent thrombosis.

TLR was performed in 12 (17.1%) of patients (9 repeat percutaneous treatment and 3 bypass surgery). Four of them

	Entire cohort SES Group		PES Group	
	( <i>n</i> = 70)	( <i>n</i> =42)	( <i>n</i> =28)	P value*
Treatment strategy (n (%))				0.001
Crush stenting	34 (48.6)	17 (40.5)	17 (60.7)	
V stenting	15 (21.4)	9 (21.4)	6 (21.4)	
T and modified T stenting	8 (11.4)	8 (19.0)	0	
Provisional stenting	8 (11.4)	8 (19.0)	0	
Culotte stenting	5 (7.1)	0	5 (17.9)	
Mean stent length (mm)				
LM-LAD	$23.4\pm7.0$	$23.5\pm7.7$	$23.1\pm6.0$	0.82
LCX	$22.4\pm8.2$	$23.4\pm8.7$	$21.0\pm7.1$	0.24
Stent-to-artery ratio (baseline)				
LM-LAD	$1.05\pm0.21$	$1.06\pm0.24$	$1.04\pm0.17$	0.81
LCX	$1.08\pm0.19$	$1.06\pm0.15$	$1.11\pm0.23$	0.29
Stent-to-artery ratio (post-procedure)				
LM-LAD	$0.92 \pm 0.14$	$0.93\pm0.14$	$0.91\pm0.15$	0.49
LCX	$0.93\pm0.12$	$0.94 \pm 0.11$	$0.93\pm0.14$	0.94
Maximal inflation pressure (kPa)				
LM-LAD	$1600.9 \pm 334.4$	$1621.2 \pm 304.0$	$1580.7 \pm 364.8$	0.63
LCX	$1590.8 \pm 202.7$	$1611.1 \pm 253.3$	$1550.3 \pm 27306$	0.36
Maximum balloon diameter (mm)				
LM-LAD	$3.38\pm0.35$	$3.36\pm0.38$	$3.41\pm0.31$	0.63
LCX	$3.11\pm0.39$	$3.05\pm0.41$	$3.16\pm0.35$	0.25
Balloon-to-artery ratio (baseline)				
LM-LAD	$1.07\pm0.19$	$1.09\pm0.22$	$1.06\pm0.15$	0.59
LCX	$1.09\pm0.18$	$1.08\pm0.16$	$1.11\pm0.21$	0.45
Balloon-to-artery ratio (post-procedure)				
LM-LAD	$0.95\pm0.13$	$0.96\pm0.12$	$0.92\pm0.13$	0.16
LCX	$0.95\pm0.11$	$0.95\pm0.10$	$0.95\pm0.13$	0.97
Usage of IABP per patient (n (%))	17 (24.3)	7 (16.7)	10 (35.7)	0.12
Kissing balloon post-dilation (n (%))	53 (75.7)	29 (69.0)	24 (85.7)	0.16

Values are presented as number (%) or mean ± SD. \*SES group vs PES group. IABP: intra-aortic balloon pump.

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Table 4. Quantitative con		analysis for LNI-LAD

	Tuble in Quantum ve coronary angrography analysis for Entre Entre			
	Entire cohort	Entire cohort SES Group (n=70) $(n=42)$	PES Group $(n = 28)$	P value*
	( <i>n</i> = 70)			1 value
Baseline				
RVD (mm)	$3.23\pm0.59$	$3.20\pm0.65$	$3.27\pm0.52$	0.63
MLD (mm)	$1.25\pm0.52$	$1.17\pm0.54$	$1.36\pm0.47$	0.13
Diameter stenosis (%)	$61.4 \pm 15.1$	$63.8 \pm 14.7$	$57.9 \pm 15.2$	0.11
Mean lesion length (mm)	$9.1 \pm 4.7$	$9.6\pm5.0$	$8.5\pm4.2$	0.35
Post procedure				
RVD (mm)	$3.63\pm0.53$	$3.54\pm0.49$	$3.78\pm0.55$	0.06
MLD (mm)	$3.21 \pm 0.52$	$3.13\pm0.51$	$3.34\pm0.52$	0.09
Diameter stenosis (%)	$11.5 \pm 8.6$	$11.6\pm7.8$	$11.3\pm9.8$	0.90
Acute gain (mm)	$1.96\pm0.66$	$1.95\pm0.70$	$1.98\pm0.62$	0.89
Follow-up				
RVD (mm)	$3.62\pm0.55$	$3.61\pm0.57$	$3.63\pm0.53$	0.90
MLD (mm)	$2.88\pm0.84$	$2.80\pm0.92$	$3.03\pm0.70$	0.37
Diameter stenosis (%)	$20.8\pm20.4$	$23.6\pm21.7$	$16.1 \pm 17.6$	0.23
Mean lesion length (mm)	$6.2 \pm 4.9$	$5.4 \pm 4.2$	$7.5\pm5.7$	0.13
Late lumen loss (mm)	$0.29\pm0.31$	$0.26\pm0.34$	$0.35\pm0.27$	0.72
Restenosis (n (%))	6/56 (10.7)	3/34 (8.8)	3/22 (13.6)	0.67

Values are presented as number (%) or mean ± SD. \*SES group vs PES group. MLD: minimal lumen diameter. RVD: reference vessel diameter.

had angina, 1 had objective evidence of ischemia while the other 4 asymptomatic patients were treated due to the severity of the restenotic lesions found. TVR was performed in 18 (25.7%) patients, 12 of them were due to TLR and the remaining 6 patients for distal lesions (remote TVR). The rate of survival-free from TLR at 1-year was 82.9% and MACE-free survival rate was 77.1% (Fig.). Lesion length was identified as a predictor of TLR (HR: 1.09, 95% CI 1.03 to 1.15, P=0.005).

## DISCUSSION

The main findings of this study are: (1) treatment of LM bifurcation using DES is safe and feasible; (2) all restenosis was focal and occurred in the lesions treated with a stent with stent size to post-procedural reference vessel diameter ratio <1.0; (3) contrary to prior experience with BMS, adverse events in the present study were mainly due to TLR, with a low incidence of cardiac

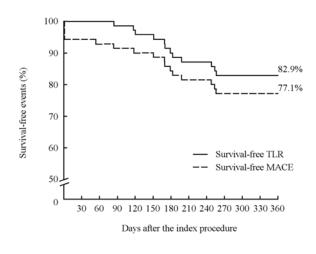
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	Entire cohort	SES Group	PES Group	P value*
	( <i>n</i> =70)	( <i>n</i> =42)	( <i>n</i> = 28)	I value
Baseline				
RVD (mm)	$2.94\pm0.58$	$2.88 \pm 0.56$	$3.03 \pm 0.61$	0.29
MLD (mm)	$1.14\pm0.65$	$1.18\pm0.76$	$1.09 \pm 0.44$	0.56
Diameter stenosis (%)	$60.3 \pm 22.1$	$58.0\pm25.6$	$63.6 \pm 15.1$	0.30
Mean lesion length (mm)	$9.8\pm5.9$	$10.5 \pm 6.7$	$8.7 \pm 4.4$	0.19
Post procedure				
RVD (mm)	$3.23\pm0.59$	$3.25\pm0.57$	$3.49\pm0.46$	0.07
MLD (mm)	$2.89\pm0.42$	$2.83\pm0.47$	$2.99\pm0.32$	0.10
Diameter stenosis (%)	$12.7\pm8.9$	$12.0 \pm 9.1$	$13.8 \pm 8.7$	0.42
Acute gain (mm)	$1.75\pm0.76$	$1.65\pm0.89$	$1.91\pm0.47$	0.15
Follow-up				
RVD (mm)	$3.26\pm0.53$	$3.25\pm0.59$	$3.26\pm0.42$	0.99
MLD (mm)	$2.36\pm0.82$	$2.26\pm0.85$	$2.53 \pm 0.77$	0.30
Diameter stenosis (%)	$27.5 \pm 23.9$	$30.8 \pm 22.7$	$21.8\pm25.8$	0.24
Mean lesion length (mm)	$6.5 \pm 4.3$	$5.8 \pm 3.6$	$7.6 \pm 5.1$	0.19
Late lumen loss (mm)	$0.30 \pm 0.35$	$0.23 \pm 0.34$	$0.43\pm0.37$	0.41
Restenosis (n (%))	9/56 (16.1)	5/34 (14.7)	4/22 (18.2)	0.73

Values are presented as number (%) or mean  $\pm$  SD. \*SES group vs PES group.

	SES group PES group				
	Entire cohort (n=70)	( <i>n</i> =42)	(n=28)	P value*	
In-hospital MACE (n (%))	4 (5.7)	1 (2.4)	3 (10.7)	0.29	
Cardiac Death	0	0	0		
MI					
Q-wave MI	0	0	0		
Non-Q-wave MI	4 (5.7)	1 (2.4)	3 (10.7)	0.29	
TLR	0	0	0		
TVR	0	0	0		
Cumulative 1 year MACE (n (%))	16 (22.9)	9 (21.4)	7 (25.0)	0.78	
Cardiac Death	3 (4.3)	2 (4.8)	1 (3.6)	1.0	
MI					
Q-wave MI	1 (1.4)	1 (2.4)	0	0.84	
Non-Q-wave MI	4 (5.7)	1 (2.4)	3 (10.7)	0.29	
TLR	12 (17.1)	7 (16.7)	5 (17.9)	1.0	
Remote TVR	6 (8.6)	3 (7.1)	3 (10.7)	0.68	
Any revascularization	18 (25.7)	10 (23.8)	8 (28.6)	0.78	
Stent thrombosis (n (%))					
Intra-procedural	1 (1.4)	0	1 (3.6)	0.84	
Subacute	0	0	0	-	
Late	2 (3.9)	1 (2.4)	1 (3.6)	0.66	

Values are presented as number (%) or mean ± SD. \*SES group vs PES group. MACE: major adverse cardiac events. TLR: target lesion revascularization. TVR: target vessel revascularization.



**Fig.** Kaplan-Meier curve of survival-free from events during 1 year follow-up. Solid line: Survival-free from of target lesions revascularization; Dash line: Survival-free from of major adverse cardiac events.

death (4.3%); (4) the 21.4% restenosis rate per patient demands for further improvements.

#### **Comparison with historical controls**

Contrary to the previously published studies on BMS, adverse events during follow-up in the present study are mainly due to TLR, rather than AMI or death. In the era of BMS, the one-year mortality for unprotected LM stenting was approximately 2%-5% for good surgical candidates and 11%-21% for poor surgical candidates.<sup>1,8,9</sup> Recently, one study reported that one-year mortality was 28% following unprotected LM stenting with BMS.<sup>2</sup> In our study, one year mortality was 4.3%, of which 3.6% (2/56) and 7.1% (1/14) were found in patients with EuroSCORE <6 and  $\geq 6$  respectively. These favourable results concur with 3 recently published papers regarding SES implantation in LM (no cardiac death).<sup>18-20</sup> LM restenosis following BMS implantation usually manifests itself as cardiac death rather than ischemic symptoms.<sup>2,5</sup>

It is possible that the reduction in mortality could be explained by a combination of less restenosis and perhaps a more "benign" pattern of restenosis. The restenosis rates between LM-LAD and LCX in present study were similar (10.7% vs 16.1%, P=0.58); this result differs from the SES randomized bifurcation study in which more restenosis occurred in the side branch.<sup>7</sup> Large vessel size and more "Crush" stenting technique usage might, at least in part, contribute to this difference.<sup>7,11,21-23</sup> It is worth noting that all restenotic lesions in our study were focal and almost all were amenable to percutaneous therapy. This hypothesis is intriguing, however, it is important to realise that there is no evidence to support a mortality benefit for DES currently.<sup>24</sup> In this study, the small number of patients and only one-year follow-up should prevent us from drawing any premature conclusions regarding this issue. A randomized study with long-term follow-up is warranted.

Contrary to the findings of Kim's,<sup>25</sup> when we compared LM bifurcation lesions treated with "Crush" technique versus other techniques, we did not find statistical significant differences in outcomes. The restenosis rate was 10.0% in the LAD and 23.3% in the LCX treated with "Crush" technique, 11.5% and 7.7% treated with other techniques, respectively. The small number does not allow any conclusions. Still we need to acknowledge that the lesions treated with "Crush" had a slightly higher risk profile (baseline RVD 3.16 mm vs 3.30 mm for LAD and 2.89 mm vs 2.98 mm for LCX, with lesion length 11.2 mm vs 8.5 mm in LCX.

Despite the significant improvement in restenosis, it is important to realise that the rate of TLR in the present study remains a two digit number. The high angiographic follow-up rate may have contributed to the increased usage of revascularization; however it is understandable that many operators are reluctant to ignore a restenotic lesion in the LM in light of the historical data on its association with cardiac death.

# Predictors of restenosis and TLR

Consistent with other studies, lesion length was identified as a predictor of restenosis and TLR.<sup>26,27</sup> Recently, one study suggested that LM stenting using a 3.0 mm SES resulted in a relatively high TLR rate (18.7%).<sup>28</sup> In our study, the restenosis rate in the lesions treated with  $\leq$ 3.0 mm stents (either SES or PES) was 20.0% (12/60) and 6.5% (3/46) in the ones treated with >3.0 mm stents (P=0.06), with the rate of TLR 29.4% (10/34) and 5.6% (2/36), respectively (P=0.01). It might be reasonable to postulate that an undersized stent might not achieve adequate or homogenous drug delivery in large vessels. Even if the numbers are small it is important to consider that when the size of the LM bifurcation is over 3 mm we can expect single digit restenosis rates. A higher usage of IVUS could have helped to determine the correct size of the LM and utilize and post-dilate stents to a more appropriate size.

# Limitations

The limitations of present study are: (1) it is a retrospective study, the choice of stenting strategy was at the operators' discretion and was non-randomized. The number of patients in each stenting technique is too small to prevent us from finding the most appropriate approach for treatment LM bifurcation; (2) not all patients underwent angiographic follow-up and only 20% of patients underwent angioplasty with IVUS guidance; (3) clinical follow-up was limited to 1 year. Despite these limitations, the efficacy of DES implantation in LM bifurcation lesions appears promising.

# Conclusions

Treatment of LM bifurcation lesions using DES is safe and feasible with a low 1 year mortality. The need for revascularization in 17% of patients demands for improvement.

#### REFERENCES

- Park SJ, Hong MK, Lee CW, Kim JJ, Song JK, Kang DH, et al. Elective stenting of unprotected left main coronary artery stenosis: effect of debulking before stenting and intravascular ultrasound guidance. J Am Coll Cardiol 2001; 38: 1054-1060.
- 2. Kelley MP, Klugherz BD, Hashemi SM, Meneveau NF, Johnston JM, Matthai WH Jr, et al. One-year clinical outcomes of protected and unprotected left main coronary artery stenting. Eur Heart J 2003; 24: 1554-1559.
- 3. Brueren BR, Ernst JM, Suttorp MJ, ten Berg JM, Rensing BJ, Mast EG, et al. Long term follow up after elective percutaneous coronary intervention for unprotected non-bifurcational left main stenosis: is it time to change the guidelines? Heart 2003; 89: 1336-1339.
- 4. Hu FB, Tamai H, Kosuga K, Kyo E, Hata T, Okada M, et al. Intravascular ultrasound-guided directional coronary atherectomy for unprotected left main coronary stenoses with distal bifurcation involvement. Am J Cardiol 2003; 92: 936-940.
- Takagi T, Stankovic G, Finci L, Toutouzas K, Chieffo A, Spanos V, et al. Results and long-term predictors of adverse clinical events after elective percutaneous interventions on unprotected left main coronary artery. Circulation 2002; 106: 698-702.
- Park SJ, Lee CW, Kim YH, Lee JH, Hong MK, Kim JJ, et al. Technical feasibility, safety, and clinical outcome of stenting of unprotected left main coronary artery bifurcation narrowing. Am J Cardiol 2002; 90: 374-378.
- Colombo A, Moses JW, Morice MC, Ludwig J, Holmes DR Jr, Spanos V, et al. Randomized study to evaluate sirolimus-eluting stents implanted at coronary bifurcation lesions. Circulation 2004; 109: 1244-1249.
- Black A, Cortina R, Bossi I, Choussat R, Fajadet J, Marco J. Unprotected left main coronary artery stenting: correlates of midterm survival and impact of patient selection. J Am Coll Cardiol 2001; 37: 832-838.
- 9. Silvestri M, Barragan P, Sainsous J, Bayet G, Simeoni JB, Roquebert PO, et al. Unprotected left main coronary artery stenting: immediate and medium-term outcomes of 140

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elective procedures. J Am Coll Cardiol 2000; 35: 1543-1550.

- Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg 1999; 16: 9-13.
- Colombo A, Stankovic G, Orlic D, Corvaja N, Liistro F, Airoldi F, et al. Modified T-stenting technique with crushing for bifurcation lesions: immediate results and 30-day outcome. Catheter Cardiovasc Interv 2003; 60: 145-151.
- Colombo A, Gaglione A, Nakamura S, Finci L. "Kissing" stents for bifurcational coronary lesion. Cathet Cardiovasc Diagn 1993; 30: 327-330.
- Schampaert E, Fort S, Adelman AG, Schwartz L. The V-stent: a novel technique for coronary bifurcation stenting. Cathet Cardiovasc Diagn 1996; 39: 320-326.
- Sheiban I, Albiero R, Marsico F, Dharmadhikari A, Tzifos V, Pagnotta P, et al. Immediate and long-term results of "T" stenting for bifurcation coronary lesions. Am J Cardiol 2000; 85: 1141-1144.
- Chevalier B, Glatt B, Royer T, Guyon P. Placement of coronary stents in bifurcation lesions by the "culotte" technique. Am J Cardiol 1998; 82: 943-949.
- Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. N Engl J Med 2004; 350: 221-231.
- Lefevre T, Louvard Y, Morice MC, Dumas P, Loubeyre C, Benslimane A, et al. Stenting of bifurcation lesions: classification, treatments, and results. Catheter Cardiovasc Interv 2000; 49: 274-283.
- Arampatzis CA, Lemos PA, Hoye A, Saia F, Tanabe K, van der Giessen WJ, et al. Elective sirolimus-eluting stent implantation for left main coronary artery disease: six-month angiographic follow-up and 1-year clinical outcome. Catheter Cardiovasc Interv 2004; 62: 292-296; discussion 297.
- Park S, Kim Y, Lee B, Lee S, Lee C, Hong M, et al. Sirolimus-eluting stent implantation for unprotected left main coronary artery stenosisPulmonary artery stenting for recurrent lung cancer after left pneumonectomy. J Am Coll Cardiol 2005; 45: 351-356.
- de Lezo JS, Medina A, Pan M, Delgado A, Segura J, Pavlovic D, et al. Rapamycin-eluting stents for the treatment of

unprotected left main coronary disease. Am Heart J 2004; 148: 481-485.

- Ajani AE, Waksman R, Cha DH, Gruberg L, Satler LF, Pichard AD, et al. The impact of lesion length and reference vessel diameter on angiographic restenosis and target vessel revascularization in treating in-stent restenosis with radiation. J Am Coll Cardiol 2002; 39: 1290-1296.
- 22. Ge L, Airoldi F, Iakovou I, Cosgrave J, Michev I, Sangiorgi GM, et al. Clinical and angiographic outcome after implantation of drug-eluting stents in bifurcation lesions with the crush stent technique: importance of final kissing balloon post-dilation. J Am Coll Cardiol 2005; 46: 613-620.
- 23. Hoye A, Iakovou I, Ge L, van Mieghem CA, Ong AT, Cosgrave J, et al. Long-term outcomes after stenting of bifurcation lesions with the "crush" technique: predictors of an adverse outcome. J Am Coll Cardiol 2006; 47: 1949-1958.
- Babapulle MN, Joseph L, Belisle P, Brophy JM, Eisenberg MJ. A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. Lancet 2004; 364: 583-591.
- 25. Kim YH, Park SW, Hong MK, Park DW, Park KM, Lee BK, et al. Comparison of simple and complex stenting techniques in the treatment of unprotected left main coronary artery bifurcation stenosis. Am J Cardiol 2006; 97: 1597-1601.
- Singh M, Gersh BJ, McClelland RL, Ho KK, Willerson JT, Penny WF, et al. Clinical and angiographic predictors of restenosis after percutaneous coronary intervention: insights from the Prevention of Restenosis With Tranilast and Its Outcomes (PRESTO) trial. Circulation 2004; 109: 2727-2731.
- 27. Singh M, Gersh BJ, McClelland RL, Ho KK, Willerson JT, Penny WF, et al. Predictive factors for ischemic target vessel revascularization in the Prevention of Restenosis with Tranilast and its Outcomes (PRESTO) trial. J Am Coll Cardiol 2005; 45: 198-203.
- Chieffo A, Stankovic G, Bonizzoni E, Tsagalou E, Iakovou I, Montorfano M, et al. Early and mid-term results of drug-eluting stent implantation in unprotected left main. Circulation 2005; 111: 791-795.

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