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Long-Term Outcomes After Stenting of Bifurcation Lesions With the "Crush" Technique

Predictors of an Adverse Outcome

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OBJECTIVES The purpose of this study was to evaluate predictors of an adverse outcome after "crush" bifurcation stenting.

BACKGROUND The "crush" technique is a recently introduced strategy with limited data regarding long-term outcomes.

METHODS We identified 231 consecutive patients treated with drug-eluting stent implantation with the "crush" technique for 241 de novo bifurcation lesions. Clinical follow-up was obtained in 99.6%.

RESULTS The in-hospital major adverse cardiac event (MACE) rate was 5.2%. At 9 months, 10 (4.3%) patients had an event consistent with possible post-procedural stent thrombosis. Survival free of target lesion revascularization (TLR) was 90.3%; the only independent predictor of TLR was left main stem (LMS) therapy (odds ratio [OR] 4.97; 95% confidence interval [CI] 2.00 to 12.37, $p = 0.001$). Survival free of MACE was 83.5% and independent predictors of MACE were LMS therapy (OR 3.79; 95% CI 1.76 to 8.14, $p = 0.001$) and treatment of patients with multivessel disease (OR 4.21; 95% CI 0.95 to 18.56, $p = 0.058$). Angiographic follow-up was obtained in 77% of lesions at 8.3 ± 3.7months. The mean late loss of the main vessel and side branch were 0.30 ± 0.64 mm and 0.41 ± 0.67 mm, respectively, with binary restenosis rates of 9.1% and 25.3%. Kissing balloon post-dilation significantly reduced the side branch late lumen loss (0.24 ± 0.50 mm vs. 0.58 ± 0.77 mm, $p < 0.001$).

CONCLUSIONS The crush technique of bifurcation stenting with drug-eluting stents is associated with favorable outcomes for most lesions; however, efficacy appears significantly reduced in LMS bifurcations, and further research is needed before the technique can be routinely recommended in this group. Furthermore, the incidence of possible stent thrombosis is of concern and requires further investigation. Kissing balloon post-dilatation is mandatory to reduce side branch restenosis. (J Am Coll Cardiol 2006;47:1949–58) © 2006 by the American College of Cardiology Foundation

The outcome of percutaneous coronary intervention of bifurcation lesions with bare-metal stents (BMS) is hindered by increased rates of procedural complications and long-term major adverse cardiac events (MACE) compared with non-bifurcated lesions (1). Randomized studies have demonstrated that drug-eluting stents (DES) reduce restenosis when used in relatively simple lesions (2–5); and recent data have demonstrated efficacy of the sirolimus-eluting stent (SES) (Cypher, Cordis/Johnson & Johnson, Warren, New Jersey) for bifurcation lesions compared with historical data of BMS (6–8). In one study of bifurcation lesions (6), the overall restenosis rate was 23%, with the majority of side branch restenoses occurring at the ostium after use of a T-stenting technique. Indeed, side branch restenosis occurred in 16.7% after T-stenting, compared with 7.1% after other stenting techniques. We hypothesized that these restenoses might relate to incomplete coverage of the side branch ostium thereby reducing the efficacy of the DES.

The "crush" technique of bifurcation stenting with DESs was introduced by Colombo et al. (9) in 2002 as a relatively simple technique that ensures complete coverage of the side branch ostium (Fig. 1) thereby facilitating drug delivery at this site. Initial data of 20 patients treated with this technique with SES suggest that it is a safe method, with an acceptable rate of procedural complications and no further adverse events up to 30 days' follow-up. Recently, angiographic data have shown the importance of simultaneous

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Abbreviations and Acronyms

AMI = acute myocardial infarction
BMS = bare-metal stent
CABG = coronary artery bypass graft
CI = confidence interval
DES = drug-eluting stent
LMS = left main stem
MACE = major adverse cardiac event
MLD = minimal lumen diameter
OR = odds ratio
PES = paclitaxel-eluting stent
SES = sirolimus-eluting stent
TLR = target lesion revascularization
TVR = target vessel revascularization

kissing balloon post-dilation in reducing restenosis and need for target lesion revascularization (10). We evaluated the clinical and angiographic outcomes of patients treated with either SES or paclitaxel-eluting stent (PES) (Taxus, Boston Scientific, Natick, Massachusetts) implantation with this strategy at our institutions and evaluated the predictors of an adverse outcome.

METHODS

Study population. Demographic and procedural data regarding all patients undergoing angioplasty at EMO Centro Cuore Columbus, San Raffaele Hospital (Italy), and Thoraxcenter (the Netherlands) are prospectively entered into dedicated databases. We identified all consecutive patients who underwent bifurcation stenting with the crush technique with DESs. Initially, therapy was undertaken with the SES beginning in April 2002, when the SES received Conformité Européenne (CE) mark approval. In the first quarter of 2003, patients could also be treated with the PES. Patients with either stable or unstable angina were included if they were treated for a de novo bifurcation lesion. Those with acute ST-segment elevation myocardial infarction were excluded. Sirolimus-eluting stents were available in diameters from 2.25 mm to 3.00 mm and lengths from 8 mm to 33 mm; PESs were available in diameters from 2.25 mm to 3.5 mm and lengths from 8 mm to 32 mm.

Procedures and intervention medications. The crush technique is depicted in Figure 1 and has been previously described (9). In short, the procedure requires a guide catheter of ≥7-F. Both the main vessel and side branch are wired and prepared for stent implantation with pre-dilatation as necessary. The stents are both positioned such that the proximal part of the side branch lies well within the main vessel but is completely covered by the stent within the main vessel (Fig. 1B). The side branch stent is deployed and the balloon carefully removed ensuring that the stent in the main vessel remains fixed. The wire within the side branch is commonly also removed, although providing that the wire is not hydrophilic, it might be kept in position. The stent in the main vessel is deployed, thereby crushing the proximal part of the side branch stent (and trapping the side branch wire if still in situ). If present, the wire in the side branch can then be withdrawn, and post-dilation of the main vessel stent with high-pressure balloon inflation facilitates use of a wire to re-cross into the side branch to allow kissing balloon post-dilation. Kissing balloon post-dilation was undertaken at the operator's discretion. The protocol was approved by the institutional ethics committees and is in accordance with the principles of Good Clinical Practice for Trials of Medicinal Products in the European Community and the Declaration of Helsinki. All patients signed a written informed consent.

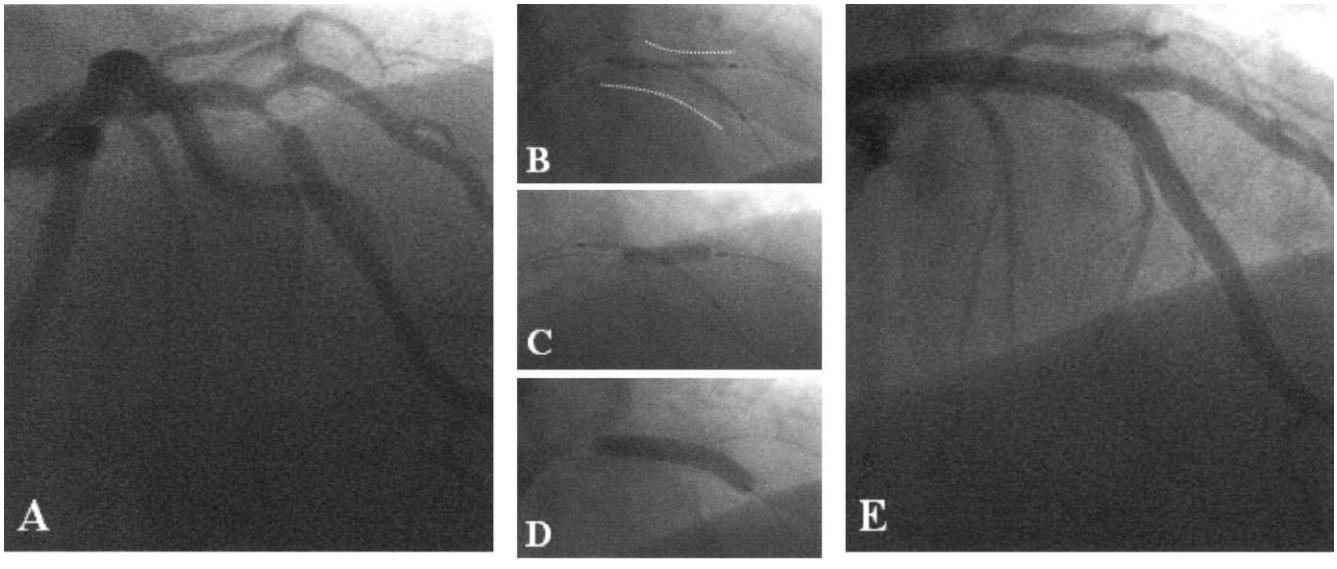

Figure 1. The crush technique of bifurcation stenting. **(A)** Baseline angiogram with significant stenosis of the left anterior descending/first diagonal bifurcation. **(B)** Both vessels are wired, and both stents are positioned. A 2.5 × 12 mm Taxus stent is positioned in the side branch with its proximal part well within the main vessel; at the same time, a 3.0 × 24 mm Taxus stent is within the main vessel, ensuring it completely covers the proximal part of the side branch stent. **(C)** The side branch stent is deployed, and the balloon is withdrawn. **(D)** The stent in the main vessel is deployed. **(E)** Final result.

Table 1. Baseline Patient Demographics

	All n = 231	SES n = 130	PES n = 101	p Value
Mean age (yrs)	62.8 ± 11.2	62.9 ± 11.2	62.6 ± 11.1	0.76
Male (%)	193 (83.5)	113 (86.9)	80 (79.2)	0.15
Current smoker (%)	44 (19.0)	24 (18.5)	20 (19.8)	0.87
Diabetes mellitus (%)	46 (19.9)	25 (19.2)	21 (20.8)	0.74
Hypertension (%)	125 (54.1)	76 (58.5)	49 (48.5)	0.14
Hypercholesterolemia (%)	162 (70.1)	91 (70.0)	71 (70.3)	1.0
Family history (%)	103 (44.6)	53 (40.8)	50 (49.5)	0.23
Previous myocardial infarction (%)	95 (41.1)	48 (36.9)	47 (46.5)	0.22
Previous CABG (%)	33 (14.3)	18 (13.8)	15 (14.9)	0.85
Multivessel disease (%)	174 (75.3)	98 (75.4)	76 (75.2)	1.0
Clinical presentation				1.0
Stable angina (%)	172 (74.5)	96 (73.8)	76 (75.2)	
Unstable angina (%)	59 (25.5)	34 (26.2)	25 (24.8)	
Glycoprotein IIb/IIIa inhibitor usage (%)	73 (31.6)	53 (40.8)	20 (19.8)	0.001

p value for the sirolimus-eluting stent (SES) group versus paclitaxel-eluting stent (PES) group.
CABG = coronary artery bypass graft surgery.

During the procedure, intravenous heparin was given to maintain an activated clotting time ≥250 s. Patients were preloaded with 300 mg clopidogrel and received life-long aspirin together with 75 mg clopidogrel/day for at least 6 months. The use of glycoprotein IIb/IIIa inhibitors was at the operator's discretion.

Clinical definitions and follow-up. Clinical follow-up was obtained with either telephone calls or office visit and evaluated the rate of MACE, pre-defined as death, acute myocardial infarction (AMI), or target vessel revascularization (TVR). The diagnosis of AMI both peri-procedural and at follow-up required an elevation of creatine kinase levels to twice the upper limit of normal, together with a rise in creatine kinase-MB fraction. When in addition to enzyme elevation there were new pathological Q waves on the electrocardiogram, the event was defined as Q-wave myocardial infarction. Target lesion revascularization (TLR) was defined as either surgical or percutaneous reintervention driven by significant (>50%) luminal diameter narrowing either within the stent or the 5 mm borders proximal and distal to the stent and was undertaken in the presence of either anginal symptoms or objective evidence of ischemia. Target vessel revascularization was defined as revascularization within the target vessel including encompassing the target lesion.

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 acute AMI in the distribution of the treated vessel or death not clearly attributable to other causes (11,12). Stent thrombosis was categorized according to the timing of the event into: intra-procedural (angiographic, confirmed intra-luminal filling defect within the stent that occurred during the index procedure) (13), acute (occurred within the first 24 h after the procedure), subacute (from 24 h to 30 days), and late (>30 days after the index procedure).

Table 2. Baseline Procedural Characteristics

	All n = 241	SES n = 137	PES n = 104	p Value
Target vessel				0.15
LAD/diagonal (%)	130 (53.9)	82 (59.9)	48 (46.2)	
LCX/obtuse marginal (%)	52 (21.6)	28 (20.4)	24 (23.1)	
RCA bifurcation (%)	12 (5.0)	6 (4.4)	6 (5.8)	
LMS (%)	47 (19.5)	21 (15.3)	26 (25.0)	
Mean number of stents in the main vessel	1.2 ± 0.5	1.24 ± 0.51	1.22 ± 0.50	0.82
Mean nominal diameter of stent in the main vessel (mm)	3.01 ± 0.32	2.95 ± 0.29	3.09 ± 0.34	0.001
Mean total length of stents in the main vessel (mm)	29.3 ± 11.3	30.31 ± 10.96	28.05 ± 11.58	0.12
Mean number of stents in the side branch	1.1 ± 0.3	1.08 ± 0.32	1.03 ± 0.26	0.18
Mean nominal diameter of stent in the side branch (mm)	2.62 ± 0.32	2.58 ± 0.30	2.68 ± 0.34	0.02
Mean total length of stents in the side branch (mm)	21.3 ± 9.3	21.45 ± 10.11	21.01 ± 8.28	0.72
Post-dilation with kissing balloons (%)	122 (50.6)	58 (42.3)	64 (61.5)	0.004

p value for the sirolimus-eluting stent (SES) group versus paclitaxel-eluting stent (PES) group.
LAD = left anterior descending artery; LCX = circumflex artery; LMS = left main stem; RCA = right coronary artery.

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Table 3. Clinical Outcomes

	All n = 231	SES n = 130	PES n = 101	p Value
In-hospital MACE, n (%)	11 (4.8)	5 (3.8)	6 (5.9)	0.5
Cardiac death, n (%)	0	0	0	1.0
Acute myocardial infarction, n (%)	11 (4.8)	5 (3.8)	6 (5.9)	0.5
Q-wave myocardial infarction	1 (0.4)	1 (0.8)	0	0.4
Non–Q-wave myocardial infarction	10 (4.3)	4 (3.1)	6 (5.9)	0.3
Target lesion revascularization, n (%)	1 (0.4)	1 (0.8)	0	0.4
Target vessel revascularization, n (%)	1 (0.4)	1 (0.8)	0	0.4

p value for the sirolimus-eluting stent (SES) group versus paclitaxel-eluting stent (PES) group.
MACE = major adverse cardiac events.

Angiographic evaluation. Procedural angiographic success was defined as a post-procedural final residual stenosis <50% with Thrombolysis In Myocardial Infarction flow grade 3 in both the main vessel and side branch. Between 6 and 12 months after the index procedure, all living patients were invited back for angiographic follow-up. Coronary angiograms were obtained in multiple views after intracoronary injection of nitrates. Quantitative coronary angiographic (QCA) analysis was performed with one of two validated edge detection systems (CMS, version 5.2, MEDIS, Leiden, the Netherlands; and the Cardiovascular Angiography Analysis System II [CAAS II], Pie Medical, Maastricht, the Netherlands). The reference vessel diameter, minimal lumen diameter (MLD), and percent diameter stenosis were measured at pre-procedure, post-procedure, and follow-up. Reference vessel diameter for the side branch was taken as the diameter of the normal vessel distal to the bifurcation. The late lumen loss was calculated as the difference between the post-procedure and follow-up MLD (14). Binary restenosis was defined as the presence of >50% diameter stenosis within the target lesion.

Statistical analysis. Discrete variables are presented as percentages and compared with Fisher exact test. Continuous variables are expressed as mean ± standard deviation and compared with Student *t* test. Cumulative survival free of adverse events was calculated according to the Kaplan-Meier method. Logistic regression models were established to investigate independent predictors of TLR and MACE. The following clinical variables were entered into the analysis model: age, gender, diabetes, stent type, unstable angina, premature antiplatelet therapy discontinuation, left main stem (LMS) bifurcation, glycoprotein IIb/IIIa inhibitor use, kissing balloon post-dilation, nominal stent diameter, and stent length. Odds ratios (ORs) with corresponding 95% confidence intervals (CIs) are reported. All tests were two-tailed, and a p value of <0.05 was considered significant.

RESULTS

The crush technique was used in 231 patients (241 lesions), with SES in 137 (56.8%), and PES in 104 (43.2%). The baseline patient and procedural characteristics are presented in Tables 1 and 2. The use of glycoprotein IIb/IIIa inhibitor therapy was significantly higher in the SES group than in the PES group (40.8% vs. 19.8%, p = 0.001). Attempted kissing balloon post-dilatation was undertaken in 128 lesions and was successful in 122 (95%) cases; it was carried out more frequently in the PES group (61.5% vs. 42.3% in SES, p = 0.004).

Clinical outcomes. The rate of in-hospital adverse events is shown in Table 3. There were three (1.3%) intraprocedural stent thromboses (two in the SES group, one in the PES group); two of these developed non–Q-wave AMI. The mean total stent length of these three cases was 69 mm, and no glycoprotein IIb/IIIa inhibitor had been given electively. After thrombolytic therapy and further balloon inflation, thrombosis resolved. One additional patient in the SES group developed a Q-wave myocardial infarction in hospital due to occlusion of septal branches during the index procedure. By logistic regression analysis, the only predictor for in-hospital MACE was the use of a glycoprotein IIb/IIIa inhibitor in patients (OR 3.25; 95% CI 0.99 to 10.60, p = 0.051).

Clinical follow-up data at nine months was available in 99.6% of patients. The cumulative rates of survival free of

Table 4. Cumulative Survival Free of MACE at Nine Months

	All n = 241	SES n = 137	PES n = 104	p Value
Survival (%)	98.7	99.2	98.0	0.42
Survival free of Q-wave AMI (%)	96.5	96.9	96.0	0.72
Survival free of AMI (Q-wave or non–Q-wave) (%)	90.8	93.1	88.0	0.20
Survival free of target lesion revascularization (%)	90.3	93.8	85.5	0.046
Survival free of target vessel revascularization (%)	89.0	93.0	83.6	0.028
Survival free of MACE (%)	83.5	87.7	78.0	0.053

p value for the sirolimus-eluting stent (SES) group versus paclitaxel-eluting stent (PES) group.
AMI = acute myocardial infarction; MACE = major adverse cardiac event.

Table 5. Patients With a Definite or Probable Post-Procedural Stent Thrombosis

Patient No.	Age/ Gender	Stent Type	DM	Multivessel Disease	Previous CABG	Target Vessel	Index Presentation	Index Use of GP IIb/IIIa Inhibitor	Kissing Balloon Post-Dilation	Time to Definite or Probable Thrombosis, days	Dual Antiplatelet Therapy at the Time of the Event	Presentation and Therapy of Thrombosis
1	74 yrs/ F	SES	N	Y	N	LAD	SA	N	Y	1	Y	AMI: underwent TLR with PCI, alive
2	66 yrs/ F	PES	N	Y	N	LCx	UA	N	N	7	Y	AMI: underwent TLR with PCI, alive
3	67 yrs/ M	PES	N	Y	Y	LMS	SA	N	Y	145	Y	AMI: managed medically, alive
4	73 yrs/ M	PES	Y	Y	Y	LMS	SA	N	N	204	N Stopped clopidogrel at 6 months	Sudden death
5	41 yrs/ M	PES	N	Y	N	LAD	UA	N	N	211	N Stopped clopidogrel at 6 months	AMI: managed medically, alive
6	82 yrs/ M	SES	Y	Y	N	LMS	UA	Y	Y	55	N Stopped clopidogrel because of pancreatitis	Death
7	61 yrs/ M	PES	N	Y	Y	LMS	SA	Y	Y	63	Y	AMI and death
8	71 yrs/ M	PES	N	Y	N	LMS	SA	N	Y	117	Y	AMI: managed medically, alive
9	65 yrs/ F	PES	Y	N	N	LAD	SA	Y	N	166	Y	AMI: managed medically, alive
10	80 yrs/ M	SES	Y	Y	N	LAD	SA	Y	N	28	N Stopped clopidogrel because of abdominal surgery	AMI: managed medically, alive

AMI = acute myocardial infarction; CABG = coronary artery bypass graft surgery; DM = diabetes mellitus; LAD = left anterior descending artery; LCx = left circumflex artery; LMS = left main stem; N = no; PCI = percutaneous coronary intervention; PES = paclitaxel-eluting stent; SA = stable angina; SES = sirolimus-eluting stent; TLR = target lesion revascularisation; UA = unstable angina; Y = yes.

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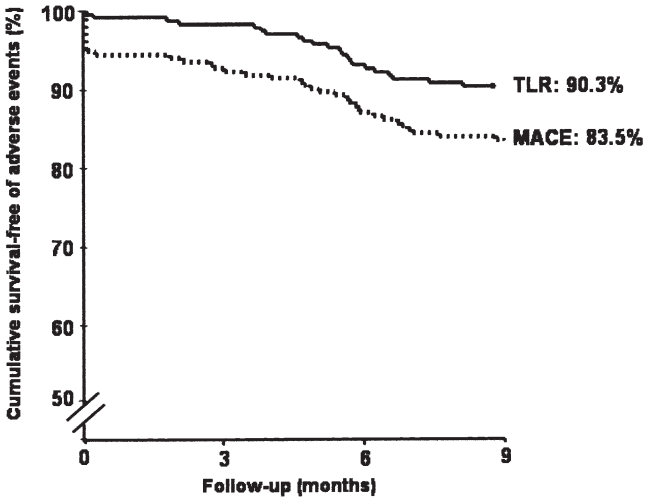

Figure 2. Cumulative survival free of target lesion revascularization (TLR) and major adverse cardiac events (MACE) after bifurcation stenting with the crush technique.

MACE are shown in Table 4. Post-procedural, angiographically confirmed stent thrombosis occurred in two (0.9%) patients (one acute, one subacute) who were both subsequently treated with glycoprotein IIb/IIIa inhibitor therapy and percutaneous TLR. In addition, three patients died, and five patients had an AMI within the territory of the treated vessel, giving a total rate of possible post-procedural stent thrombosis of 4.3%. The demographics of these 10 patients are presented in Table 5. The incidence of post-procedural stent thrombosis was higher for the PES group than the SES group (6.9% vs. 2.2%, $p = 0.08$).

The overall rates of survival free of MACE and TLR were 83.5% and 90.3%, respectively (Fig. 2). Independent predictors for MACE were therapy of the LMS (OR 3.79; 95% CI 1.76 to 8.14, $p = 0.001$) and therapy of patients with multivessel disease (OR 4.21; 95% CI 0.95 to 18.56, $p = 0.058$). Significantly fewer of the SES treated patients required TLR compared with those treated with PES; however, logistic regression demonstrated that the only independent factor for TLR was therapy of the LMS (OR 4.97; 95% CI 2.00 to 12.37, $p = 0.001$). The rate of survival free of TLR was 77.8% in those who underwent LMS stenting compared with 94.2% in the remainder (Fig. 3).

Quantitative angiographic analysis. Procedural angiographic success was achieved in 99.6% of lesions. Follow-up coronary angiography was undertaken in 186 (77.2%) lesions, at a mean period of 8.3 ± 3.7 months. Angiographic data with respect to the stent type and the use of kissing balloon post-dilation are presented in Tables 6 and 7. There was no significant difference in angiographic results with respect to the type of stent used; however, kissing balloon post-dilation significantly reduced the side branch late lumen loss and binary restenosis. Among the 47 restenotic lesions at the side branch, 34 (72.3%) were focal (<10 mm) and located at the ostium.

DISCUSSION

The main findings of this report are: 1) treatment of most bifurcation lesions with DES by the "crush" technique is associated with low rates of TLR and MACE at nine months, however, therapy of the LMS was an independent predictor of both TLR and MACE; 2) at nine months, the incidence of possible post-procedural stent thrombosis was 4.3%; and 3) the rate of side branch restenosis was significantly lower in lesions treated with kissing balloon post-dilation compared with those without.

Stent coverage of the ostium of the side branch and clinical outcomes. Bifurcation lesions are subject to increased rates of restenosis and need for TLR compared with non-bifurcated lesions. Historical data of BMSs suggest a TLR rate of 16% to 38%, with a tendency toward increased restenosis after stenting of both the main vessel and side branch compared with single vessel stenting (15–19). In the same studies, the rate of MACE at six months ranged between 17% and 51%. In randomized studies of relatively simple lesions, DESs reduce restenosis compared with BMSs, although bifurcation lesions were excluded (2–5). Preliminary data for the SES has recently suggested efficacy in bifurcation lesions (6–8); however, the most effective stenting strategy is currently unknown. Previous data of the SES suggested a higher restenosis rate after T-stenting, with the hypothesis that this might relate to incomplete coverage of the side branch ostium (6,7). In most bifurcations, the angle at the carina is significantly smaller than 90°, meaning that even with precise positioning, the stents are unable to make a "T" and completely cover the bifurcation (18). The crush technique is a relatively simple strategy that ensures complete lesion coverage, even for bifurcation lesions that have extensive disease within the side branch. Preliminary data have pointed to acceptable short-term results suggesting that it might therefore be an effective strategy for bifurcation lesions (9).

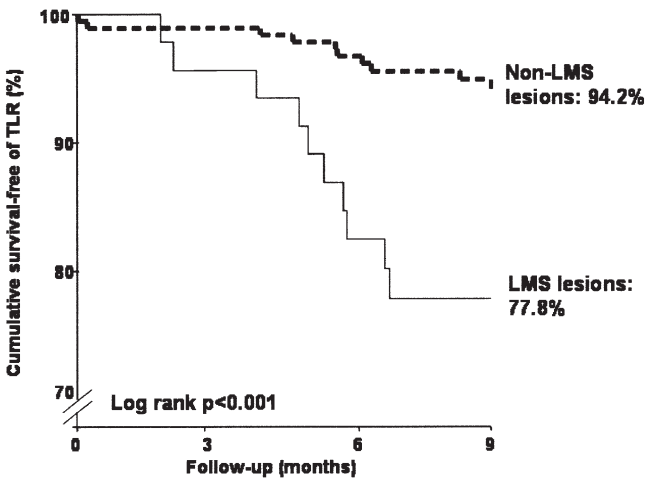

Figure 3. Cumulative survival free of target lesion revascularization (TLR) for patients treated with the crush technique of bifurcation stenting for a left main stem (LMS) lesion compared with those treated for lesions outside the left main stem (non-LMS).

Table 6. Quantitative Coronary Angiography

	All	SES	PES	p Value
Follow-up angiography, n (%)	186 (77.2)	107 (78.1)	79 (76.0)	0.8
Main branch				
Reference diameter (mm)	2.71 ± 0.59	2.71 ± 0.58	2.71 ± 0.61	1.0
Length of lesion (mm)	15.38 ± 10.46	15.99 ± 9.09	14.57 ± 12.06	0.4
Minimal lumen diameter (mm)				
Pre-procedure	0.93 ± 0.52	0.90 ± 0.53	0.98 ± 0.52	0.3
Post-procedure	2.73 ± 0.56	2.70 ± 0.51	2.77 ± 0.62	0.4
6-month follow-up	2.43 ± 0.81	2.40 ± 0.76	2.47 ± 0.89	0.6
Diameter stenosis (%)				
Pre-procedure	65.9 ± 17.5	67.3 ± 17.1	63.9 ± 18.0	0.2
Post-procedure	13.0 ± 8.6	13.6 ± 8.3	12.1 ± 9.0	0.3
6-month follow-up	22.9 ± 19.9	24.1 ± 19.1	21.3 ± 21.1	0.3
Late lumen loss (mm)	0.30 ± 0.64	0.30 ± 0.60	0.30 ± 0.70	1.0
Binary restenosis rate (%)	17 (9.1)	10 (9.3)	7 (8.9)	1.0
Side branch				
Reference diameter (mm)	2.39 ± 0.51	2.36 ± 0.45	2.41 ± 0.60	0.6
Length of lesion (mm)	8.99 ± 6.03	9.64 ± 6.12	8.04 ± 5.80	0.09
Minimal lumen diameter (mm)				
Pre-procedure	0.89 ± 0.52	0.92 ± 0.51	0.86 ± 0.53	0.5
Post-procedure	2.26 ± 0.51	2.26 ± 0.49	2.26 ± 0.55	1.0
6-month follow-up	1.85 ± 0.86	1.89 ± 0.85	1.81 ± 0.87	0.5
Diameter stenosis at 6 months (%)				
Pre-procedure	62.3 ± 20.5	60.9 ± 20.6	64.3 ± 20.3	0.3
Post-procedure	15.5 ± 9.5	15.0 ± 9.7	16.2 ± 9.3	0.4
6-month follow-up	30.7 ± 0.67	29.4 ± 27.7	32.5 ± 27.3	0.5
Late lumen loss (mm)	0.41 ± 0.67	0.37 ± 0.71	0.46 ± 0.60	0.4
Restenosis rate (%)	47 (25.3)	29 (27.1)	18 (22.8)	0.6

p value for the sirolimus-eluting stent (SES) group versus paclitaxel-eluting stent (PES) group.

In the present study, we have demonstrated encouraging long-term results, with a high rate of survival free of TLR of 90.3%. Although TLR rates were higher in those treated with PES compared with SES, there were more patients in this group treated for LMS bifurcation (25.0% vs. 15.3%). By logistic regression analysis, therapy of the LMS was the only independent predictor of TLR. Indeed, at nine months, the rate of survival free of TLR was 77.8% in those who underwent LMS stenting, compared with 94.2% in the remainder. The rate of in-hospital MACE was 4.8%, the majority comprising non–Q-wave AMI. The MACE rate was higher in those who received a glycoprotein IIb/IIIa inhibitor; however, this is likely to reflect the operators' decision to use such an agent only in the situation of a difficult or complicated procedure. There is evidence to suggest improved efficacy of glycoprotein IIb/IIIa inhibitors with early administration. Further work is needed to evaluate whether routine pre-procedural administration of such agents to all patients undergoing crush stenting might reduce the occurrence of in-hospital events.

At nine months, the overall rate of survival free of MACE was 83.5%. Independent predictors were the treatment of multivessel disease and treatment of the LMS. Recent data have been published specifically evaluating the results of LMS stenting with DES implantation (20–23). In all these studies, results suggested lower rates of restenosis compared with historical data of BMS. The incidence of TLR ranged from 2.0% to 14.1%. This appears to be much lower than the LMS cohort in our study where the rate of survival free of TLR was just 77.8% (compared with 94.2% for non-LMS lesions); however, in the aforementioned studies, restenosis after LMS bifurcation stenting was higher compared with lesions localized to the ostium or body of the LMS. Chieffo et al. (22) evaluated 85 patients, including 69 (81.2%) with disease of the distal LMS. The majority of these patients were treated with stent implantation to both branches, most (59%) with crush stenting. All 12 patients who required TLR were initially treated with a two-stent strategy. Park et al. (21) demonstrated excellent results after LMS angioplasty, with a binary restenosis rate of 7.0%. In this study, 70.6% patients were treated for the LMS bifurcation, and all restenoses occurred in these patients.

Kissing balloon post-dilation. Although the overall rate of TLR in the present study was relatively low, kissing balloon post-dilation had a significant impact on the angiographic results, leading to a significantly larger post-procedural MLD within both the main vessel and side branch. This larger MLD was maintained in both vessels at follow-up but was particularly evident within the side branch. As previously demonstrated by Ge et al. (10), kissing balloon post-dilation in the present study significantly reduced both the side branch late lumen loss (0.24 ± 0.50 mm vs. 0.58 ± 0.77 mm, $p < 0.001$) and binary restenosis rate (9.6% vs. 41.3%, $p < 0.000001$).

The majority (72.3%) of these side branch restenoses were focal and occurred at the ostium. Bench study results have demonstrated the crush technique to effectively cover the bifurcation lesion; however, the absence of kissing

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Table 7. Quantitative Coronary Angiography With Respect to the Use of Kissing Balloon Post-Dilation

	Kissing Balloon Post-Dilation	No Kissing Balloon Post-Dilation	p Value
Follow-up angiography, n (%)	94 (77.0)	92 (77.3)	1.0
Main branch			
Reference diameter (mm)	2.78 ± 0.61	2.64 ± 0.57	0.1
Length of lesion (mm)	14.84 ± 10.40	15.97 ± 10.55	0.5
Minimal lumen diameter (mm)			
Pre-procedure	0.97 ± 0.53	0.89 ± 0.52	0.3
Post-procedure	2.89 ± 0.54	2.55 ± 0.53	<0.0001
6-month follow-up	2.64 ± 0.81	2.21 ± 0.75	<0.001
Diameter stenosis (%)			
Pre-procedure	65.5 ± 17.1	66.4 ± 18.0	0.7
Post-procedure	12.2 ± 8.7	13.8 ± 8.5	0.2
6-month follow-up	19.9 ± 20.2	26.1 ± 19.3	0.04
Late lumen loss (mm)	0.26 ± 0.65	0.35 ± 0.64	0.3
Binary restenosis rate (%)	6 (6.4)	11 (12.0)	0.2
Side branch			
Reference diameter (mm)	2.45 ± 0.53	2.32 ± 0.49	0.1
Length of lesion (mm)	9.01 ± 6.06	8.97 ± 6.03	1.0
Minimal lumen diameter (mm)			
Pre-procedure	0.90 ± 0.53	0.88 ± 0.52	0.8
Post-procedure	2.43 ± 0.53	2.10 ± 0.44	<0.00001
6-month follow-up	2.18 ± 0.71	1.52 ± 0.86	<0.0000001
Diameter stenosis at 6 months (%)			
Pre-procedure	62.7 ± 20.7	61.9 ± 20.3	0.8
Post-procedure	12.8 ± 8.7	18.3 ± 9.5	<0.0001
6-month follow-up	20.5 ± 17.9	41.0 ± 31.5	<0.000001
Late lumen loss (mm)	0.24 ± 0.50	0.58 ± 0.77	<0.001
Restenosis rate (%)	9 (9.6)	38 (41.3)	<0.000001

balloon post-dilation leads to under-expansion and mal-apposition of the side branch stent struts (24). Kissing balloon post-dilation opens the struts, thereby facilitating access to the side branch, and corrects stent deformation to provide optimal scaffolding and delivery of drug. The crush technique is technically relatively quick and simple; kissing balloon post-dilation increases the procedural time and cost, although our results suggest that it is a necessity.

After stent implantation, it can be difficult and time-consuming to re-cross the side branch with a wire and/or balloon. We recommend routine post-dilation of the main vessel stent with a balloon (≥nominal stent diameter) taken to high pressure. After this, successful access of the side branch and subsequent post-dilation can be achieved in >95% of procedures. Stent under-expansion remains one of the major reasons for restenosis (25), even in the DES era (26–28). To enable full stent strut expansion at the side branch ostium, we initially perform high-pressure (>12 atm) balloon inflation in the side branch with a balloon ≥nominal stent diameter (29). Once both the main vessel and side branch stents have been individually post-dilated at high pressure, kissing balloon post-dilation is then undertaken. Notably, the aforementioned bench study (24) emphasized that optimal kissing dilation requires the size of the balloon in the main vessel greater than or equal to the nominal stent diameter.

Bifurcation stenting is known to increase the risk of restenosis with BMS. Accordingly, compared with the results of randomized studies of non-bifurcation lesions, our results suggest that this also applies to DESs. Compared with the Sirolimus-Eluting Stent in De Novo Native Coronary Lesions (SIRIUS) study (4), the SES patients in our study demonstrated a higher rate of TLR (5.4% vs. 4.1%). Similarly, compared with the results of Paclitaxel-Eluting Coronary Stent System (TAXUS)-IV (5), the PES patients in our study demonstrated a higher rate of TLR (11.9% vs. 3.0%). In addition, compared with these published studies, both groups of patients in our study had a higher main vessel late lumen loss (0.30 ± 0.60 mm vs. 0.24 ± 0.47 mm for the SES, and 0.30 ± 0.70 mm vs. 0.23 ± 0.44 mm for the PES).

Stent thrombosis. The 1.3% incidence of intra-procedural stent thrombosis in the present report is slightly higher than the incidence previously reported in a large series of patients treated with SES (0.7%) (12). The 4.3% incidence of post-procedural stent thrombosis is of concern and is higher than the findings of the trials that evaluated DES implantation in relatively simple lesions (0.4% for SES and 0.6% for PES) (4,5). This might reflect the complexity of the technique with an increased risk of thrombosis perhaps reflecting the triple layer of stent struts, polymer, and drug at the site of the carina. Notably, in the present study, kissing balloon post-dilation did not appear to reduce the risk of stent thrombosis.

The incidence of post-procedural stent thrombosis tended to be higher in the cohort treated with the PES

compared with the SES (6.9% vs. 2.2%). This is in accordance with the recently presented results of the Prospective Randomized Multi-center Head-to-Head Comparison of the Sirolimus-Eluting Stent (REALITY) study (30). This multicenter study randomized 1,353 patients (1,911 lesions) to therapy with either SES or PES. There was a higher rate of stent thrombosis in the PES-treated group (1.8% vs. 0.4%, $p = 0.02$). In the present study, such a high incidence of thrombosis emphasizes the importance of an aggressive strategy of antiplatelet therapy, with administration of dual antiplatelet therapy for a prolonged (though as yet undefined) period of time. Indeed, 4 of the 10 patients had stopped clopidogrel before the presumed thrombotic event. A recent study has shown that premature discontinuation of dual antiplatelet therapy is associated with an approximately 30-fold greater risk of stent thrombosis after SES implantation (11). For patients treated with the crush technique, premature discontinuation of antiplatelet therapy has been shown to be a predictor of stent thrombosis (10) and, in conjunction with our results, suggests that the technique should not be recommended in patients who cannot receive or tolerate dual antiplatelet therapy. Further work is needed to evaluate the potential benefit of routine pre-procedural administration of glycoprotein IIb/IIIa inhibitor therapy to all patients treated with this technique.

Study limitations. The main limitation of the present report is its non-randomized design; therefore, caution must be taken in evaluating any differences between the stent types. Furthermore, the study does not make comparison with alternative stenting strategies. The decision to use both glycoprotein IIb/IIIa inhibitor therapy and the use of kissing balloon post-dilation was at the operators' discretion and was therefore also not randomized.

Conclusions. The crush technique of bifurcation stenting with DESs is associated with favorable clinical outcomes when compared with historical data of BMS; however, the incidence of possible post-procedural stent thrombosis is of concern and is higher than that after therapy of more simple lesions, suggesting that an aggressive strategy of antiplatelet therapy might be of importance. Notably, the efficacy of the technique appears to be reduced in LMS bifurcation lesions, and further research is needed before the technique can be routinely recommended in this group of patients. When using this technique, kissing balloon post-dilatation is mandatory to reduce the rate of restenosis of the side branch. Randomized studies are warranted to directly compare the technique with other bifurcation stenting strategies.

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