

FOCUS ISSUE: TREATMENT OF BIFURCATION LESIONS

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

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OBJECTIVES	The purpose of this research was to evaluate the long-term outcomes after implantation of drug-eluting stents (DES) in bifurcation lesions with the “crush” technique.
BACKGROUND	The long-term outcome of “crush” stenting technique has yet to be determined.
METHODS	We identified 181 consecutive patients who were treated with DES with the “crush” stent technique from April 2002 to April 2004. Based on the usage of final kissing balloon post-dilation (FKB), the patients were divided into an FKB group (n = 116) and a non-FKB group (n = 65).
RESULTS	Clinical follow-up at nine months was available in all patients, and angiographic follow-up in 80% of patients. Three cases (1.7%) of intraprocedural stent thrombosis and five (2.8%) cases of postprocedural stent thrombosis occurred. Restenosis rate of the main branch in the entire cohort lesions was 11.5%. Restenosis rate of the side branch was lower in the FKB group than that in the non-FKB group (11.1% vs. 37.9%, $p < 0.001$). The target lesion revascularization (TLR) rate for all patients was 14.9%. The lack of FKB was a predictor for TLR (hazard ratio [HR] 4.17; 95% confidence interval [CI] 1.30 to 14.3, $p = 0.02$). Diabetes was also a predictor for TLR (HR 1.79; 95% CI 1.14 to 2.80, $p = 0.01$). Premature discontinuation of dual antiplatelet therapy (odds ratio [OR] 16.8; 95% CI 1.31 to 159.5, $p = 0.03$) and age (OR 1.10; 95% CI 1.00 to 1.21, $p = 0.048$) was associated with the occurrence of postprocedural stent thrombosis.
CONCLUSIONS	Compared to the absence of FKB, the “crush” stenting technique with FKB appears to be associated with more favorable long-term outcomes. When utilizing the “crush” stenting technique, FKB is mandatory. (J Am Coll Cardiol 2005;46:613–20) © 2005 by the American College of Cardiology Foundation

Implantation of one stent in the main branch with balloon dilation of the side branch seems to be the best approach for treatment of most coronary bifurcation lesions with bare-metal stents or drug-eluting stents (DES) (1,2). A limitation of this approach is that some bifurcation lesions have extensive disease in the side branch requiring stenting of this vessel as well. “Crush” stenting technique has been proposed as a method to implant two DES in a bifurcation with the intent to ensure optimal stent coverage and drug delivery to the ostium of the side branch. Despite the fact that short-term outcomes of “crush” stenting are encouraging (3), the mid- or long-term outcomes of this technique remain uncertain. The aim of this study was to evaluate the long-term outcomes after implantation of either sirolimus-eluting stents (SES) (Cypher, Cordis/Johnson & Johnson, Warren, New Jersey) or paclitaxel-eluting stents (PES)

(Taxus, Boston Scientific, Natick, Massachusetts) in bifurcation lesions with the “crush” stenting technique.

METHODS

Study population. Demographic and procedural data regarding all patients undergoing angioplasty at EMO Centro Cuore Columbus and San Raffaele Hospital were prospectively entered into a dedicated database. All consecutive patients treated with either SES or PES by the “crush” stenting technique between April 2002 and April 2004 were identified. Based on the usage of final kissing balloon post-dilation (FKB), the entire cohort was divided into FKB group and non-FKB group. Patients with revascularization in the setting of acute myocardial infarction (AMI) were not considered in this report because we do not implant DES in these patients.

Procedures and postintervention medications. All patients were pretreated with aspirin and either ticlopidine or clopidogrel. A 300-mg loading dose of clopidogrel before the index procedure was administered if patients were not pretreated. During the procedure, patients received intrave-

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Abbreviations and Acronyms

AMI	= acute myocardial infarction
CI	= confidence interval
DES	= drug-eluting stent
FKB	= final kissing balloon after dilation
HR	= hazard ratio
MACE	= major adverse cardiac events
OR	= odds ratio
PES	= paclitaxel-eluting stent
SES	= sirolimus-eluting stent
TLR	= target lesion revascularization
TVR	= target vessel revascularization

nous unfractionated heparin (100 IU/kg) to maintain activated clotting time between 250 to 300 s. The administration of glycoprotein IIb/IIIa inhibitors was left to the operator's discretion. All patients were on maintenance aspirin therapy and clopidogrel or ticlopidine continued for at least six months after DES implantation.

The "crush" technique has been previously described (3). In patients who underwent FKB, wire recrossing into the side branch followed by high-pressure balloon inflation (12 to 14 atm) was always performed before FKB. A floppy wire or an intermediate wire or occasionally a hydrophilic wire (Pilot 150, Guidant, Temecula, California) was chosen to recross into the side branch.

Clinical definitions and follow-up. Clinical follow-up was performed by telephone contact or office visit at nine months for both groups. Angiographic follow-up was scheduled for between six and eight months after the procedure unless clinically indicated earlier.

Major adverse cardiac events (MACE) were defined as cardiac death, AMI, and target vessel revascularization (TVR), either percutaneous or surgical. Cumulative MACE were defined as the in-hospital and nine-month follow-up MACE. All deaths were considered cardiac unless otherwise documented. A non-Q-wave AMI was defined as creatine kinase-MB enzyme elevation ≥ 3 times the upper limit of the normal value; when in addition to enzyme elevation there were new pathological Q waves in the electrocardiogram, the event was defined as a Q-wave AMI. Target lesion revascularization (TLR) was defined as a repeat revascularization with a stenosis $\geq 50\%$ within the stent or in the 5-mm distal or proximal segments adjacent to the stent; TVR was defined as repeat revascularization within the treated vessel.

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 (4). Stent thromboses were categorized according to the timing of the event into: intraprocedural, subacute thrombosis (from the end of the procedure to 30 days), and late stent thrombosis (>30 days).

Quantitative coronary angiographic analysis. Cineangiograms were analyzed using a validated edge detection system (CMS, version 5.2, MEDIS, Leiden, the Netherlands) in main branch and in side branch. When analyzing left main bifurcations, the main branch was the distal left main continuing into the left anterior descending. Angiographic restenosis was defined as diameter stenosis $\geq 50\%$ within a previously stented segment (stent and 5 mm proximal and distal) at the follow-up angiogram. Angiographic success was defined as a final residual stenosis $<30\%$ with Thrombolysis In Myocardial infarction flow grade 3 in either the main branch or the side branch (5). Procedural success was defined as the achievement of angiographic success without in-hospital MACE.

Statistical analysis. Continuous variables are presented as mean \pm SD and categorical variables as frequency (%). Continuous variables were compared using independent sample *t* test. Categorical variables were compared with chi-square statistics or Fisher exact test. Fisher exact test was used when any expected cell count was <5 (not resulting from missing rows or columns in a larger table). Because of a low number of thrombotic events, exact logistic regression models (6) based on permutation resampling were used to determine the association of postprocedural stent thrombosis with several clinical variables (7). The following clinical variables were entered into this analysis model: age, gender, diabetes, ejection fraction, stent type, unstable angina, premature discontinuation antiplatelet therapy, left main bifurcation, the lack of use of glycoprotein IIb/IIIa inhibitors, FKB, calcific lesions, reference vessel diameter, lesion length, minimal lumen diameter at baseline and at postprocedure, balloon size, maximal balloon pressure, and stent length. The results are presented as odds ratios (OR) with exact 95% confidence interval (CI) and exact *p* values. Survival free of TLR was estimated using the Kaplan-Meier method, and the differences between the two survival curves were compared with the log-rank test. The Cox regression model was used to identify the predictors of TLR at nine months. The results are presented as hazard ratios (HR) with exact 95% CI. A *p* value of <0.05 was considered to be statistically significant, and all reported *p* values are two-sided. Analysis was performed with SAS version 8.2 (SAS Inc., Cary, North Carolina).

RESULTS

Baseline and procedural characteristics. A total of 181 consecutive patients undergoing angioplasty with DES by the "crush" stenting technique were identified (SES were implanted in 106 patients with 110 bifurcations and PES in 75 patients with 75 bifurcations). Of them, 116 patients (with 118 bifurcations) were included in the FKB group and 65 patients (with 67 bifurcations) in the non-FKB group. The baseline clinical, lesion, and procedural characteristics are shown in Tables 1, 2, and 3. Compared to the non-FKB group, the FKB group had a larger maximum balloon

Table 1. Baseline Clinical Characteristics

	Entire Cohort n = 181 Patients	FKB Group n = 116 Patients	Non-FKB Group n = 65 Patients	p*
Age, yrs	62 ± 11	62 ± 12	62 ± 11	0.82
Male, n (%)	158 (87.3)	102 (87.9)	56 (86.2)	0.82
Current smoker, n (%)	31 (17.1)	20 (17.2)	11 (16.9)	0.88
Hypercholesterolemia, n (%)	130 (71.8)	81 (69.8)	49 (75.4)	0.49
Hypertension, n (%)	108 (59.7)	67 (57.8)	41 (63.1)	0.53
Diabetes mellitus, n (%)	40 (22.1)	25 (21.6)	15 (23.1)	0.96
Prior MI, n (%)	76 (42.5)	51 (44.7)	25 (38.5)	0.44
Prior PCI, n (%)	60 (33.1)	42 (36.2)	18 (27.7)	0.26
Prior CABG, n (%)	35 (19.3)	24 (20.7)	11 (16.9)	0.70
Unstable angina, n (%)	46 (25.4)	31 (26.7)	15 (23.1)	0.72
GP IIb/IIIa inhibitors, n (%)	71 (39.2)	48 (41.4)	23 (35.4)	0.53
LVEF, %	52.0 ± 9.5	51.7 ± 10.3	52.6 ± 7.9	0.56

Values are presented as numbers (%) or mean ± SD. *FKB group versus non-FKB group.
 CABG = coronary artery bypass graft surgery; FKB = final kissing balloon after dilation; GP = glycoprotein; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

diameter (3.25 ± 0.37 mm vs. 3.06 ± 0.39 mm, $p = 0.01$) and shorter stent length (26.8 ± 8.0 mm vs. 32.5 ± 12.8 mm, $p < 0.001$) in the main branch.

Quantitative angiographic analysis. Serial quantitative coronary angiography analysis results for the main branch and side branch are shown in Tables 4 and 5. Angiographic follow-up was available in 145 (80.1%) patients (with 148 bifurcations) at a mean period of 7.6 ± 2.8 months after the index procedure. Of these, 87 (75.0%) patients (with 90 bifurcations) were in the FKB group and 58 (89.2%) patients (with 58 bifurcations) in the non-FKB group. Late lumen loss in the side branch was lower in the FKB group than that in the non-FKB group (0.32 ± 0.16 mm vs. 0.52 ± 0.38 mm, $p = 0.04$), resulting in a lower incidence of restenosis (11.1% vs. 37.9%, $p < 0.001$) (Fig. 1). Among the 32 restenotic lesions at the side branch, 24 (75.0%) were focal (<10 mm) restenosis and located at the ostium of the side branch.

Clinical outcomes. In-hospital results and clinical follow-up outcomes are shown in Table 6. There were three (1.7%) cases of intraprocedural stent thrombosis (two in the FKB group treated with SES, one in the non-FKB group treated with PES); two of these developed non-Q-wave AMI. All intraprocedural stent thrombosis occurred before performing FKB. The mean total stent length of these three cases was 69 mm, and no elective glycoprotein IIb/IIIa inhibitors were given. One patient treated with SES developed a Q-wave AMI in-hospital due to the occlusion of septal branches during the index procedure. Clinical follow-up at nine months was available in all patients. Compared to the non-FKB group, the rate of cumulative MACE was lower in the FKB group (19.8% vs. 38.5%, $p = 0.008$). Survival free from TLR was 90.5% in the FKB group and 75.4% in the non-FKB group ($p = 0.008$) (Fig. 2).

During clinical follow-up, five (2.8%) cases of stent thrombosis were recorded, two (1.9%) of these treated with

Table 2. Baseline Lesion Characteristics

	Entire Cohort n = 185 Lesions	FKB Group n = 118 Lesions	Non-FKB Group n = 67 Lesions	p*
Calcification				
Main branch	31 (16.8)	24 (20.3)	7 (10.4)	0.13
Side branch	19 (10.3)	15 (12.7)	4 (6.0)	0.23
Total occlusion				
Main branch	16 (8.6)	8 (6.8)	8 (11.9)	0.28
Side branch	19 (10.3)	10 (8.5)	9 (13.4)	0.32
Restenotic lesions				
Main branch	13 (7.0)	11 (9.3)	2 (3.0)	0.14
Side branch	12 (6.5)	10 (8.5)	2 (3.0)	0.22
Lesions location, n (%)				
LM	49 (26.5)	38 (32.2)	11 (16.4)	0.03
LAD/diagonal	83 (44.9)	51 (43.2)	32 (47.8)	0.66
LAD/septal	1 (0.5)	0	1 (1.5)	0.77
LCX/OM	40 (21.6)	26 (22.0)	14 (20.9)	0.99
RCA/RCA-PL/RCA-PD	12 (6.5)	3 (2.5)	9 (13.4)	0.01

Values are presented as numbers (%). Calcification was defined as a radiopaque area found before contrast injection and was moderate when visible only during the cardiac cycle or severe if visible also on still frames. *FKB group versus non-FKB group.

FKB = final kissing balloon after dilation; LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main; OM = obtuse marginal; PD = posterior descending; PL = posterior lateral; RCA = right coronary artery.

Table 3. Procedural Characteristics

	Entire Cohort n = 185 Lesions	FKB Group n = 118 Lesions	Non-FKB Group n = 67 Lesions	p*
Adjunctive debulking, n (%)				
Main branch	5 (2.7)	2 (1.7)	3 (4.5)	0.35
Side branch	1 (0.5)	0	1 (1.5)	0.36
Mean stent length, mm				
Main branch	28.9 ± 10.4	26.8 ± 8.0	32.5 ± 12.8	<0.001
Side branch	24.7 ± 8.4	24.1 ± 7.3	25.6 ± 10.0	0.23
Maximal inflation pressure, atm				
Main branch	15.6 ± 3.1	16.2 ± 2.3	15.1 ± 3.4	0.06
Side branch	14.5 ± 2.8	14.4 ± 2.9	14.9 ± 2.7	0.2
Maximum balloon diameter, mm				
Main branch	3.19 ± 0.38	3.25 ± 0.37	3.06 ± 0.39	0.01
Side branch	2.85 ± 0.40	2.89 ± 0.39	2.80 ± 0.42	0.17

Values are presented as numbers (%) or mean ± SD. *FKB group versus non-FKB group.
FKB = final kissing balloon after dilation.

SES and three (4.0%) treated with PES (Table 7). All five patients had clinical events, and two patients died. The mean age of these five patients was 72 years compared to 62 years in the other patients ($p = 0.06$). There were eight patients who stopped dual antiplatelet therapy prematurely. Of these, two (25%) patients suffered thrombotic events presenting as AMI within 7 and 10 days after stopping aspirin and clopidogrel (one due to pancreatitis, the other due to abdominal surgery), respectively. In the remaining patients who continued taking dual antiplatelet therapy, there were three (1.7%) episodes of stent thrombosis (1.7% vs. 25%, $p = 0.005$, Fisher exact test). The incidence of postprocedural stent thrombosis was not statistically significantly different between the FKB group and the non-FKB group (2.6% vs. 3.1%, $p = 0.78$, Fisher exact test).

Predictors of TLR and stent thrombosis. The absence of FKB (HR 4.17; 95% CI 1.30 to 14.3, $p = 0.02$) was a predictor of TLR. Diabetes (HR 1.79; 95% CI 1.14 to 2.80, $p = 0.01$) was also identified as a predictor of TLR. Premature discontinuation of dual antiplatelet therapy (OR

16.8; 95% CI 1.31 to 159.5, $p = 0.03$) and age (OR 1.10; 95% CI 1.00 to 1.21, $p = 0.048$) were associated with the occurrence of postprocedural stent thrombosis.

DISCUSSION

The main findings of this report are: 1) compared to the absence of FKB, the "crush" stenting with FKB appears to be associated with a lower rate of restenosis in side branch, and low rates of MACE and need for revascularization; the absence of FKB was identified as one of the predictor factors of TLR; and 2) the incidence of postprocedural stent thrombosis during nine months follow-up was 2.8%. Premature discontinuation of dual antiplatelet therapy was strongly associated with the occurrence of postprocedural stent thrombosis.

Full coverage of the ostium of the side branch and FKB. In the randomized SES bifurcation study (2), the rate of restenosis in the side branch was 21.8%. Incomplete coverage of the side branch was advocated as a possible

Table 4. Quantitative Coronary Angiography Analysis for the Main Branch

	Entire Cohort n = 185 Lesions	FKB Group n = 118 Lesions	Non-FKB Group n = 67 Lesions	p*
Baseline				
RVD, mm	2.81 ± 0.58	2.85 ± 0.60	2.74 ± 0.53	0.23
MLD, mm	0.95 ± 0.51	0.95 ± 0.51	0.95 ± 0.52	0.97
Diameter stenosis, %	66.3 ± 16.6	67.0 ± 15.9	65.2 ± 17.6	0.49
Mean lesion length, mm	15.9 ± 8.7	14.5 ± 7.2	16.4 ± 10.3	0.14
After procedure				
RVD, mm	3.36 ± 0.53	3.44 ± 0.56	3.23 ± 0.47	0.01
MLD, mm	2.92 ± 0.54	3.04 ± 0.54	2.80 ± 0.50	0.03
Diameter stenosis, %	11.9 ± 7.9	11.1 ± 8.1	13.1 ± 7.5	0.11
Acute gain, mm	1.98 ± 0.59	2.07 ± 0.58	1.85 ± 0.60	0.02
Follow-up				
RVD, mm	3.28 ± 0.59	3.37 ± 0.58	3.21 ± 0.61	0.11
MLD, mm	2.57 ± 0.96	2.78 ± 0.85	2.48 ± 0.92	0.04
Diameter stenosis, %	23.3 ± 23.8	19.1 ± 20.8	22.5 ± 23.5	0.38
Mean lesion length, mm	7.8 ± 6.6	7.8 ± 6.6	7.8 ± 6.6	0.97
Late lumen loss, mm	0.27 ± 0.18	0.21 ± 0.26	0.34 ± 0.10	0.10
Restenosis, n (%)	17/148 (11.5)	8/90 (8.9)	9/58 (15.5)	0.33

Values are presented as numbers (%) or mean ± SD. *FKB group versus non-FKB group.
FKB = final kissing balloon after dilation; MLD = minimal lumen diameter; RVD = reference vessel diameter.

Table 5. Quantitative Coronary Angiography Analysis for Side Branch

	Entire Cohort n = 185 Lesions	FKB Group n = 118 Lesions	Non-FKB Group n = 67 Lesions	p*
Baseline				
RVD, mm	2.44 ± 0.58	2.46 ± 0.61	2.40 ± 0.52	0.54
MLD, mm	0.87 ± 0.51	0.87 ± 0.51	0.88 ± 0.52	0.84
Diameter stenosis, %	64.1 ± 19.5	64.1 ± 19.6	63.9 ± 19.4	0.96
Mean lesion length, mm	10.9 ± 6.7	10.5 ± 6.8	11.4 ± 6.5	0.39
After procedure				
RVD, mm	2.87 ± 0.46	2.89 ± 0.45	2.84 ± 0.48	0.44
MLD, mm	2.46 ± 0.46	2.54 ± 0.47	2.33 ± 0.40	0.004
Diameter stenosis, %	14.2 ± 9.5	12.3 ± 9.2	17.1 ± 9.4	0.001
Acute gain, mm	1.58 ± 0.65	1.67 ± 0.64	1.44 ± 0.64	0.03
Follow-up				
RVD, mm	2.84 ± 0.52	2.88 ± 0.53	2.77 ± 0.48	0.20
MLD, mm	1.98 ± 0.88	2.22 ± 0.77	1.70 ± 0.91	0.001
Diameter stenosis, %	30.7 ± 27.1	23.5 ± 22.0	37.9 ± 32.2	0.004
Mean lesion length, mm	6.3 ± 3.9	6.1 ± 4.2	6.5 ± 3.5	0.60
Late lumen loss, mm	0.40 ± 0.27	0.32 ± 0.16	0.52 ± 0.38	0.04
Restenosis, n (%)	32/148 (21.6)	10/90 (11.1)	22/58 (37.9)	<0.001

Values are presented as numbers (%) or mean ± SD. *FKB group versus non-FKB group. Abbreviations as in Table 4.

cause for the high restenosis rate (2,8). In order to guarantee full coverage of the ostium of the side branch, the “crush” stent technique was introduced (3). Our preliminary experience with the “crush” stenting technique did not show a clear improvement in the rate of restenosis at the side branch. At that time FKB was not performed routinely when no residual stenosis was observed at ostium of the side

branch. Learning from follow-up results led to more frequent performance of FKB. Since January 2003, kissing inflation became standard procedure. In the present study, the restenosis rate of the side branch in the FKB group was 11.1%. Compared to the SES bifurcation study, a 49% relative reduction in the restenosis rate in the side branch was achieved (2). The significant reduction of late loss in the

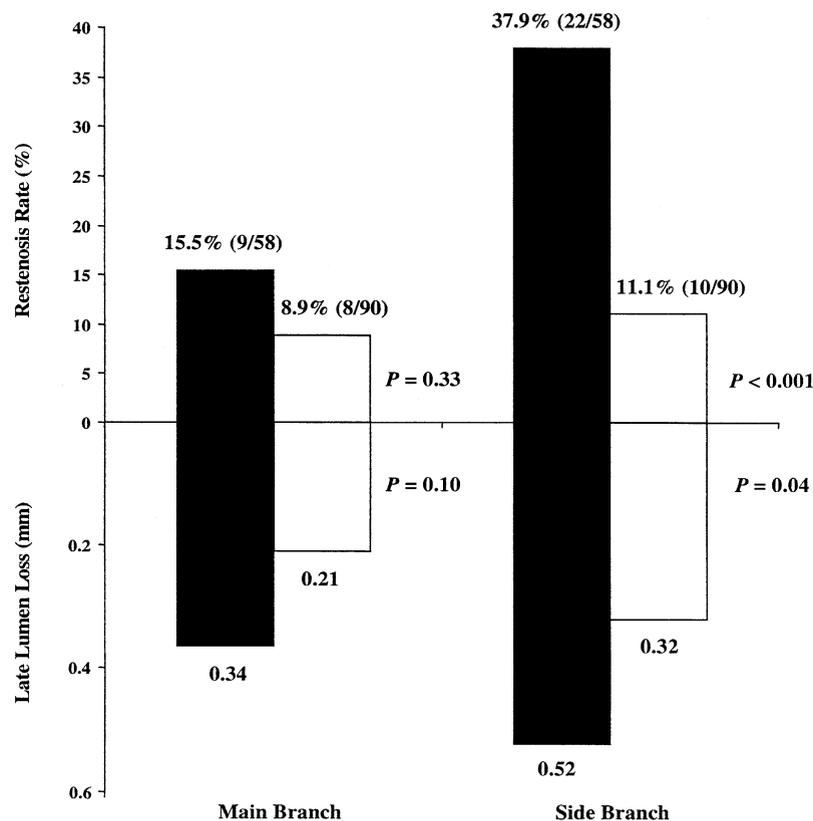


Figure 1. Restenosis rate and late lumen loss of drug-eluting stent implantation in bifurcation lesions with the “crush” stent technique. **Black bars** = without kissing balloon after dilation; **open bars** = kissing balloon after dilation.

Table 6. Clinical Outcomes

	Entire Cohort n = 181 Patients	FKB Group n = 116 Patients	Non-FKB Group n = 65 Patients	p*
Angiographic success, n (%)	178 (98.3)	116 (100)	62 (95.4)	0.13
Procedural success, n (%)	162 (89.5)	106 (91.4)	56 (86.2)	0.40
In-hospital MACE, n (%)	16 (8.8)	10 (8.6)	6 (9.2)	1.0
Cardiac death	0	0	0	—
Q-wave MI	1 (0.6)	0	1 (1.5)	0.77
Non-Q-wave MI	15 (8.3)	10 (8.6)	5 (7.7)	0.95
TLR	0	0	0	—
TVR	0	0	0	—
Cumulative nine-month MACE, n (%)	48 (26.5)	23 (19.8)	25 (38.5)	0.008
Cardiac death	2 (1.1)	2 (1.7)	0	0.54
Q-wave MI	6 (3.3)	2 (1.7)	4 (6.2)	0.28
Non-Q-wave MI	15 (8.3)	10 (8.6)	5 (7.7)	0.95
TLR	27 (14.9)	11 (9.5)	16 (24.6)	0.008
TVR	31 (17.1)	12 (10.3)	19 (29.2)	0.002
Postprocedural stent thrombosis	5 (2.8)	3 (2.6)	2 (3.1)	0.78
Subacute	1 (0.6)	0	1 (1.5)	0.77
Late	4 (2.2)	3 (2.6)	1 (1.5)	0.95

Values are presented as numbers (%). *FKB group versus non-FKB group.
 MACE = major adverse cardiac events; TLR = target lesion revascularization; TVR = target vessel revascularization; other abbreviations as in Table 1.

side branch after FKB can be explained by better strut contact to the vessel wall and better drug delivery. The numerical and not significant reduction of late loss in the main branch with FKB could just be a consequence of a lower tissue growth at the ostium of the side branch with a lower chance to extend into the main branch (9). Stent underexpansion is one of the major reasons for restenosis (10), even in the DES era (11,12); FKB may correct stent deformation and ensure optimal stent scaffolding (9,13). To guarantee full stent strut expansion, we always performed balloon inflation in the side branch at high pressure (12 to 14 atm) before FKB. We think that this “two-step proce-

sure” is essential to ensure full strut apposition at the ostium of the side branch (14).

Similar to the findings of the SES bifurcation study (2), the 24 (75.0%) restenosis cases of the side branch observed in the present report were focal. However, it is important to mention that among these 24 restenotic lesions, only 8 (33.3%) lesions underwent FKB. An intriguing and unanswered question is why, despite apparent full coverage of the ostium of the side branch and despite performing FKB, a double digit restenosis rate at the ostium of the side branch still occurred. Possible explanations could be the breakage of the polymer secondary to the overlap of multiple struts layers and uneven distribution of the stent struts at the ostium of the side branch (9). To resolve this problem, specific stent designs addressing the proper coverage of the ostium of the side branch may be needed.

Stent thrombosis. The 1.7% incidence of intraprocedural stent thrombosis in the present report was higher than the one that we reported earlier (0.7%) (7). It is important to note that three patients who developed intraprocedural stent thrombosis were not treated with glycoprotein IIb/IIIa inhibitors. In order to reduce the incidence of acute stent thrombosis, we should consider a more liberal usage of glycoprotein IIb/IIIa inhibitors and a more aggressive usage of loading dose clopidogrel (15–17).

The 2.8% incidence of postprocedural stent thrombosis is also different from the findings of the corresponding trials for DES in selected lesions (0.4% for SES and 0.6% for PES) (4,18). It is also important to mention that, in the present study, there was a 1.7% incidence of postprocedural stent thrombosis in patients who did not discontinue dual antiplatelet therapy. This finding is similar to the result of a recently published study, in which the incidence of postprocedural stent thrombosis was 1.1% in nonselected lesions

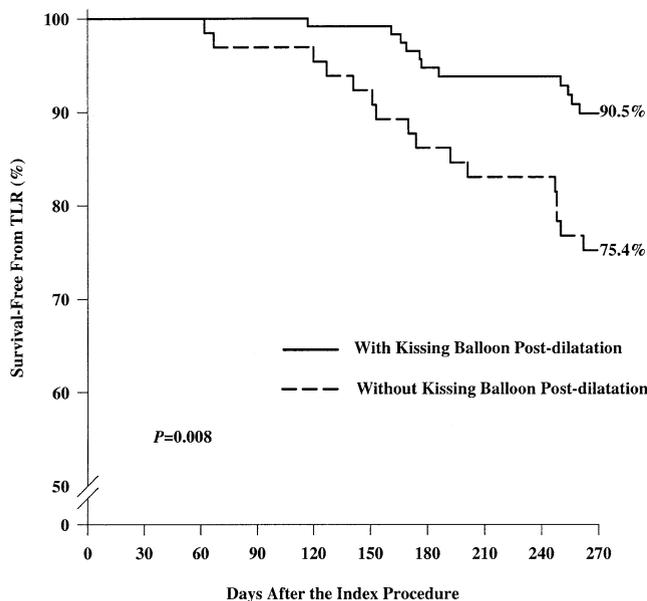


Figure 2. Kaplan-Meier curve of survival free from target lesion revascularization (TLR) during nine-month follow-up.

Table 7. Clinical Characteristics and Outcomes of Patients With Postprocedure Stent Thrombosis

Patient	Stent Type	Age, yrs	Time of Stent Thrombosis, Days	Location	Diabetes	LVEF, %	Stent Length, mm	Premature Discontinue Antiplatelet Therapy	Presentation	Outcome
1	SES	80	28	LAD/diagonal	Yes	50	66	Yes (at 18 days after the index procedure)	AMI	Alive
2	SES	82	55	LM	Yes	42	51	Yes (at 48 days after the index procedure)	AMI	Death
3	PES	71	103	LM	No	35	52	No	AMI	Alive
4	PES	61	64	LM	No	45	64	No	AMI	Death
5	PES	65	90	LAD/diagonal	Yes	60	68	No	AMI	Alive

Time of stent thrombosis: from the index procedure to the day stent thrombosis occurred.

AMI = acute myocardial infarction; LVEF = left ventricular ejection fraction; PES = paclitaxel-eluting stent; SES = sirolimus-eluting stent; other abbreviations as in Table 2.

(19). An additional finding, which may raise concerns, is a four-fold increase in the incidence of late stent thrombosis in the patients treated with PES compared to the ones treated with SES (0.9% [1 of 106] vs. 4.0% [3 of 75], $p = 0.39$, Fisher exact test); the small number of patients should prevent us from drawing premature conclusions. Recently, late stent thrombosis after PES and SES implantation were reported (20). All these data seem to point out that, when two DES are implanted in a bifurcation, there is a higher risk of stent thrombosis and a strong need to adhere to dual antiplatelet therapy for a currently “unknown” time period.

By exact logistic regression analysis, the strongest predictor of postprocedural stent thrombosis was premature discontinuation of antiplatelet therapy. Recently, one study showed that premature discontinuation of dual antiplatelet therapy was associated with an approximately 30-fold greater risk of stent thrombosis (19). In accordance with the finding of another study, age was also identified as a significant predictor of stent thrombosis (21).

Study limitations. The main limitations of the present report are its nonrandomized design with lack of comparison with alternative strategies such as the implantation of a single stent in the main branch, a strategy that is viewed as a default approach no matter how severe the disease in the side branch (22). The lack of randomization between FKB and non-FKB constitutes another limitation. It is of importance to mention that, in the present study, the definition of late stent thrombosis did not require angiographic documentation; therefore, we cannot exclude that the incidence was slightly inflated.

Conclusions. Compared to the absence of kissing balloon after dilation, the “crush” stenting with kissing balloon after dilation appears to be associated with more favorable long-term outcomes. When utilizing the “crush” stenting technique, kissing balloon after dilation is mandatory to reduce the restenosis rate of side branch and the need for TLR.

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REFERENCES

1. Yamashita T, Nishida T, Adamian MG, et al. Bifurcation lesions: two stents versus one stent—immediate and follow-up results. *J Am Coll Cardiol* 2000;35:1145–51.
2. Colombo A, Moses JW, Morice MC, et al. Randomized study to evaluate sirolimus-eluting stents implanted at coronary bifurcation lesions. *Circulation* 2004;109:1244–9.
3. Colombo A, Stankovic G, Orlic D, et al. Modified T-stenting technique with crushing for bifurcation lesions: immediate results and 30-day outcome. *Catheter Cardiovasc Interv* 2003;60:145–51.
4. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;350:221–31.
5. Sheehan FH, Braunwald E, Canner P, et al. The effect of intravenous thrombolytic therapy on left ventricular function: a report on tissue-type plasminogen activator and streptokinase from the Thrombolysis In Myocardial Infarction (TIMI phase I) trial. *Circulation* 1987;75:817–29.
6. Mehta CR, Patel NR. Exact logistic regression: theory and examples. *Stat Med* 1995;14:2143–60.
7. Chieffo A, Bonizzoni E, Orlic D, et al. Intraprocedural stent thrombosis during implantation of sirolimus-eluting stents. *Circulation* 2004;109:2732–6.
8. Tanabe K, Hoye A, Lemos PA, et al. Restenosis rates following bifurcation stenting with sirolimus-eluting stents for de novo narrowings. *Am J Cardiol* 2004;94:115–8.
9. Ormiston JA, Currie E, Webster MW, et al. Drug-eluting stents for coronary bifurcations: insights into the crush technique. *Catheter Cardiovasc Interv* 2004;63:332–6.
10. Castagna MT, Mintz GS, Leiboff BO, et al. The contribution of “mechanical” problems to in-stent restenosis: an intravascular ultrasonographic analysis of 1,090 consecutive in-stent restenosis lesions. *Am Heart J* 2001;142:970–4.
11. Fujii K, Mintz GS, Kobayashi Y, et al. Contribution of stent underexpansion to recurrence after sirolimus-eluting stent implantation for in-stent restenosis. *Circulation* 2004;109:1085–8.
12. Takebayashi H, Kobayashi Y, Dangas G, et al. Restenosis due to underexpansion of sirolimus-eluting stent in a bifurcation lesion. *Catheter Cardiovasc Interv* 2003;60:496–9.
13. Lefevre T, Louvard Y, Morice MC, et al. Stenting of bifurcation lesions: classification, treatments, and results. *Catheter Cardiovasc Interv* 2000;49:274–83.
14. Colombo A. Bifurcational lesions and the “crush” technique: understanding why it works and why it doesn’t—a kiss is not just a kiss. *Catheter Cardiovasc Interv* 2004;63:337–8.
15. The EPISTENT Investigators. Randomised placebo-controlled and balloon angioplasty-controlled trial to assess safety of coronary stenting with use of platelet glycoprotein IIb/IIIa blockade. Evaluation of Platelet IIb/IIIa Inhibitor for Stenting. *Lancet* 1998;352:87–92.
16. Angiolillo DJ, Fernandez-Ortiz A, Bernardo E, et al. High clopidogrel loading dose during coronary stenting: effects on drug response and interindividual variability. *Eur Heart J* 2004;25:1903–10.

17. Angiolillo DJ, Fernandez-Ortiz A, Bernardo E, et al. Identification of low responders to a 300-mg clopidogrel loading dose in patients undergoing coronary stenting. *Thromb Res* 2005;115:101–8.
18. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;349:1315–23.
19. Jeremias A, Sylvia B, Bridges J, et al. Stent thrombosis after successful sirolimus-eluting stent implantation. *Circulation* 2004;109:1930–2.
20. McFadden EP, Stabile E, Regar E, et al. Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy. *Lancet* 2004;364:1519–21.
21. Schuhlen H, Kastrati A, Dirschinger J, et al. Intracoronary stenting and risk for major adverse cardiac events during the first month. *Circulation* 1998;98:104–11.
22. Louvard Y, Lefevre T, Morice MC. Percutaneous coronary intervention for bifurcation coronary disease. *Heart* 2004;90:713–22.