Randomized Comparison of Final Kissing Balloon Dilatation Versus No Final Kissing Balloon Dilatation in Patients With Coronary Bifurcation Lesions Treated With Main Vessel Stenting

The Nordic-Baltic Bifurcation Study III

Matti Niemelä, MD; Kari Kervinen, MD; Andrejs Erglis, MD; Niels R. Holm, MD; Michael Maeng, MD; Evald H. Christiansen, MD; Indulis Kumsars, MD; Sanda Jegere, MD; Andis Dombrovskis, MD; Pål Gunnes, MD; Sindre Stavnes, MD; Terje K. Steigen, MD; Thor Trovik, MD; Markku Eskola, MD; Saila Vikman, MD; Hannu Romppanen, MD; Timo Mäkikallio, MD; Knud N. Hansen, MD; Per Thayssen, MD; Lars Åberge, MD; Lisette O. Jensen, MD; Anders Hervold, MD; Juhani Airaksinen, MD; Mikko Pietilä, MD; Ole Frobert, MD; Thomas Kellerth, MD; Jan Ravkilde, MD; Jens Aarøe, MD; Jan S. Jensen, MD; Steffen Helqvist, MD; Iwar Sjögren, MD; Stefan James, MD; Heikki Miettinen, MD; Jens F. Lassen, MD; Leif Thuesen, MD; for the Nordic-Baltic PCI Study Group

Background—It is unknown whether the preferred 1-stent bifurcation stenting approach with stenting of the main vessel (MV) and optional side branch stenting using drug-eluting stents should be finalized by a kissing balloon dilatation (FKBD). Therefore, we compared strategies of MV stenting with and without FKBD.

Methods and Results—We randomized 477 patients with a bifurcation lesion to FKBD (n=238) or no FKBD (n=239) after MV stenting. The primary end point was major adverse cardiac events: cardiac death, non–procedure-related index lesion myocardial infarction, target lesion revascularization, or stent thrombosis within 6 months. The 6-month major adverse cardiac event rates were 2.1% and 2.5% (P=1.00) in the FKBD and no-FKBD groups, respectively. Procedure and fluoroscopy times were longer and more contrast media was needed in the FKBD group than in the no-FKBD group. Three hundred twenty-six patients had a quantitative coronary assessment. At 8 months, the rate of binary (re)stenosis in the entire bifurcation lesion (MV and side branch) was 11.0% versus 17.3% (P=0.11), in the MV was 3.1% versus 2.5% (P=0.68), and in the side branch was 7.9% versus 15.4% (P=0.039) in the FKBD versus no-FKBD groups, respectively. In patients with true bifurcation lesions, the side branch restenosis rate was 7.6% versus 20.0% (P=0.024) in the FKBD and no-FKBD groups, respectively.

Conclusions—MV stenting strategies with and without FKBD were associated with similar clinical outcomes. FKBD reduced angiographic side branch (re)stenosis, especially in patients with true bifurcation lesions. The simple no-FKBD procedures resulted in reduced use of contrast media and shorter procedure and fluoroscopy times. Long-term data on stent thrombosis are needed.

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Key Words: angioplasty, balloon ■ coronary disease ■ drug-eluting stents ■ bifurcation

Bifurcation lesions represent 15% to 20% of percutaneous coronary interventions (PCIs).[1] PCI of bifurcation lesions is challenging and associated with increased procedural costs, greater complication rates, and worse outcomes compared with PCI of simple coronary lesions.[2] The rate of PCI-associated restenosis in the bare metal stent era was reported to be up to 40%, and even worse in the side branch (SB).[3] The introduction of drug-eluting stents

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From the Division of Cardiology, Department of Internal Medicine, University of Oulu, Oulu, Finland (M.N., K.K., H.R.); Latvian Center of Cardiology, Paul Stradins Clinical Hospital, Riga, Latvia (A.E., I.K., S. Jegere, A.D.); Department of Cardiology, Aarhus University Hospital, Skejby, Aarhus, Denmark (N.R.H., M.M., E.H.C., J.F.L., L.T.); Department of Cardiology, The Feiring Clinic, Feiring, Norway (P.G., S.S.); Department of Cardiology, University Hospital of Tromsoe, Tromsoe, Norway (T.K.S., T.T.); Heart Center, Tampere University Hospital, Tampere, Finland (M.E., S.V.); Department of Cardiology, Kainuu Central Hospital, Lansi-Pohja Central Hospital, and Lapland Central Hospital, Kemi, Finland (T.M.); Department of Cardiology, Odense University Hospital, Odense, Denmark (K.N.H., P.T., L.O.J.); Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway (L.A., A.H.); Division of Cardiology, Turku University Hospital, Turku, Finland (J. Airaksinen); Department of Cardiology, Örebro University Hospital, Örebro, Sweden (O.F., T.K.); Department of Cardiology, Aalborg University Hospital, Aalborg, Denmark (J.R., J. Aarøe); Department of Cardiology, Gentofte University Hospital, Gentofte, Denmark (J.S.J.); Department of Cardiology, Rigshospitalet, Copenhagen, Denmark (S.H.); Department of Cardiology, Falun Hospital, Falun, Sweden (I.S.); Department of Cardiology, Uppsala University Hospital, Uppsala, Sweden (S. James); and Division of Cardiology, Kuopio University Central Hospital, Kuopio, Finland (H.M.).

Correspondence to Matti Niemelä, Division of Cardiology, Department of Internal Medicine, University of Oulu, Finland. E-mail matti.niemela@ppshp.fi

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improved outcomes and resulted in low rates of main vessel (MV) restenosis. However, SB ostial residual stenosis and restenosis remained a problem. Bifurcation treatment involves a number of steps: predilatation, implantation of 1 or 2 stents, and postdilatation with single or kissing balloon techniques. Several studies have compared a 1-stent technique and a 2-stent technique using drug-eluting stents for bifurcation lesions.[4–7] These studies reported that 2-stent techniques did not offer any advantage over stenting of the MV only but were associated with increased use of contrast, longer procedure times, and higher rates of procedure-related myocardial infarctions (MIs).[4,7] Therefore, the provisional SB stenting strategy has emerged as the preferred bifurcation treatment strategy. In the Nordic Bifurcation Study, the optional SB stenting strategy resulted in a 20% SB restenosis rate at follow-up. In that study, the SB was dilated through the MV stent in one third of the patients.[4] In 2-stent techniques such as culotte and crush techniques, final kissing balloon dilatation (FKBD) is currently considered mandatory.[8] Whether FKBD will improve clinical and angiographic outcomes after successful stenting of the MV remains unknown. Therefore, the present study assessed, in a randomized multicenter setting, whether routine FKBD after successful stenting of the MV would improve outcomes in patients with coronary artery bifurcation lesions.

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Methods

Patients and Study Design

The study, designed as a nonblinded randomized multicenter trial, was conducted at 13 hospitals in Denmark, Finland, Latvia, Sweden, and Norway. The patients were recruited from the general PCI populations of the participating centers. From April 2007 through October 2008, a total of 477 patients were enrolled, by estimate 20% of eligible patients. A few patients (<5%) were excluded from the study because of impaired SB flow after MV stenting. A flow diagram of the study is shown in Figure 1. National ethics committees approved the study protocol. All patients gave their written informed consent before randomization.

Patients were eligible for randomization if they had either stable or unstable angina pectoris or silent ischemia attributable to a de novo coronary bifurcation lesion involving the MV. For inclusion, the MV diameter had to be ≥2.5 mm and the SB had to be ≥2.25 mm by visual estimate. No patients with SB lesion and no MV stenosis were included. The exclusion criteria were ST-segment elevation MI within 24 hours, life expectancy <1 year, serum creatinine ≥200 μmol/L, and allergy to any of the drugs used (aspirin, clopidogrel, and sirolimus).

Randomization

Patients were enrolled after successful stenting of the MV and with preserved normal Thrombolysis in Myocardial Infarction blood flow in the SB. The patients were allocated to treatment groups by use of stratified block randomization with strata defined by site, gender, and diabetes status (yes/no), each with separate computer-generated treatment allocation sequences with permuted block sizes of 2, 4, and 6 in random order. Treatment allocation was properly concealed by the use of an automated telephone allocation service provided by an independent organization.

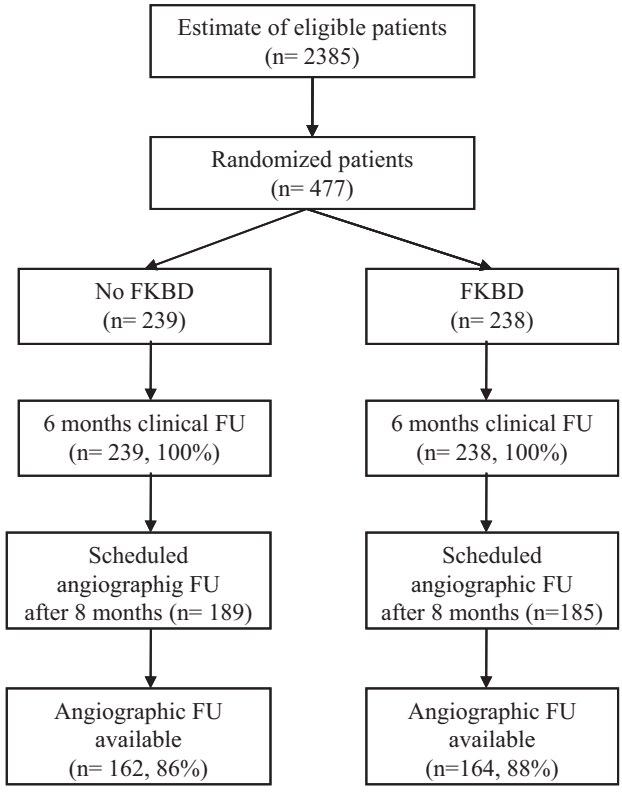

Figure 1. Flow diagram of the Nordic-Baltic Bifurcation Study III. FU indicates follow-up.

Stent Implantation

In the patients not receiving aspirin, 250 to 500 mg aspirin was administered before the procedure. All patients received a loading dose of 300 to 600 mg clopidogrel unless they were on long-term treatment. In the catheterization laboratory, heparin or low-molecular-weight heparin was administrated. Glycoprotein receptor inhibitor and bivalirudin were used at the discretion of the operator. After PCI, lifelong aspirin (≥75 mg/d) and clopidogrel (75 mg/d) for 12 months were recommended.

The operator was requested to avoid pretreatment (balloon dilatation) of MV segments that were not going to be covered by the stent. The sirolimus-eluting Cypher Select+ (Cordis/Johnson & Johnson, Miami Lakes, FL) coronary stent was used in the study.

The main treatment principles of the PCI procedure were as follows: wiring of both the MV and SB, predilatation of the stenosed areas of the MV and SB at the discretion of the operator, followed by stenting of the MV and thus jailing of the SB wire. If there was Thrombolysis in Myocardial Infarction grade 3 flow in the SB after MV stenting, the patient was randomized to FKBD or no FKBD. If the patient was randomized to the no-FKBD group, the procedure was terminated even if a high-grade ostial SB stenosis was present. In the FKBD group, the SB was rewired through the MV stent, and simultaneous kissing balloon dilation was performed. There were no specific recommendations for performing the simultaneous kissing balloon dilatation. In case of SB Thrombolysis in Myocardial Infarction flow less than grade 3 after FKBD, the SB was treated with a stent.

If the study stent could not be delivered, another drug-eluting stent or a bare metal stent was allowed. Different types of drug-eluting stents in the same vessel were not allowed. Implantation of additional stents to cover the whole lesion or to cover a dissection was allowed.

Cardiac Biomarkers and ECG

Creatine kinase-MB mass and cardiac troponin T or troponin I were measured before intervention and 12 to 18 hours after intervention.

Troponin T was used as the primary marker; creatine kinase-MB mass or troponin I was measured only if troponin T was not available. To avoid confounding by non–procedure-related marker elevation, unstable patients were included in the biomarker analysis only if preprocedure and postprocedure markers were normal. An increase in biomarker values to ≥3 times the upper limit of normal was considered significant. A 12-lead ECG was obtained before and 12 to 18 hours after the procedure.

Follow-Up

Information on death and other major adverse cardiac events (MACEs) was obtained by phone contact at 1 month. Clinical follow-up visit was performed at 6 months for primary end-point registration. An 8-month control coronary angiography was scheduled at randomization for patients who consented. If patients included in the angiographic substudy had clinical driven target lesion revascularization (TLR) in the follow-up period, their event angiogram before PCI was used for their angiographic follow-up. No patients were lost to follow-up.

Quantitative Coronary Angiography Analysis at 8 Months

Coronary angiograms obtained at baseline, at the completion of the stenting procedure, and at the 8-month follow-up were submitted to the joint angiographic core laboratory (Aarhus University Hospital, Skejby, Aarhus, Denmark, and Paul Stradins Clinical Hospital, Riga, Latvia) and analyzed with the use of a computer-based system dedicated to bifurcation analysis (QAngio XA version 7.2, Medis, Leiden, the Netherlands). Quantitative coronary analysis of the bifurcation lesion was obtained in 3 segments: the proximal MV segment, the distal MV segment, and the SB. The MV edge segments comprised the 5-mm margins to the stented segment. The first 5 mm of the SB was used for analysis regardless of the treatment. The analyses were not blinded.

Study End Points

The primary end point of the study was the clinical combined end point of the MACEs: cardiac death, non–procedure-related index lesion MI, stent thrombosis, or TLR by PCI or coronary artery bypass surgery within 6 months. Secondary end points were (1) the individual end points of total death, cardiac death, non–procedure-related MI, or TLR; (2) procedure-related increase in biochemical markers to ≥3 times the decision limit of MI (99th percentile) given a coefficient of variation <10% of creatine kinase-MB mass, troponin T, and/or troponin I; (3) the angiographic end point of significant in-segment and in-stent restenosis (≥50% diameter stenosis) of the MV and/or SB; and (4) Canadian Cardiovascular Society (CCS) angina score ≥2. The clinical study end points were adjudicated blindly by an independent end-point committee.

Definitions

Non–procedure-related MI was defined as a level of biochemical markers exceeding the decision limit of MI (99th percentile) with at least 1 of the following: ischemic symptoms, ECG changes indicative of ischemia (ST-segment elevation or depression), or development of pathological Q wave with no relation to a PCI procedure. Definite stent thrombosis was defined according to the Academic Research Consortium classification.[9] TLR was defined as repeat revascularization by PCI or surgery of the target lesion. Percent diameter stenosis was defined as follows: (reference diameter−minimal luminal diameter)/reference diameter×100. Restenosis was defined as a minimum of 50% diameter stenosis at the 8-month angiographic follow-up. Late lumen loss was defined as postprocedure minimal luminal diameter minus minimal luminal diameter (in millimeters) at the 8-month follow-up.

Statistical Analysis

We expected a MACE rate of 2% in the FKBD group and 8% in the no-FKBD group. With an α of 5% and power of 80%, 206 patients were needed in each group (2-sided χ^2 test) to demonstrate this difference. By including 225 patients in each group, we accounted for a possible dropout before follow-up, and we would expect >350 patients to schedule an angiographic follow-up.

Differences in categorical variables between the 2 groups were analyzed with the χ^2 test or the Fisher exact test. Continuous variables were analyzed with independent-sample t test and Mann-Whitney U test, and time-to-event data were analyzed with the Kaplan-Meier method and the log-rank test. All P values were 2 sided. The level of significance was 5%. The analysis was performed on an intention-to-treat basis. All analyses were performed with SPSS 13.0 (SPSS Inc, Chicago, IL).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Table 1. Baseline Clinical Characteristics

	No FKBD (n=239)	FKBD (n=238)	P
Age, y	64.2±10	65.2±10	0.25
Male, n (%)	173 (72.4)	174 (73.1)	0.91
Current smoker, n (%)	55 (22.6)	48 (20.3)	0.57
Hypercholesterolemia, n (%)	201 (84.1)	198 (83.2)	0.80
Hypertension, n (%)	158 (66.1)	145 (61.3)	0.29
Diabetes mellitus, n (%)	38 (15.9)	43 (17.7)	0.62
Family history, n (%)	146 (61.1)	133 (56.4)	0.30
Prior PCI, n (%)	74 (31.0)	57 (24.4)	0.12
Prior CABG, n (%)	5 (1.7)	7 (2.9)	0.38
CCS class ≥2 angina, n (%)	233 (97.5)	232 (97.4)	1.00
Indication, n (%)			
Stable angina pectoris	177 (74.1)	177 (74.4)	1.00
Unstable angina pectoris	61 (25.6)	60 (25.2)	0.91
Silent ischemia	1 (0.4)	1 (0.4)	1.00
Antiplatelet therapy, n (%)			
Aspirin	238 (99.6)	238 (100)	1.00
Clopidogrel	236 (98.7)	236 (99.2)	1.00
GP IIb/IIIa inhibitors	69 (28.9)	69 (29.1)	1.00
Bivalirudin	50 (20.9)	62 (26.2)	0.19

CABG indicates coronary artery bypass graft surgery; GP, glycoprotein receptor. Values are mean± SD when appropriate.

Results

Baseline Clinical Characteristics

Baseline clinical characteristics listed in Table 1 showed no significant differences between the 2 treatment groups. The mean age of study group was 65 years; 73% were male; and 17% had diabetes mellitus. The indication was stable angina pectoris in three fourths of the patients and unstable angina pectoris in one fourth of the patients. The use of aspirin, clopidogrel, glycoprotein IIb/IIIa inhibitors, and bivalirudin was similar in both groups.

Procedural and Lesion Characteristics

Details on procedural and lesion characteristics for the 2 groups are reported in Table 2. In the FKBD group, the target bifurcation lesion was located in the left anterior descending artery in 76% of patients compared with 67% of the no-FKBD group (P=0.03), whereas 12% in the FKBD group had a treatment of the circumflex artery compared with 21%

Table 2. Procedural Characteristics

	No FKBD n=239	FKBD n=238	*P*
LVEF, %	59±10	58±11	0.44
Lesion location, n (%)			
Left anterior descending artery	160 (66.9)	182 (76.5)	0.03
Circumflex artery	51 (21.3)	28 (11.8)	0.01
Right coronary artery	13 (5.4)	9 (3.8)	0.51
Left main stem	17 (7.1)	19 (8.0)	0.73
True bifurcation lesion (Medina 1,1,1; 1.0.1; 0,1,1), n (%)*	117 (49.0)	129 (50.8)	0.71
Mean lesion length, mm*			
MV	17.7±10.2	17.3±8.6	0.58
SB	3.6±4.2	3.4±3.9	0.62
MV mean stent length, mm*	22.9±10.5	23.6±11.1	0.50
Proximal reference diameter, mm*			
MV	3.4±0.4	3.4±0.6	0.58
SB	2.7±0.4	2.6±0.3	0.05
MV stented, n (%)	238 (99.6)	238 (100)	1.00
SB stented, n (%)	0 (0)	3 (1.3)	0.12
SB dilatation through MV stent, n (%)	3 (1.3)	79 (33.3)	0.0001
FKBD, n (%)	2 (0.8)	231 (97.1)	0.0001
SB dilatation through MV stent or FKBD, n (%)	4 (1.7)	231 (97.1)	0.0001
Treatment successful, n (%)†	236 (98.7)	236 (99.2)	1.00
Procedure time, min	47±22	61±28	0.0001
Fluoroscopy time, min	11±10	16±12	0.0001
Contrast volume, mL	200±92	235±97	0.0001

LVEF indicates left ventricular ejection fraction. Values are mean±SD when appropriate.

*By visual estimate.

†Residual stenosis <30% of MV and Thrombolysis in Myocardial Infarction grade 3 flow in SB.

in the no-FKBD group. The left main bifurcation was treated in 8% of the patients. According to the Medina classification,[10] a "true bifurcation" lesion (Medina 1,1,1; 1,0,1; 0,1,1) was observed in 50% of the patients by operator assessment. The average vessel sizes, as evaluated by the operator, were 3.4 mm in the proximal MV and 2.7 mm in the SB, with lesion lengths of 17.5 and 3.5 mm, respectively. The SB was predilated in 29.0% and 27.6% ($P=0.76$) in the FKBD and the no-FKBD groups, respectively. The SB had a single balloon dilatation through the MV stent in 33.3% of the FKBD group and in 1.3% of the no-FKBD group ($P=0.0001$). Kissing balloon dilatation was performed after MV stenting in 97.1% of the FKBD group and 0.8% of the no-FKBD group. Procedure duration, fluoroscopic time, and contrast media volume were significantly lower in the no-FKBD group. Procedural success was similar in both groups.

Clinical Outcome

Clinical follow-up data at 6 months were available in all patients, and the primary composite end point of 6-month MACEs (cardiac death, nonprocedure-related index lesion MI, TLR, definite stent thrombosis) is shown in Figure 2. The

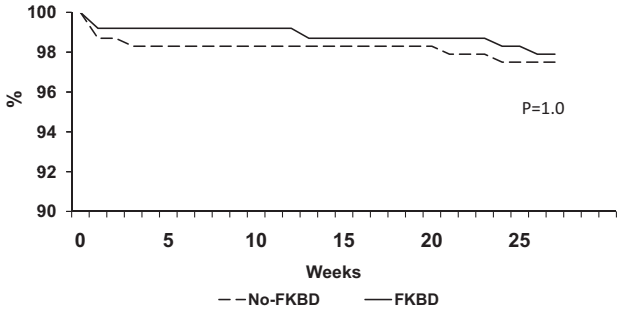

Figure 2. Kaplan-Meier curves for MACE-free survival (cardiac death, non–procedure-related index lesion MI, TLR, definite stent thrombosis) in the FKBD and no-FKBD groups during the 6-month of follow-up.

6-month MACE rate was 2.1% in the FKBD and 2.5% ($P=1.00$) in the no-FKBD group. The individual end-point rates of the components of MACE by 6 months (Table 3) showed no differences between the 2 groups. The proportion of CCS angina class ≥2 was similar in the study groups before (97.4% versus 97.5%; $P=1.00$; Table 1) and 6 months after PCI (11.7% versus 12.0%; $P=1.00$; Table 3).

Procedure-Related Elevation of Biomarkers

Procedure-related biomarker release was evaluated in 350 patients (175 in each group). Significant marker elevation was observed in 6.3% of patients in both study groups.

Quantitative Coronary Angiography Analysis

A total of 374 patients were scheduled for 8-month angiographic follow-up, and a complete angiographic data set was available in 326 patients (87%). The results of the quantitative coronary analysis are shown in Table 4. The reference vessel diameters of the MV and SB at baseline, after stenting, and at follow-up were similar in both groups. The minimal luminal diameter of the SB tended to be larger in the FKBD group at follow-up (1.74±0.48 versus 1.63±0.59 mm; $P=0.06$). At follow-up, the percentage of binary (re)stenosis (diameter stenosis ≥50%) in the entire bifurcation lesion (MV and SB) was 11.0% in the FKBD and 17.3% in the no-FKBD group ($P=0.11$). In the in-segment MV, restenosis occurred in 3.1% and 2.5% ($P=0.68$) in the FKBD and no-FKBD groups, respectively. In the SB segment, the rates were 7.9% versus 15.4% ($P=0.039$), respectively. No patients in the FKBD group had a ≥75% diameter SB binary

Table 3. Individual Components of MACEs and Clinical Outcomes at 6 Months

	No FKBD (n=239), n (%)	FKBD (n=238), n (%)	*P*
Noncardiac death	0 (0)	1 (0.4)	0.49
Cardiac death	0 (0)	2 (0.8)	0.24
Index lesion MI*	3 (1.3)	1 (0.4)	0.62
TLR	4 (1.7)	3 (1.3)	1.00
CCS class ≥2 angina	29 (12.0)	28 (11.7)	1.00
Stent thrombosis	1 (0.4)	1 (0.4)	1.00

The χ^2 test was used.

*Not procedure related.

Table 4. Results of Quantitative Angiography in the 3 Bifurcation Segments

	Proximal MV			Distal MV			SB		
Variable	FKBD (n=164)	No FKBD (n=162)	*P*	FKBD (n=164)	No FKBD (n=162)	*P*	FKBD (n=164)	No FKBD (n=162)	*P*
In-stent* minimal luminal diameter, mm									
Before	1.39±0.57	1.43±0.63	0.54	1.47±0.57	1.42±0.57	0.39	1.59±0.56	1.54±0.60	0.65
After	2.70±0.44	2.64±0.45	0.16	2.43±0.41	2.44±0.40	0.88	1.60±0.46	1.54±0.53	0.22
Follow-up	2.76±0.54	2.65±0.56	0.06	2.48±0.49	2.42±0.53	0.30	1.74±0.48	1.63±0.59	0.06
In-stent* reference diameter, mm									
Before	2.78±0.58	2.83±0.59	0.51	2.49±0.57	2.50±0.57	0.87	2.31±0.46	2.35±0.75	0.59
After	3.06±0.45	3.00±0.41	0.25	2.70±0.41	2.69±0.39	0.77	2.26±0.49	2.24±0.51	0.81
Follow-up	3.16±0.48	3.11±0.47	0.27	2.79±0.42	2.77±0.42	0.65	2.32±0.51	2.33±0.53	0.80
In-stent* diameter stenosis, %									
Before	49±21	48±22	0.80	40±20	43±22	0.25	31±20	33±20	0.43
After	12±8	12±10	0.49	10±9	9±9	0.47	28±17	31±19	0.12
Follow-up	12±13	15±13	0.06	11±12	13±13	0.18	25±15	30±20	0.009
In-stent* late lumen loss, mm	−0.06±0.51	−0.01±0.53	0.42	−0.05±0.50	0.02±0.47	0.23	−0.13±0.42	−0.10±0.46	0.52
Edge minimal luminal diameter, mm									
After	2.92±0.62	2.88±0.57	0.60	2.06±0.46	2.10±0.48	0.47			
Follow-up	2.97±0.66	2.98±0.60	0.86	2.16±0.47	2.23±0.47	0.23			
Restenosis, n (%)									
In-stent*	3 (1.8)	3 (1.9)	1.00	2 (1.2)	3 (1.9)	1.00	13 (7.9)	25 (15.4)	0.039
Edge	2 (1.2)	0 (0)	0.50	2 (1.2)	0 (0)	0.50			

Restenosis was defined as ≥50% diameter stenosis at the 8-month follow-up. The Fisher exact test, χ^2 test, or independent-samples *t* test was used.
*In-stent segments included the stented areas of the MV or the first 5 mm of the SB.

(re)stenosis compared with 4 patients (2.5%) in the no-FKBD group ($P=0.06$). Late lumen loss was similar both in the MV segments and in the SB between treatment groups.

True Versus Nontrue Bifurcation Subgroup Analysis

A total of 239 patients (50.1%) had a true bifurcation lesion according to the Medina classification as assessed by the operator. In this group, the 6-month MACE rates were 1.7% and 2.5% ($P=0.68$) and TLR rates were 0.8% and 1.7% ($P=0.62$) in the FKBD and no-FKBD groups, respectively. In patients with nontrue bifurcations, the 6-month MACE rates were 2.6% and 2.5% ($P=1.00$) and TLR rates were 1.7% and 1.7% ($P=1.00$) in the FKBD and no-FKBD groups, respectively. Quantitative coronary analysis was available for 172 patients in the true bifurcation and in 154 in the nontrue bifurcation subgroups. In the true bifurcation subgroup, angiographic SB results were improved by FKBD (SB minimal luminal diameter: 1.71*0.42 versus 1.50*0.53, $P=0.005$; SB diameter stenosis: 25*14 versus 32*21, $P=0.009$; and SB binary (re)stenosis: n=7 [7.6%] versus n=16 [20.0%], $P=0.024$). Angiographic outcome was not improved by FKBD in the non-true bifurcation subgroup (Table 5).

Discussion

Our trial demonstrates that a simple MV stenting technique without FKBD provides excellent clinical results that are similar to those of the more complex strategy of MV stenting with FKBD in patients with coronary bifurcation lesions. At the 8-month angiographic follow-up, there was no significant

Table 5. True Versus Nontrue Bifurcation Subgroup Comparison: 8-Month Angiographic Follow-Up

	True Bifurcation Subgroup			Nontrue Bifurcation Subgroup		
Variable	FKBD (n=92)	No FKBD (n=80)	*P*	FKBD (n=72)	No FKBD (n=82)	*P*
In-segment MV						
DS, %	22±15	22±15	0.85	22±14	21±12	0.90
≥50% DS, n (%)	3 (3.8)	2 (2.2)	0.67	3 (4.2)	1 (1.2)	0.34
Ostial 5 mm of the SB						
MLD, mm	1.71±0.42	1.50±0.53	0.005	1.79±0.54	1.77±0.61	0.79
DS, %	25±14	32±21	0.009	23±15	27±19	0.21
≥50% DS, n (%)	7 (7.6)	16 (20)	0.024	6 (8.3)	9 (11)	0.79

DS indicates diameter stenosis; MLD, minimal luminal diameter. The Fisher exact test, χ^2 test, or independent-samples *t* test was used.

difference in the binary (re)stenosis rate of the entire bifurcation lesion (MV plus SB) in the 2 treatment arms, but the rate of SB (re)stenosis was increased in the no-FKBD group, primarily as a result of increased (re)stenosis in true bifurcation lesions treated without FKBD.

The optimal stenting technique for bifurcation lesions has been debated, and several techniques using either 1 or 2 stents have been introduced.[11,12] The available data indicate that most patients can be treated safely and effectively with a provisional SB stenting strategy. However, it is not known whether the MV stent should always be opened at the SB ostium by SB rewiring through the MV stent and subsequent balloon dilatation. It might be expected that SB blood flow would improve after opening the MV stent at the SB ostium. On the other hand, distortion of the MV stent might be a concern. Meticulous bench testing has shown that stent deformation is consistently seen after opening of a stent, but this deformation can be corrected by FKBD.[13,14] Therefore, the present study compared FKBD and no FKBD to investigate both the clinical and angiographic effects of routine opening of the MV stent struts at the SB ostium in bifurcation lesions treated with MV stenting.

Stringent criteria for SB stenting were applied in our study. The crossover rate was low, allowing a true comparison of the 2 study groups. Thus, any SB dilatation was performed in only 1.7% of the patients in the no-FKBD group, and the crossover rate from no-FKBD to FKBD strategy was only 0.8%. Furthermore, no patients in the no-FKBD group and 1.3% of patients in the FKBD group received a SB stent. Therefore, the treatment principles used in our study seem applicable to almost all bifurcation lesions with normal SB blood flow after MV stenting.

Our results are consistent with a recent study that randomized 110 patients to mandatory kissing balloon inflation or to provisional kissing after stenting.[15] However, only 73% of the patients in that study compared with 97.1% in our study underwent kissing balloon dilatation in the FKBD arm, and 17.9% of the patients had stenting of the SB in the FKBD arm[15] compared with 1.3% in the present study.

Clinical Outcomes

Both study groups had excellent clinical results. Mortality and incidence of MI were low and comparable to recent randomized bifurcation studies using drug-eluting stents that did not include procedure-related MI[4] and slightly lower than in studies that included procedure-related MI.[5–7] The rate of definite stent thrombosis was 0.4% in the 2 groups. Thus, MV stenting without FKBD could be performed without increasing the risk of stent thrombosis within the observation period. A considerable longer follow-up is needed to obtain a reliable assessment of the risk of stent thrombosis. It has been suggested that postdilatation would facilitate subsequent SB access.[14] We found that the need for TLR was $<2\%$ after 6 months, indicating that the need for subsequent SB access was low.

An important observation of the present study relates to the favorable results relative to the occurrence of angina pectoris. The majority of patients had severe angina pectoris at baseline. At the 6-month follow up, symptom relief was substantial and similar in both groups.

Quantitative Coronary Angiography Analysis

The 8-month quantitative coronary analysis revealed excellent results in the MV segment and improved angiographic results in the SB in the FKBD group. The follow-up percent diameter stenosis and the incidence of (re)stenosis in the SB were higher in the no-FKBD arm compared with patients assigned to FKBD. This difference was not due to greater late lumen loss, which was similar in both treatment arms. Significant residual SB stenosis potentially causes significant angina pectoris and subsequent TLR. However, in our study, CCS class 2 or higher angina occurred with similar frequency during follow-up in both treatment arms. Furthermore, the need for clinical driven TLR in the patients included in the angiographic substudy was only 0.6% and 1.9% in the FKBD and no-FKBD groups, respectively. Thus, the clinical relevance of angiographic SB (re)stenosis, although assessed 2 months later, was negligible in the present study. Accordingly, the assessment of SB stenosis with fractional flow reserve found that this functional assessment correlated only weakly with angiography.[16]

True and Nontrue Bifurcation Lesions

Clinical end point rates in true and nontrue bifurcation lesions were low. Hence, possible differences in the clinical outcome between the 2 treatment groups were not detectable. In the true bifurcation lesion subgroup, FKBD reduced SB (re)stenosis significantly, an effect that might become clinically relevant and justify the more complex FKBD procedure. In the subgroup of nontrue bifurcation lesions, no difference in angiographic outcome between FKBD and no-FKBD was found.

Study Limitations

The open-label design with operators and patients being aware of the treatment assignment is a limitation of the study. It is, however, impossible to blind the operator in this type of study. Data completeness and consistency were audited centrally at the PCI Research Unit, Aarhus University Hospital, Skejby, but there were no onsite audits. The lack of onsite study monitoring might have led to an underreporting of events. MACEs were adjudicated by a blinded event committee, which should reduce the bias of the open-label design.

Mortality and incidence of MI were low in our study, and procedure-related MI was excluded from our primary end point. Hence, comparison to results from other bifurcation studies should be made cautiously. Given the observed clinical event rates, the study was underpowered. However, considering the low event rates, a properly powered study with a 6-month clinical follow-up is not realistic. Future studies will have to focus on imaging or fractional flow reserve end points or possibly longer-term follow-up.

Importantly, the average SB reference 2.33 mm by quantitative coronary analysis and 2.63 mm by visual estimation, while the SB lesion length was 3.5 mm by visual estimation. Furthermore, the prevalence of nontrue bifurcation lesions according to the Medina classification was 50% in our study.

Extrapolation of the results to all types of bifurcations, especially to genuine bifurcation lesions with a large SB or long SB lesions, should be done cautiously. Because the clinical follow-up was restricted to 6 months, no conclusions can be drawn about the long-term safety profile of either treatment strategy.

Conclusions

In coronary bifurcation lesions, MV stenting with and without FKBD was associated with favorable and similar 6-month clinical outcomes. The simple no-FKBD procedure resulted in reduced use of contrast media and shorter procedure and fluoroscopy times. Angiographic SB outcome was improved by FKBD, especially in patients with true bifurcation lesions. In nontrue bifurcation lesions, no effect of FKBD was detected by either clinical or angiographic end points. Long-term safety data are needed.

Appendix

The Nordic-Baltic PCI Study Group

The purpose of the Nordic-Baltic PCI Study Group is to conduct academic randomized clinical trials and to optimize PCI treatment in the Nordic and Baltic countries.

Steering Committee

Leif Thuesen, Jens Flensted Lassen, Per Thayssen, Terje Steigen, Pål Gunnes, Lars Åberge, Saila Vikman, Matti Niemelä, Kari Kervinen, Juhani Airaksinen, Andrejs Erglis, Indulis Kumsars.

Quantitative Coronary Angiography Core Laboratories

Aarhus University Hospital, Skejby, Denmark: Michael Maeng, Niels R. Holm, and Helle Højdahl. Latvian Center of Cardiology, Paul Stradins Clinical Hospital, Riga, Latvia: Sanda Jegere.

Participating Centers and Inclusions per Center

Finland: Division of Cardiology, Department of Internal Medicine, University of Oulu (149); Department of Cardiology, Tampere University Hospital, Tampere (24); Department of Cardiology Turku University Hospital, Turku (13); Department of Cardiology, Kajaani Central Hospital, Kajaani (12); Department of Cardiology, Rovaniemi Central Hospital, Rovaniemi (5); Department of Cardiology, Kemi Central Hospital, Kemi (1); Department of Cardiology, Kuopio University Hospital, Kuopio (1); Denmark: Aarhus University Hospital, Skejby (81); Odense University Hospital, Odense (17); Aalborg University Hospital (7); Gentofte Hospital (4); Rigshospitalet, Copenhagen (2); Sweden: Department of Cardiology, Örebro Central Hospital, Örebro (10); Department of Cardiology, Falun Hospital, Falun (1); Department of Cardiology, Uppsala University Hospital, Uppsala (1); Norway: Department of Cardiology, The Feiring Clinic, Feiring (33); Department of Cardiology, University Hospital of Tromsoe, Tromsoe (32); Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo (13); Latvia: Latvian Center of Cardiology, Paul Stradins Clinical Hospital, Riga (71).

Coordination and Data Entry

Helle Bargsteen, study secretary.

Data Monitoring and Safety

Members of the Steering Committee.

Statistics

Helle Højdahl, MPH, and Michael Maeng, MD, Department of Cardiology, Aarhus University Hospital, Skejby, Denmark.

Clinical End Point Committee

Kristian Thygesen, MD, Department of Medicine and Cardiology, Aarhus University Hospital, Aarhus, Denmark; Kjell Nikus, MD, Department of Cardiology, Tampere University Hospital, Tampere, Finland.

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Disclosures

None.

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CLINICAL PERSPECTIVE

The 1-stent bifurcation stenting approach with stenting of the main vessel and optional side branch stenting using drug-eluting stents is the preferred strategy to treat coronary bifurcation lesions. It is unknown whether a successful main vessel stenting procedure should be finalized by a simultaneous kissing balloon dilatation (FKBD). In the present study, 477 patients with successful main vessel stenting were randomized to FKBD versus no FKBD. The 6-month rates of major adverse cardiac events (cardiac death, non–procedure-related index lesion myocardial infarction, target lesion revascularization, or stent thrombosis) were similar and low in the study groups. FKBD reduced angiographic side branch (re)stenosis, especially in patients with true bifurcation lesions. The simple no-FKBD procedures resulted in reduced use of contrast media and shorter procedure and fluoroscopy times. FKBD may be recommended in genuine bifurcation lesions treated with main vessel stenting but may be avoided in bifurcations without side branch stenosis. Long-term data on stent thrombosis are needed.