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ORIGINAL RESEARCH

Final kissing balloon dilatation in patients with coronary bifurcation lesions treated with an upfront provisional stenting strategy

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ABSTRACT

BACKGROUND: The impact of final kissing balloon inflation (FKB) in patients treated with an upfront provisional strategy for coronary bifurcation lesions is controversial.

AIMS: We aimed to assess the impact of FKB on patient- and lesion-oriented outcomes in a large real-world cohort.

METHODS: The ULTRA-BIFURCAT registry was obtained by patient-level merging the BIFURCAT and ULTRA registries. Pairs of patients were generated with propensity score matching (PSM). The primary outcome of interest was major adverse cardiac events (MACE) – a composite of all-cause death, myocardial infarction (MI), target lesion revascularisation (TLR) or stent thrombosis. A lesion-oriented composite outcome (LOCO) – a composite of target vessel MI (TVMI) or TLR – along with each single component of MACE represented the secondary outcomes. Subgroup analyses included the site of bifurcation (unprotected left main [ULM] vs non-ULM), side branch involvement (true bifurcation vs non-true bifurcation), side branch diameter and lesion length. Follow-up was censored at 800 days.

RESULTS: A total of 5,607 patients undergoing a provisional stenting technique were selected for the present analysis. PSM generated 1,784 pairs. Between the matched patients with FKB versus no FKB, no significant difference in MACE was observed (9.0% vs 8.6%; p=0.68). FKB was associated with a lower rate of the LOCO (1.9% vs 2.9%; p=0.04) compared to the no FKB group, driven by lower rates of TVMI (0.2% vs 0.5%; p=0.03) and TLR (1.8% vs 2.6%; p=0.14). These results were confirmed in the subgroups of patients treated for bifurcations with side branches with a diameter >2.5 mm and for true coronary bifurcation lesions.

CONCLUSIONS: Among patients treated for coronary bifurcation lesions with provisional stenting, FKB had no significant impact on MACE but was associated with a mild reduction in the incidence of the LOCO.

KEYWORDS: coronary bifurcation; final kissing balloon; percutaneous coronary intervention; provisional stenting

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Coronary bifurcations are prone to atherosclerosis due to unique local flow patterns and shear stress, making them one of the most challenging lesion subsets in interventional cardiology, with lower procedural success and higher long-term adverse events[1-3]. Despite significant interest, treatment of bifurcations with percutaneous coronary intervention (PCI) remains contentious, with various strategies proposed[4]. Several randomised trials have shown no advantage of 2-stent techniques over 1-stent techniques, regardless of lesion type[3,5-7]. The DKCRUSH-II trial found no significant clinical differences at 6 months but did find differences in target lesion revascularisation (TLR) and target vessel revascularisation at 12 months, favouring the 2-stent strategy after systematic follow-up angiography at 8 months[8].

A network meta-analysis comparing 5 bifurcation PCI techniques showed that the double-kissing crush strategy is beneficial for bifurcation lesions with side branch lesion lengths >10 mm, while no significant differences emerged between provisional and 2-stent techniques in other settings[9]. The DEFINITION-II trial also indicated better outcomes with a systematic 2-stent approach in complex bifurcations[10]. Overall, evidence suggests that provisional stenting is preferred for most bifurcations, while 2-stent strategies are better for complex lesions involving significant side branches.

Final kissing balloon inflation (FKB), involving simultaneous post-dilatation of both branches, aims to improve stent apposition and procedural success[11-13]. FKB is considered essential for all bifurcations requiring side branch treatment, minimising distortion in the main vessel (MV) stent and bifurcation carina[14]. The impact of FKB in real-world practice, particularly with provisional stenting, remains debated, with recent studies showing conflicting outcomes[15-18]. However, the effectiveness of FKB and prevention of its potential adverse effects also depend on the manner in which it is performed[19].

This study investigates the clinical implications of FKB in a large, unselected cohort of patients undergoing PCI for coronary bifurcation lesions with an upfront provisional stenting.

Impact on daily practice

Current interventional cardiology practice suggests provisional stenting as the preferred approach for most coronary bifurcation lesions, with a 2-stent strategy reserved for complex cases. Final kissing balloon inflation (FKB) is often employed to optimise stent apposition and minimise side branch compromise, especially in 2-stent techniques. The results of this multicentre retrospective study, pooling patient-level data from three large registries, offer real-world evidence on the effectiveness of FKB among patients treated with a provisional stenting technique. While FKB did not reduce major adverse cardiac events, it showed promise in reducing lesion-associated adverse outcomes, such as target lesion revascularisation and target vessel myocardial infarction.

Methods

STUDY DESIGN AND PATIENT POPULATION

The COBIS III Registry (ClinicalTrials.gov: NCT03068494) enrolled 2,648 patients with coronary bifurcation lesions undergoing PCI with second-generation drug-eluting stents (DES) from January 2010 to December 2014. The RAIN registry (ClinicalTrials.gov: NCT03544294) included 2,889 patients treated with very thin-strut DES for coronary bifurcations and/or unprotected left main (ULM) lesions from June 2015 to December 2017. The ULTRA registry (ClinicalTrials.gov: NCT05205148) involved 2,036 patients treated with ultrathin-strut DES for complex coronary lesions from September 2016 to August 2021, with 1,293 treated for bifurcations[20]. These datasets were merged to create a unified registry with 6,830 patients **(Figure 1)**.

PCI was performed according to guidelines from the Korean Society of Interventional Cardiology and the European Society of Cardiology. All patients received aspirin and a $P2Y_{12}$ inhibitor per guidelines, with dual antiplatelet therapy (DAPT) duration and other therapies at the operator's discretion. Bifurcation lesions were classified per the Medina classification, with true bifurcations defined as Medina 1.1.1, 1.0.1, or 0.1.1 lesions[21]. Data were collected using a web-based system, and follow-up data were obtained from medical records, visits, or phone contact. For the present analysis, only patients treated with an upfront provisional stenting strategy were included, while patients treated with an upfront 2-stent strategy (regardless of the adopted strategy) were excluded. The registry was designed to capture these different scenarios by requiring practitioners to declare their strategy using specific labels: upfront provisional, conversion from provisional to 2-stent, or upfront 2-stent. These labels were derived from clinical records, angiographic procedures, and, if necessary, direct consultation with the physician who performed the procedure. The decision to implant a second stent in the side branch, within the context of the provisional stepwise approach, was at the operating physician's discretion. The included cohort was further classified into two groups based on the performance of FKB. A propensity score matching (PSM) analysis was performed to adjust for baseline and procedural characteristics.

CLINICAL ENDPOINTS

The primary outcome was major adverse cardiac events (MACE): a composite of all-cause death, any myocardial infarction (MI), TLR or stent thrombosis (ST). A lesion-oriented composite outcome (LOCO) – a composite of target vessel MI (TVMI) or TLR – along with each component of MACE represented the secondary outcomes of interest. The

Abbreviations

FKB	final kissing balloon inflation	**MACE**	major adverse cardiac events	**PCI**	percutaneous coronary intervention
LOCO	lesion-oriented composite outcome	**MV**	main vessel	**ULM**	unprotected left main

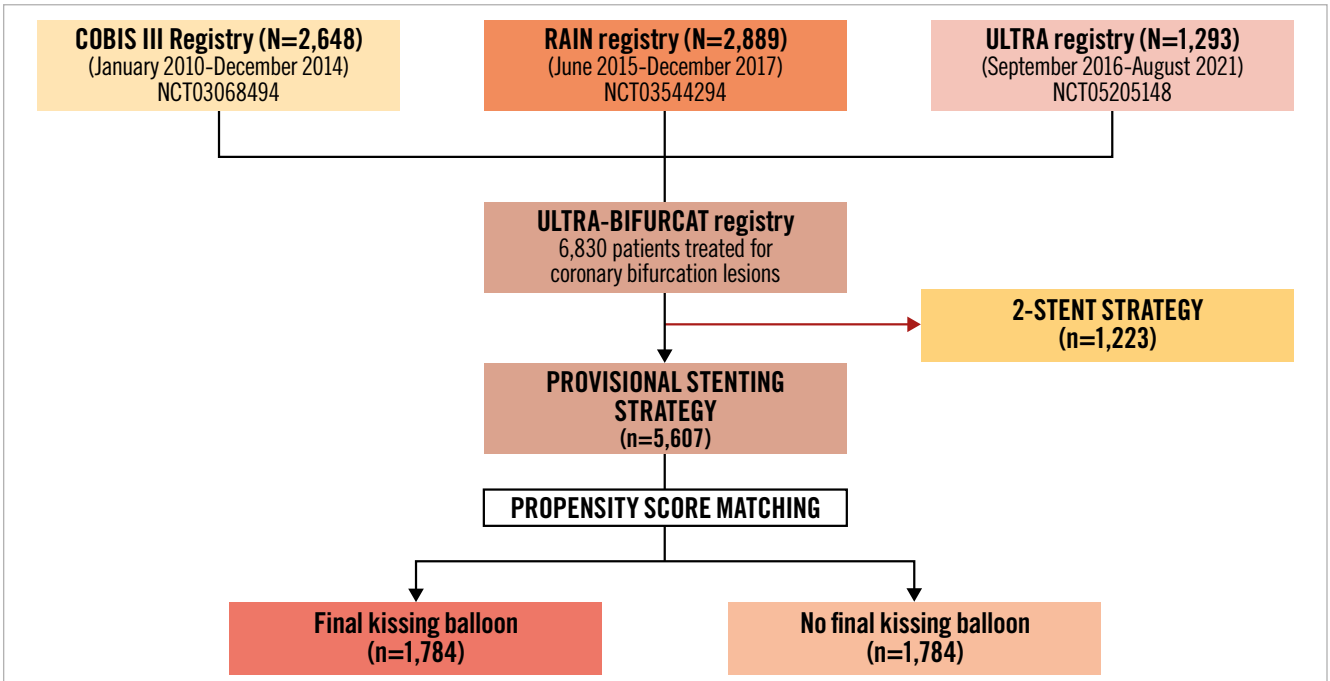


Figure 1. *Study flowchart.*

target lesion was considered the treated coronary segment during the index procedure plus a distance of 5 mm from the stent edges or the balloon angioplasty site, applied for both the MV and side branch. The target vessel was defined as the entire major intervened coronary vessel, including side branches. TLR was defined as a repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complications of the target lesion. TVMI was defined as an MI case with evidence of myocardial necrosis or direct evidence of invasive angiographic, electrocardiographic, or other imaging evidence supporting the involvement of the vascular territory of the previously treated target vessel[22]. Definitions of clinical endpoints used in the registries considered for this analysis are listed in **Supplementary Appendix 1**. Before PSM, a subgroup analysis was performed excluding patients who were ultimately treated with a 2-stent strategy. After PSM, subgroup analyses were performed according to the site of bifurcation (namely for bifurcations involving the ULM vs non-ULM), the involvement of a side branch (true bifurcations as per Medina definitions), side branch diameter, length of lesion and registries (COBIS III vs ULTRA and RAIN). All endpoints are patient based, reflecting the design of the registries to focus on overall clinical outcomes for the patients rather than individual lesion characteristics. Endpoints were primarily based on clinical outcomes. Routine angiographic follow-up was not performed for all patients; angiography was conducted as clinically indicated. Follow-up was censored at 800 days to ensure homogeneity among registries.

STATISTICAL ANALYSIS

Continuous variables are expressed as mean±standard deviation or as median with interquartile range. Continuous variables were compared using the unpaired t-test or the Mann-Whitney U test in the prematched cohort and the paired t-test in the matched cohort. Categorical variables are reported as counts and percentages. Categorical variables were compared using Pearson's χ^2 test or Fisher's exact test in the prematched cohort and the McNemar test in the matched cohort. To mitigate differences among patients included in the two subgroups of FKB versus no FKB, which are partially influenced by their inclusion in different registries across varying periods and potential selection bias, a propensity score (PS) was generated for each patient from a multivariable logistic regression model based on pretreatment covariates as independent variables with final kissing balloon inflation as a dependent outcome. Pairs of patients were derived using greedy 1:1 matching with a calliper of width equal to 0.2 of the standard deviation of the logit of the PS. The quality of the match was assessed by comparing selected pretreatment variables in PS-matched patients using the standardised mean difference, for which an absolute standardised difference of greater than 20% is suggested to represent meaningful covariate imbalance. All p-values<0.05 were considered to indicate statistical significance. Kaplan-Meier curves were generated in the PSM cohorts for the primary endpoint and compared with the log-rank test. All statistical analyses were performed using SPSS version 21 (IBM), and differences were considered significant at α=0.05.

Results

Of 6,830 patients included in the ULTRA-BIFURCAT registry, 5,607 were treated with an upfront provisional stenting strategy. Of these, 2,133 were treated with no FKB and 3,474 were treated with FKB **(Figure 1)**. The baseline features of patients are listed in **Table 1**. Patients treated without FKB were characterised by a higher prevalence of common

Table 1. Baseline features.

	Overall (n=5,607)	FKB (n=3,474)	No FKB (n=2,133)	*p*-value
Age, years	66.00±11.35	65.87±11.29	66.23±11.46	0.24
LVEF, %	56.07±9.68	56.28±9.83	55.73±9.44	0.04
Male	4,311 (76.9)	2,654 (76.4)	1,657 (77.7)	0.26
Hypertension	3,597 (64.2)	2,146 (61.8)	1,451 (68.1)	<0.001
Hyperlipidaemia	2,794 (49.8)	1,628 (46.9)	1,166 (54.7)	<0.001
Diabetes	1,746 (31.1)	1,021 (29.4)	725 (34.0)	<0.001
Insulin dependent	63 (1.1)	23 (0.67)	40 (1.9)	<0.001
Smoker	1,533 (27.4)	965 (27.7)	568 (26.6)	0.06
Previous smoker	1,462 (26.1)	929 (26.7)	533 (25.0)	
Current smoker	71 (1.3)	36 (1.0)	35 (1.6)	
CKD	716 (13.0)	354 (10.4)	362 (17.1)	<0.001
Previous PCI	1,244 (22.2)	738 (21.2)	506 (23.7)	0.03
Previous CABG	186 (3.3)	108 (3.1)	78 (3.7)	0.27
Previous MI	975 (17.4)	583 (16.8)	392 (18.4)	0.13
Previous stroke	53 (0.9)	30 (0.9)	23 (1.1)	0.42
Active cancer	42 (0.7)	19 (0.5)	23 (1.1)	0.02
COPD	65 (1.2)	30 (0.9)	35 (1.6)	0.01
History of major bleeding	9 (0.2)	2 (0.1)	7 (0.3)	0.01
Multivessel disease	521 (9.3)	260 (7.5)	261 (12.4)	<0.001
PAD	88 (1.6)	40 (1.2)	48 (2.3)	<0.001
Indication for PCI				<0.001
CCS	983 (17.5)	517 (14.9)	466 (21.8)	
ACS	2,427 (43.2)	1,506 (43.9)	897 (42.0)	
STE-ACS	1,191 (21.2)	792 (22.8)	399 (18.7)	
NSTE-ACS	1,236 (22.0)	738 (21.2)	498 (23.3)	
Other	2,197 (39.2)	1,427 (41.1)	770 (36.1)	

Data are presented as mean±standard deviation or n (%). ACS: acute coronary syndrome; CABG: coronary artery bypass graft; CCS: chronic coronary syndrome; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; FKB: final kissing balloon inflation; LVEF: left ventricular ejection fraction; MI: myocardial infarction; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; PAD: peripheral artery disease; PCI: percutaneous coronary intervention; STE-ACS: ST-segment elevation acute coronary syndrome

cardiovascular risk factors, such as hypertension, diabetes mellitus and dyslipidaemia, as compared to those treated with FKB. Patients in the no FKB group showed a higher prevalence of comorbidities such as chronic obstructive pulmonary disease (1.6% vs 0.9%; p<0.01), chronic kidney disease (17.1% vs 10.4%; p<0.001) and peripheral artery disease (2.3% vs 1.2%; p<0.001). Procedural and angiographic features are shown in **Table 2**. The use of intracoronary imaging was low overall but more frequent in the no FKB subgroup (34.3% vs 27.6%; p<0.001). The site and the complexity of the index bifurcation lesions were significantly different among the two groups, with more patients in the FKB group undergoing treatment of the distal left main artery (26.5% vs 18.4%; p<0.001) and for true coronary bifurcations (40.8% vs 36.3%; p=0.001). In the entire cohort, 82 patients were eventually treated with an additional side branch stent; this occurred more frequently in FKB group (1.8% vs 0.9%; p=0.005). PSM generated 1,784 pairs. Baseline and procedural features of the paired groups are summarised in **Supplementary Table 1**-**Supplementary Table 3**. A total of 1,142 (32%) of the selected patients were recruited in COBIS III, 1,764 (49%) in RAIN and 662 (18%) in ULTRA. No significant differences with respect to baseline characteristics were observed between the matched groups. Standardised mean differences of variables selected for the PSM are shown in **Supplementary Table 4**. Most patients were middle-aged (mean age 66.36±11.44 years old and 66.22±11.46 years old in the FKB and no FKB groups, respectively) and burdened by a relevant prevalence of cardiovascular risk factors. Left ventricular ejection fraction was, on average, preserved in both groups, and nearly half of both cohorts were treated for an acute coronary syndrome. The most frequently used DAPT regimen overall consisted of aspirin plus clopidogrel (up to 70% of patients) followed by aspirin and ticagrelor, with a median length of administration of 14.61±6.11 months, and there were no significant differences among the FKB versus no FKB PS-matched cohorts. As for the procedural features of the PS-matched cohorts, more than one-third of patients were treated for true coronary bifurcations (34.4% and 37.3% in the FKB and no FKB groups, respectively), with the left anterior descending/diagonal branches being the most frequent site of the bifurcation lesion (45.2% vs 48.9%

Table 2. Procedural features (overall population).

	Overall (n=5,607)	FKB (n=3,474)	No FKB (n=2,133)	*p*-value
Arterial access				<0.001
Radial	3,722 (66.4)	2,204 (63.4)	1,518 (71.2)	
Femoral	1,885 (33.6)	1,270 (36.6)	615 (28.8)	
Intracoronary imaging	1,690 (30.1)	939 (27.6)	726 (34.3)	<0.001
IVUS	1,649 (29.6)	934 (26.9)	715 (33.5)	
OCT	41 (0.6)	23 (0.7)	18 (0.8)	
Site of bifurcation				<0.001
Distal LM	1,311 (23.4)	920 (26.5)	391 (18.4)	
LAD-diag	2,734 (48.8)	1,683 (48.5)	1,051 (49.3)	
LCx/OM	1,077 (19.2)	617 (17.8)	460 (21.6)	
RCA/PDA-PL	327 (5.8)	203 (5.8)	124 (5.8)	
Medina classification				<0.001
0.0.1	209 (3.7)	110 (3.2)	99 (4.7)	
0.1.0	919 (16.5)	657 (19.0)	262 (12.3)	
0.1.1	317 (5.7)	197 (5.7)	121 (5.7)	
1.0.0	609 (10.9)	322 (9.3)	287 (13.5)	
1.0.1	446 (8.0)	250 (7.2)	196 (9.2)	
1.1.0	1,652 (29.6)	948 (27.4)	704 (33.1)	
1.1.1	1,428 (25.6)	971 (28.1)	457 (21.5)	
True bifurcations	2,192 (39.1)	1,418 (40.8)	774 (36.3)	0.001
Main branch diameter, mm	3.15±0.57	3.16±0.60	3.13±0.51	0.02
Main branch lesion length, mm	25.27±11.42	25.40±11.72	25.08±10.92	0.31
Side branch diameter, mm	2.11±1.81	2.13±1.42	2.09±2.18	0.51
Side branch lesion length, mm	23.59±9.85	23.32±9.66	23.91±10.06	0.08
Severe calcification	189 (20.3)	106 (22.1)	83 (18.3)	0.30
Rotational atherectomy	165 (2.9)	60 (1.7)	105 (4.9)	<0.001
Diffuse disease	1,748 (31.2)	1,060 (30.5)	688 (32.3)	0.17
Cardiogenic shock on admission	14 (0.2)	6 (0.2)	8 (0.4)	0.14
Use of MCS				0.57
IABP	4 (0.1)	2 (0.1)	2 (0.1)	
Impella	2 (0.0)	1(0.0)	1 (0.0)	
Need for inotrope/vasopressors	25 (0.4)	11 (0.3)	14 (0.6)	0.27
Additional side branch stent	82 (2)	63 (1.8)	19 (0.9)	0.005
$P2Y_{12}$ inhibitors				
Clopidogrel	4,104 (73.6)	2,612 (75.8)	1,492 (70.2)	<0.001
Ticagrelor	1,455 (25.9)	823 (23.9)	622 (29.3)	
Prasugrel	24 (0.4)	13 (0.4)	11 (0.5)	
DAPT duration, months	15.46±6.80	16.36±7.18	14.00±5.86	<0.001

Data are presented as n (%) or mean±standard deviation. DAPT: dual antiplatelet therapy; diag: diagonal branch; FKB: final kissing balloon inflation; IABP: intra-aortic balloon pump; IVUS: intravascular ultrasound; LAD: left anterior descending artery; LCx: left circumflex artery; LM: left main; MCS: mechanical circulatory support; OCT: optical coherence tomography; OM: obtuse marginal branch; PDA: posterior descending artery; PL: posterolateral branch

in the FKB and no FKB groups, respectively). Both before and after PSM, XIENCE and XIENCE Alpine (both Abbott) were the most frequently implanted stents (up to 24%), followed by Orsiro (Biotronik; up to 23%) and Resolute/Resolute Onyx (Medtronic; up to 21%) **(Supplementary Table 3)**.

OUTCOMES

MACE occurred in 276 patients (7.9%) in the FKB group and 185 patients (8.7%) in the no FKB group (p=0.33). A significantly lower rate of MI was observed in the FKB group as compared with the no FKB group (1.8% vs 3.5%; p<0.001), partially driven by a lower rate of TVMI among

patients in the FKB group (0.1% vs 0.7%; p<0.001). No significant differences between the two groups were observed with respect to all-cause death (FKB vs no FKB: 3.8% vs 4.3%; p=0.37) or TLR (FKB vs no FKB: 1.9% vs 2.4%; p=0.17). A numerically lower rate of ST, albeit not significant, was observed in the FKB group compared with patients not treated with FKB (0.7% vs 1.1%; p=0.06). As for the secondary composite endpoint of LOCO, a significantly lower rate was observed among patients treated with FKB as compared with those without FKB (1.9% vs 3.0%; p=0.013) **(Table 3)**. After excluding patients with an additional side branch stent, the benefit of FKB persisted consistently for all outcomes **(Supplementary Table 5)**.

After PSM, there were no significant differences in the primary composite outcome in the FKB and no FKB groups (9.0% vs 8.6%, respectively; p=0.68). Kaplan-Meier curves for the cumulative freedom from MACE are presented in **Figure 2**.

Patients treated with FKB were characterised by a significantly lower rate of any MI (2.0% vs 3.3%; p=0.02) and TVMI (0.1% vs 0.5%; p=0.03), and a lower, but not significant, rate of TLR (1.8% vs 2.6%; p=0.14) compared to those not treated with FKB. Overall, the LOCO occurred less frequently in the FKB group compared with the no FKB group (1.9% vs 2.9%; p=0.04).

No significant difference was observed between the two PS-matched cohorts with respect to all-cause death (5.1% vs 4.3%, in the FKB and no FKB groups, respectively; p=0.23). A marginally significant lower rate of ST was instead observed in the FKB group as compared with no FKB group (1.5% vs 0.6%, respectively; p=0.05) **(Table 3)**.

SUBGROUP ANALYSES

Results of the prespecified subgroup analysis, performed in the PS-matched cohorts, are graphically summarised in **Figure 3**. Among 1,279 patients treated for true coronary bifurcations (613 in the FKB group and 666 in the no FKB group), no significant differences were observed between the FKB and no FKB groups for the primary outcome (MACE: 9.1% vs 9.9%; p=0.64). FKB was associated with a lower rate of TLR (1.5% vs 3.2% in the FKB and no FKB groups, respectively; p=0.05) and of the LOCO (1.6% vs 3.6%; p=0.03). A lower rate of any MI was also observed in the FKB group compared with the no FKB group (2.1% vs 4.4%; p=0.02), while there were no significant differences for other secondary endpoints. Similar results were observed in the subgroup of patients treated for coronary bifurcations involving side branches with diameters >2.5 mm. A significantly lower rate of the LOCO was indeed observed among patients treated with FKB as compared with those without FKB (2.0% vs 4.4%; p=0.02). This difference was driven by significantly lower rates of TVMI (0.2% vs 1.5%; p=0.01) and lower, albeit not significant, rates of TLR (1.8% vs 3.3%; p=0.11). No significant differences were otherwise observed between FKB and no FKB in this subgroup with respect to the primary endpoint and other secondary outcomes. In the subgroup of patients treated for coronary bifurcations with side branch lesions >20 mm in length, no significant differences for any of the investigated outcomes were observed between FKB and no FKB. Among patients treated for bifurcations involving the unprotected left main, FKB was associated with a marginally significant reduction of ST (0.4% vs 1.7%; p=0.05), while no other significant differences were observed for the primary or other secondary endpoints of interest. Regarding analysis across different registries, FKB did not have an impact on MACE either for the COBIS III or the RAIN plus ULTRA registries (6% vs 8%; p=0.19, and 9% vs 10%; p=0.96, respectively), while the reduction of the LOCO was consistent (1.5% vs 3.6%; p=0.02, and 1.5% vs 3.1%; p=0.09, respectively).

Discussion

In this retrospective multicentre study, we assessed the impact of FKB in a large cohort of patients treated for coronary bifurcations using an upfront provisional stenting strategy. We generated 1,784 PS-matched pairs of patients and conducted event assessments over an 800-day follow-up period.

Our key findings are as follows **(Central illustration)**:

- FKB did not significantly reduce MACE or all-cause mortality among patients treated with the provisional technique.
- FKB was associated with a reduction in a lesion-oriented composite outcome (TLR and TVMI) and a lower rate of any myocardial infarction compared to those not treated with FKB.
- The benefit of FKB was mainly seen in patients with side branches >2.5 mm in diameter and true coronary bifurcations.

Table 3. Long-term outcomes according to final kissing balloon inflation before and after propensity score matching.

Outcomes	Crude analysis			Propensity score-matched analysis		
	FKB (n=3,474)	No FKB (n=2,133)	*p*-value	FKB (n=1,784)	No FKB (n=1,784)	*p*-value
MACE	276 (7.9)	185 (8.7)	0.33	160 (9.0)	153 (8.6)	0.68
All-cause death	133 (3.8)	92 (4.3)	0.37	91 (5.1)	76 (4.3)	0.23
Any MI	64 (1.8)	74 (3.5)	<0.001*	36 (2.0)	59 (3.3)	0.02*
TLR	66 (1.9)	52 (2.4)	0.17	33 (1.8)	46 (2.6)	0.14
ST	23 (0.7)	24 (1.1)	0.06	11 (0.6)	22 (1.5)	0.05*
TVMI	3 (0.1)	15 (0.7)	<0.001*	2 (0.1)	9 (0.5)	0.03*
LOCO	67 (1.9)	63 (3.0)	0.013*	34 (1.9)	52 (2.9)	0.04*

Data are presented as n (%). *Indicates statistical significance. FKB: final kissing balloon inflation; LOCO: lesion-oriented composite outcome; MACE: major adverse cardiac events; MI: myocardial infarction; ST: stent thrombosis; TLR: target lesion revascularisation; TVMI: target vessel myocardial infarction

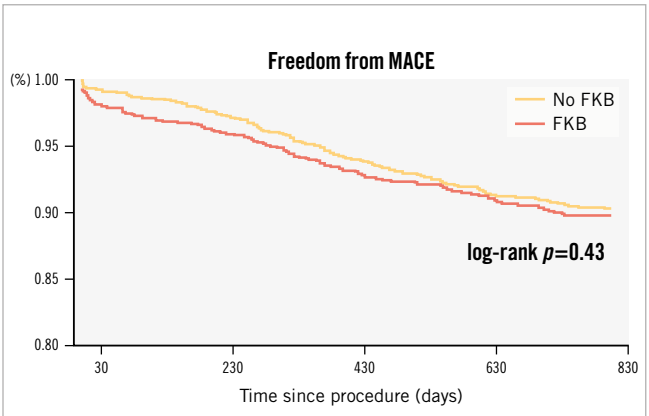


Figure 2. *Kaplan-Meier analysis for freedom from MACE according to FKB in the propensity score-matched cohort. FKB: final kissing balloon inflation; MACE: major adverse cardiac events*

The potential benefit of FKB with the provisional approach remains uncertain because of limited data. Although FKB has been considered effective for securing side branch patency after MV stenting[23], recent studies have not shown clear clinical advantages for FKB in the 1-stent technique[17,24,25]. In the COBIS III Registry, among 1,065 patients treated with a 1-stent technique, 329 were treated with FKB, while 736 were not. At a median follow-up of 22 months, most TLRs occurred in the MV rather than in the side branch, and no significant differences were observed between the groups in terms of rates of cardiac death, myocardial infarction, or stent thrombosis[16]. Similar findings were observed in the randomised CORPAL Kiss Trial over a 1-year follow-up[26]. In the Nordic Baltic Bifurcation Study III, 477 patients with a bifurcation lesion were randomised to receive FKB or not after MV stenting[15]. At the 6-month follow-up, the rates of MACE were similar (2.1% vs 2.5%; p=1.00). At the 8-month angiographic follow-up, there was a trend towards a lower rate of binary restenosis in the FKB group. Notably, FKB significantly reduced angiographic side branch restenosis, especially in true bifurcation lesions (7.6% vs 20.0%; p=0.02). Another meta-analysis confirmed that FKB significantly reduced the risk of side branch restenosis in the simple-strategy group[27]. However, some controversy regarding whether FKB reduces the risk of TLR still persists. Two reports indicated that the no-FKB strategy was associated with a lower risk of TLR compared with FKB while in the TAXUS PMS, FKB was an independent predictor of 3-year TLR[16,18]. In contrast, the COBIS II study showed that rates of TLR were higher in the no FKB group than in the FKB group[17]. This study aimed to partially address the controversial evidence about the effectiveness of FKB in the context of provisional stenting. Taken together, our results align with the existing literature indicating that, over a medium-term follow-up, FKB may offer benefits in terms of lesion-associated outcomes without affecting "hard" clinical endpoints such as all-cause death or MACE[15,17,27]. However, it should be noted that non-emergent TLR has been linked to all-cause mortality in a large meta-analysis, and a longer follow-up or larger sample size may reveal differences in hard clinical endpoints[28].

It is worth noting that our study features a larger sample size and a generally longer follow-up compared to the above-mentioned registries and trials, which prevent direct comparisons. The ULTRA-BIFURCAT registry reflects real-world clinical practice across different centres and time periods, enhancing its generalisability. However, our findings might not be directly comparable to those from more controlled clinical trial settings, which often have strict inclusion criteria and planned angiographic follow-up.

While randomised controlled trials (RCTs) conducted thus far may not adequately reflect practice patterns in real-world clinical settings due to their small to medium sample sizes, limited follow-up periods, and strict protocols, we acknowledge that the observational, retrospective nature of our study and its reliance on multiple registries introduce potential biases and confounding factors (e.g., procedural and material changes over time, selection bias) that can only be partially managed with propensity score adjustment. To account for the heterogeneous scenarios of bifurcation lesions, several subgroup analyses were performed.

After PSM, more than one-third of patients were treated for true coronary bifurcations. Patients with true bifurcation lesions are known to be at a higher risk for procedural complications than patients with other types of bifurcation lesions[21]. As observed in our registry, more patients in the FKB group were treated for true coronary bifurcations. However, after PSM there was no significant difference in the primary outcome between the FKB and no FKB groups. Unlike the remainder of the population, both before and after propensity score matching, FKB was associated with a significantly lower rate of TLR, yet the absolute difference in TLR was relatively small. A lower rate of any MI and the LOCO was also observed in the FKB group as compared to the no FKB group, whereas no significant differences were found for other secondary endpoints.

The diameter and atherosclerotic burden of the side branch play a crucial role in managing bifurcation lesions. The side branch size, often called the "ostial" orifice, significantly impacts procedural success and long-term outcomes[29]. An appropriately sized side branch is essential for maintaining adequate blood flow. If the side branch is too small, it may be compromised during the main branch intervention, leading to ischaemia and reintervention. Conversely, a large side branch may correlate with a large proximal reference diameter in the main branch. During provisional and FKB techniques, meticulous attention to the side branch diameter is crucial. Proper sizing helps prevent dissections, reduces plaque shifting, and promotes successful stent deployment in both branches. Therefore, we conducted a subgroup analysis after PSM based on side branch dimensions, specifically considering diameters >2.5 mm and lesion lengths >20 mm. FKB reduced the LOCO and TVMI for side branches with diameters >2.5 mm, while a lower, albeit not significant, rate of the LOCO was observed for lesion lengths >20 mm treated with FKB. These results suggest that side branch features should be accurately assessed during PCI of coronary bifurcation, and our approach should be tailored accordingly.

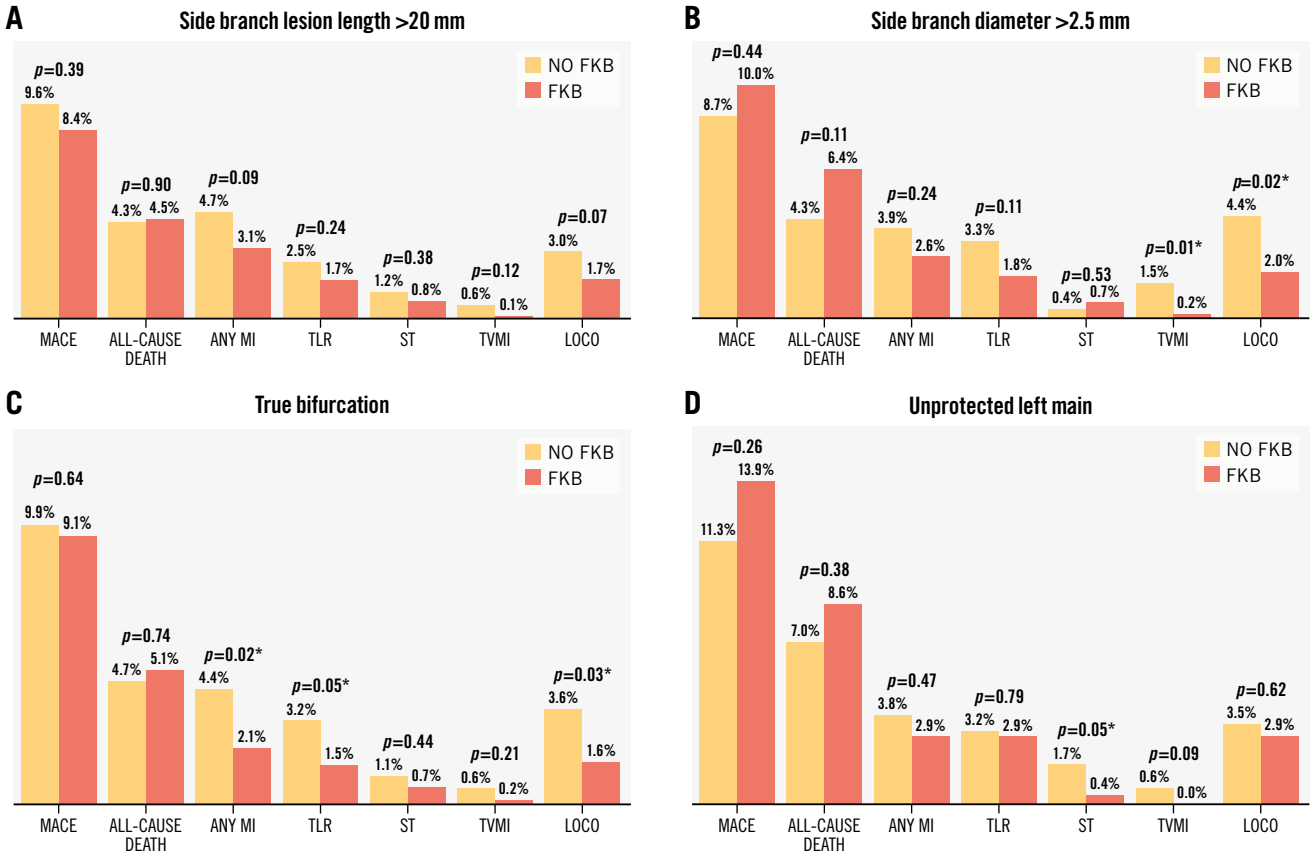


Figure 3. *Subgroup analyses. Subgroup analyses performed in the PS-matched cohorts for side branch lesion length (A), side branch diameter (B), true bifurcation (C), and unprotected left main bifurcation (D). *Indicates statistical significance. FKB: final kissing balloon inflation; LOCO: lesion-oriented composite outcome; MACE: major adverse cardiac events; MI: myocardial infarction; ST: stent thrombosis; TLR: target lesion revascularisation; TVMI: target vessel myocardial infarction*

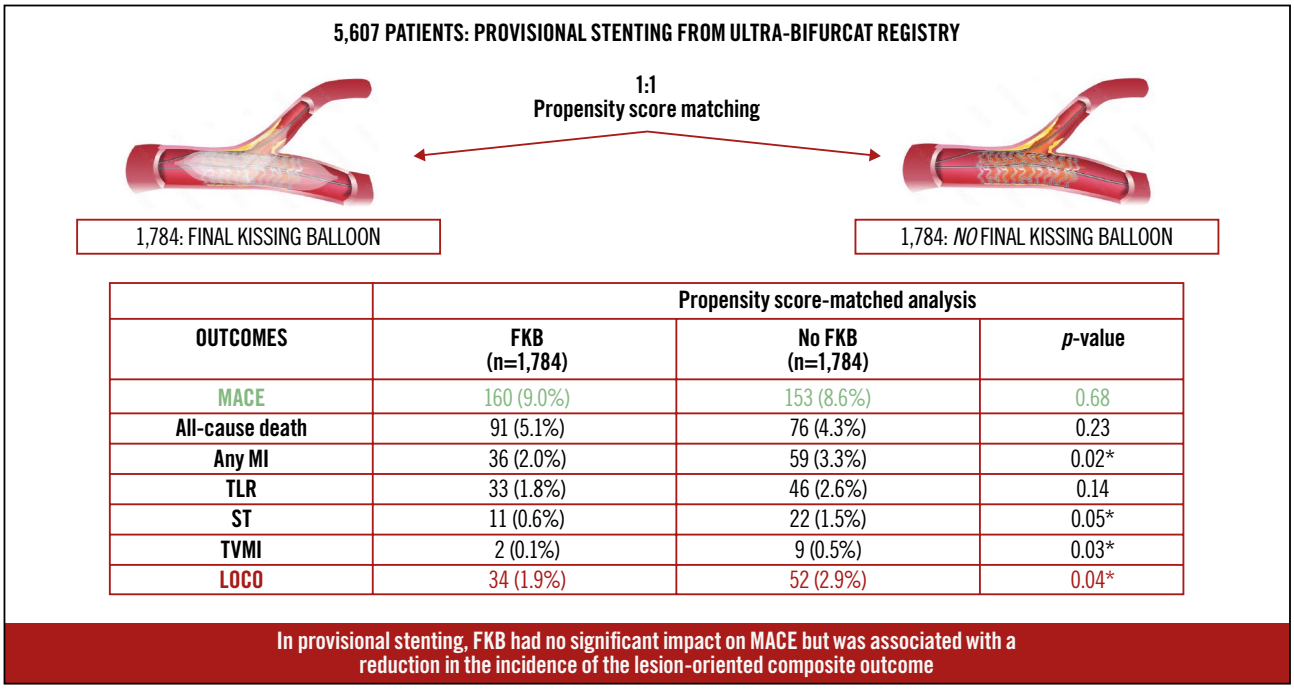
Of note, in our subgroup analysis of patients treated for ULM bifurcations, FKB was not associated with an incremental benefit. While the limited sample size of this subgroup should be considered in interpreting these findings, our results suggest that the relevance of the side branch (often left circumflex in the context of ULM bifurcations), rather than the site of the bifurcation itself, should be taken into account when deciding about FKB use in the context of provisional bifurcation stenting. The results of the currently ongoing CROSS-COBIS RCT (ClinicalTrials.gov: NCT05705362) are awaited and expected to provide insights into the impact of FKB on clinical outcome after treatment of non-left main coronary bifurcations.

Limitations

Several limitations should be acknowledged. While the sample size was large, the study design is retrospective with inherent limitations. This limitation may be partly balanced by the all-comer design with broad inclusion criteria and a 100% follow-up rate. Nevertheless, the study findings should be considered hypothesis-generating. A key limitation of our study is the use of endpoint definitions from the Academic Research Consortium-2 consensus document[22], as the new definitions from the European Bifurcation Club were published after our registries were developed[30]. This temporal difference prevented the adoption of the latest terminologies and specific endpoints, such as the bifurcation-oriented composite endpoint. However, our endpoints related to the "index" lesion inherently include side branches. Additionally, while the new guidelines recommend separate trials for left main and non-left main bifurcations, our study addresses this by including a subgroup analysis for these bifurcations.

Despite the extensive adjustment with propensity score matching, which was overall effective (as shown in **Supplementary Table 4**), the retrospective nature of our study and the utilisation of multiple registries introduce potential biases and confounding. While PSM was employed to mitigate these biases, it cannot completely eliminate the impact of unknown or unmeasured variables. Therefore, our conclusions should be considered preliminary and interpreted with caution. In particular, we acknowledge that limited data were available with respect to the proximal optimisation technique (POT). Performing POT after FKB is recommended by European consensus for the treatment of coronary bifurcation lesions, although its impact on hard outcomes is uncertain[4]. In a previous manuscript[19], we reported benefits of a short overlap between balloons. In the present analysis,

Final kissing balloon dilatation in patients with coronary bifurcation lesions treated with an upfront provisional stenting strategy.



	Propensity score-matched analysis		
OUTCOMES	**FKB (n=1,784)**	**No FKB (n=1,784)**	***p*-value**
MACE	160 (9.0%)	153 (8.6%)	0.68
All-cause death	91 (5.1%)	76 (4.3%)	0.23
Any MI	36 (2.0%)	59 (3.3%)	0.02*
TLR	33 (1.8%)	46 (2.6%)	0.14
ST	11 (0.6%)	22 (1.5%)	0.05*
TVMI	2 (0.1%)	9 (0.5%)	0.03*
LOCO	34 (1.9%)	52 (2.9%)	0.04*

In provisional stenting, FKB had no significant impact on MACE but was associated with a reduction in the incidence of the lesion-oriented composite outcome

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**Indicates statistical significance. FKB: final kissing balloon inflation; LOCO: lesion-oriented composite outcome; MACE: major adverse cardiac events; MI: myocardial infarction; ST: stent thrombosis; TLR: target lesion revascularisation; TVMI: target vessel myocardial infarction*

which comprised a larger number of patients, we were not able to systematically obtain such data, yet we suppose that a short balloon overlap might even increase the clinical benefit of FKB that was observed in the present study. Finally, all evaluated endpoints are patient based, according to the design of the registries. While this approach enhances the clinical relevance of our findings, the absence of a lesion-level analysis may be regarded as a limitation.

Conclusions

Among the patients of this large, real-world registry, treated with a provisional stenting technique for coronary bifurcation lesions and assessed during medium-term follow-up, FKB was not associated with a significant reduction of MACE but was associated with a significant reduction of lesion-associated adverse outcomes, such as TLR and TVMI. Subgroup analyses of patients who were treated for true coronary bifurcation lesions and for lesions with major side branches revealed similar results. Our results should be interpreted with caution due to the limitations inherent in the observational and retrospective nature of the data derived from the merging of three different registries, highlighting the need for confirmation in a dedicated prospective study.

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Guest Editor

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Conflict of interest statement

C. von Birgelen indicated previous institutional research funds to the research department of Thoraxcentrum Twente from Abbott, Biotronik, Boston Scientific, and Medtronic. R. Piccolo reports personal fees from Biotronik, Amarin, Abiomed, Chiesi, and Medtronic, outside the submitted work. G. Patti indicated speaker/consultant fees from Abbott, AstraZeneca, Sanofi, Amgen, Menarini, Bayer, Pfizer, BMS, Daiichi Sankyo, PIAM, Malesci, Sigma-Tau, Chiesi, Medtronic, MSD, Boehringer Ingelheim, and Servier, outside the submitted work. J. Escaned indicated speaker/advisory member fees from Abbott, Abiomed, Boston Scientific, Medis, Philips, and Shockwave Medical, outside the submitted work. G. Campo reports grants from SMT, Siemens, and Medis, outside the submitted work. D. Capodanno reports personal fees from Abbott, Novo Nordisk, Sanofi, Terumo, and Chiesi; institutional fees from Medtronic; and participation on a data safety monitoring board or advisory board with MedAlliance, all outside the submitted work. C.-W. Nam reports institutional research grant from Abbott. The other authors have no conflicts of interest to declare. The Guest Editor reports consultancy fees from Novartis and Meril Life Sciences; speaker honoraria from Boston Scientific, Amgen, Daiichi Sankyo, and Meril Life Sciences; speaker honoraria paid to his institution from BMS/Pfizer, Daiichi Sankyo, Boston Scientific, Siemens, and Amgen; and research grants paid to his institution from Boston Scientific and Abbott.

References

1. Chatzizisis YS, Jonas M, Coskun AU, Beigel R, Stone BV, Maynard C, Gerrity RG, Daley W, Rogers C, Edelman ER, Feldman CL, Stone PH. Prediction of the localization of high-risk coronary atherosclerotic plaques on the basis of low endothelial shear stress: an intravascular ultrasound and histopathology natural history study. *Circulation*. 2008;117:993-1002.
2. Latib A, Colombo A. Bifurcation disease: what do we know, what should we do? *JACC Cardiovasc Interv*. 2008;1:218-26.
3. Steigen TK, Maeng M, Wiseth R, Erglis A, Kumsars I, Narbute I, Gunnes P, Mannsverk J, Meyerdierks O, Rotevatn S, Niemelä M, Kervinen K, Jensen JS, Galløe A, Nikus K, Vikman S, Ravkilde J, James S, Aarøe J, Ylitalo A, Helqvist S, Sjögren I, Thayssen P, Virtanen K, Puhakka M, Airaksinen J, Lassen JF, Thuesen L; Nordic PCI Study Group. Randomized study on simple versus complex stenting of coronary artery bifurcation lesions: the Nordic bifurcation study. *Circulation*. 2006;114:1955-61.
4. Burzotta F, Lassen JF, Louvard Y, Lefèvre T, Banning AP, Daremont O, Pan M, Hildick-Smith D, Chieffo A, Chatzizisis YS, Džavík V, Gwon HC, Hikichi Y, Murasato Y, Koo BK, Chen SL, Serruys P, Stankovic G. European Bifurcation Club white paper on stenting techniques for patients with bifurcated coronary artery lesions. *Catheter Cardiovasc Interv*. 2020;96:1067-79.
5. Ferenc M, Gick M, Kienzle RP, Bestehorn HP, Werner KD, Comberg T, Kuebler P, Büttner HJ, Neumann FJ. Randomized trial on routine vs. provisional T-stenting in the treatment of de novo coronary bifurcation lesions. *Eur Heart J*. 2008;29:2859-67.
6. Colombo A, Bramucci E, Saccà S, Violini R, Lettieri C, Zanini R, Sheiban I, Paloscia L, Grube E, Schofer J, Bolognese L, Orlandi M, Niccoli G, Latib A, Airoldi F. Randomized study of the crush technique versus provisional side-branch stenting in true coronary bifurcations: the CACTUS (Coronary Bifurcations: Application of the Crushing Technique Using Sirolimus-Eluting Stents) Study. *Circulation*. 2009;119:71-8.
7. Hildick-Smith D, de Belder AJ, Cooter N, Curzen NP, Clayton TC, Oldroyd KG, Bennett L, Holmberg S, Cotton JM, Glennon PE, Thomas MR, Maccarthy PA, Baumbach A, Mulvihill NT, Henderson RA, Redwood SR, Starkey IR, Stables RH. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: the British Bifurcation Coronary Study: old, new, and evolving strategies. *Circulation*. 2010;121:1235-43.
8. Chen SL, Santoso T, Zhang JJ, Ye F, Xu YW, Fu Q, Kan J, Paiboon C, Zhou Y, Ding SQ, Kwan TW. A randomized clinical study comparing double kissing crush with provisional stenting for treatment of coronary bifurcation lesions: results from the DKCRUSH-II (Double Kissing Crush versus Provisional Stenting Technique for Treatment of Coronary Bifurcation Lesions) trial. *J Am Coll Cardiol*. 2011;57:914-20.
9. Di Gioia G, Sonck J, Ferenc M, Chen SL, Colaiori I, Gallinoro E, Mizukami T, Kodeboina M, Nagumo S, Franco D, Bartunek J, Vanderheyden M, Wyffels E, De Bruyne B, Lassen JF, Bennett J, Vassilev D, Serruys PW, Stankovic G, Louvard Y, Barbato E, Collet C. Clinical Outcomes Following Coronary Bifurcation PCI Techniques: A Systematic Review and Network Meta-Analysis Comprising 5,711 Patients. *JACC Cardiovasc Interv*. 2020;13:1432-44.
10. Zhang JJ, Ye F, Xu K, Kan J, Tao L, Santoso T, Munawar M, Tresukosol D, Li L, Sheiban I, Li F, Tian NL, Rodríguez AE, Paiboon C, Lavarra F, Lu S, Vichairuangthum K, Zeng H, Chen L, Zhang R, Ding S, Gao F, Jin Z, Hong L, Ma L, Wen S, Wu X, Yang S, Yin WH, Zhang J, Wang Y, Zheng Y, Zhou L, Zhou L, Zhu Y, Xu T, Wang X, Qu H, Tian Y, Lin S, Liu L, Lu Q, Li Q, Li B, Jiang Q, Han L, Gan G, Yu M, Pan D, Shang Z, Zhao Y, Liu Z, Yuan Y, Chen C, Stone GW, Han Y, Chen SL. Multicentre, randomized comparison of two-stent and provisional stenting techniques in patients with complex coronary bifurcation lesions: the DEFINITION II trial. *Eur Heart J*. 2020;41:2523-36.
11. Ge L, Airoldi F, Iakovou I, Cosgrave J, Michev I, Sangiorgi GM, Montorfano M, Chieffo A, Carlino M, Corvaja N, Colombo A. Clinical and angiographic outcome after implantation of drug-eluting stents in bifurcation lesions with the crush stent technique: importance of final kissing balloon post-dilation. *J Am Coll Cardiol*. 2005;46:613-20.
12. Hoye A, Iakovou I, Ge L, van Mieghem CA, Ong AT, Cosgrave J, Sangiorgi GM, Airoldi F, Montorfano M, Michev I, Chieffo A, Carlino M, Corvaja N, Aoki J, Rodriguez Granillo GA, Valgimigli M, Sianos G, van der Giessen WJ, de Feyter PJ, van Domburg RT, Serruys PW, Colombo A.

Long-term outcomes after stenting of bifurcation lesions with the "crush" technique: predictors of an adverse outcome. *J Am Coll Cardiol.* 2006;47:1949-58.

13. D'Ascenzo F, Omedè P, De Filippo O, Cerrato E, Autelli M, Trabattoni D, Ryan N, Venuti G, Muscoli S, Montabone A, Wojakowski W, Rognoni A, Helft G, Gallo D, Parma R, De Luca L, Figini F, Mitomo S, Boccuzzi G, Mattesini A, Wańha W, Smolka G, Huczek Z, Cortese B, Sheiban I, Escaned J, Biolè C, Conrotto F, Templin C, Quadri G, Rolfo C, Capodanno D, Chieffo A, Nuñez-Gil I, Morbiducci U, Iannaccone M, Gili S, Mario CD, Moretti C, D'Amico M, Varbella F, Romeo F, Lüscher TF. Impact of Final Kissing Balloon and of Imaging on Patients Treated on Unprotected Left Main Coronary Artery With Thin-Strut Stents (From the RAIN-CARDIOGROUP VII Study). *Am J Cardiol.* 2019;123:1610-9.

14. Murasato Y, Finet G, Foin N. Final kissing balloon inflation: the whole story. *EuroIntervention.* 2015;11:V81-5.

15. Niemelä M, Kervinen K, Erglis A, Holm NR, Maeng M, Christiansen EH, Kumsars I, Jegere S, Dombrovskis A, Gunnes P, Stavnes S, Steigen TK, Trovik T, Eskola M, Vikman S, Romppanen H, Mäkikallio T, Hansen KN, Thayssen P, Aberge L, Jensen LO, Hervold A, Airaksinen J, Pietilä M, Frobert O, Kellerth T, Ravkilde J, Aarøe J, Jensen JS, Helqvist S, Sjögren I, James S, Miettinen H, Lassen JF, Thuesen L; Nordic-Baltic PCI Study Group. 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. *Circulation.* 2011;123:79-86.

16. Gwon HC, Hahn JY, Koo BK, Song YB, Choi SH, Choi JH, Lee SH, Jeong MH, Kim HS, Seong IW, Yang JY, Rha SW, Jang Y, Yoon JH, Tahk SJ, Seung KB, Park SJ. Final kissing ballooning and long-term clinical outcomes in coronary bifurcation lesions treated with 1-stent technique: results from the COBIS registry. *Heart.* 2012;98:225-31.

17. Yu CW, Yang JH, Song YB, Hahn JY, Choi SH, Choi JH, Lee HJ, Oh JH, Koo BK, Rha SW, Jeong JO, Jeong MH, Yoon JH, Jang Y, Tahk SJ, Kim HS, Gwon HC. Long-Term Clinical Outcomes of Final Kissing Ballooning in Coronary Bifurcation Lesions Treated With the 1-Stent Technique: Results From the COBIS II Registry (Korean Coronary Bifurcation Stenting Registry). *JACC Cardiovasc Interv.* 2015;8:1297-307.

18. Song YB, Park TK, Hahn JY, Yang JH, Choi JH, Choi SH, Lee SH, Gwon HC. Optimal Strategy for Provisional Side Branch Intervention in Coronary Bifurcation Lesions: 3-Year Outcomes of the SMART-STRATEGY Randomized Trial. *JACC Cardiovasc Interv.* 2016;9:517-26.

19. Gaido L, D'Ascenzo F, Imori Y, Wojakowski W, Saglietto A, Figini F, Mattesini A, Trabattoni D, Rognoni A, Tomassini F, Bernardi A, Ryan N, Muscoli S, Helft G, De Filippo O, Parma R, De Luca L, Ugo F, Cerrato E, Montefusco A, Pennacchi M, Wańha W, Smolka G, de Lio G, Bruno F, Huczek Z, Boccuzzi G, Cortese B, Capodanno D, Omedè P, Mancone M, Nuñez-Gil I, Romeo F, Varbella F, Rinaldi M, Escaned J, Conrotto F, Burzotta F, Chieffo A, Perl L, D'Amico M, di Mario C, Sheiban I, Gagnor A, Giammaria M, De Ferrari GM. Impact of Kissing Balloon in Patients Treated With Ultrathin Stents for Left Main Lesions and Bifurcations: An Analysis From the RAIN-CARDIOGROUP VII Study. *Circ Cardiovasc Interv.* 2020;13:e008325.

20. de Filippo O, Bruno F, Pinxterhuis TH, Gąsior M, Perl L, Gaido L, Tuttolomondo D, Greco A, Verardi R, Lo Martire G, Iannaccone M, Leone A, Liccardo G, Caglioni S, González Ferreiro R, Rodinò G, Musumeci G, Patti G, Borzillo I, Tarantini G, Wańha W, Casella B, Ploumen EH, Pyka Ł, Kornowski R, Gagnor A, Piccolo R, Roubin SR, Capodanno D, Zocca P, Conrotto F, De Ferrari GM, von Birgelen C, D'Ascenzo F; ULTRA Collaborators. Predictors of target lesion failure after treatment of left main, bifurcation, or chronic total occlusion lesions with ultrathin-strut drug-eluting coronary stents in the ULTRA registry. *Catheter Cardiovasc Interv.* 2023;102:221-32.

21. Park TK, Park YH, Song YB, Oh JH, Chun WJ, Kang GH, Jang WJ, Hahn JY, Yang JH, Choi SH, Choi JH, Lee SH, Jeong MH, Kim HS, Lee JH, Yu CW, Rha SW, Jang Y, Yoon JH, Tahk SJ, Seung KB, Park JS, Gwon HC. Long-Term Clinical Outcomes of True and Non-True Bifurcation Lesions According to Medina Classification- Results From the COBIS (COronary BIfurcation Stent) II Registry. *Circ J.* 2015;79:1954-62.

22. Garcia-Garcia HM, McFadden EP, Farb A, Mehran R, Stone GW, Spertus J, Onuma Y, Morel MA, van Es GA, Zuckerman B, Fearon WF, Taggart D, Kappetein AP, Krucoff MW, Vranckx P, Windecker S, Cutlip D, Serruys PW; Academic Research Consortium. Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. *Circulation.* 2018;137:2635-50.

23. Sgueglia GA, Chevalier B. Kissing balloon inflation in percutaneous coronary interventions. *JACC Cardiovasc Interv.* 2012;5:803-11.

24. Yamawaki M, Muramatsu T, Kozuma K, Ito Y, Kawaguchi R, Kotani J, Yokoi H, Nakamura M, Saito S. Long-term clinical outcome of a single stent approach with and without a final kissing balloon technique for coronary bifurcation. *Circ J.* 2014;78:110-21.

25. Biondi-Zoccai G, Sheiban I, De Servi S, Tamburino C, Sangiorgi G, Romagnoli E. To kiss or not to kiss? Impact of final kissing-balloon inflation on early and long-term results of percutaneous coronary intervention for bifurcation lesions. *Heart Vessels.* 2014;29:732-42.

26. Pan M, Medina A, Suárez de Lezo J, Romero M, Segura J, Martín P, Suárez de Lezo J, Hernández E, Mazuelos F, Moreno A, Pavlovic D, Ojeda S, Toledano F, Leon C. Coronary bifurcation lesions treated with simple approach (from the Cordoba & Las Palmas [CORPAL] Kiss Trial). *Am J Cardiol.* 2011;107:1460-5.

27. Niccoli G, Ferrante G, Porto I, Burzotta F, Leone AM, Mongiardo R, Mazzari MA, Trani C, Rebuzzi AG, Crea F. Coronary bifurcation lesions: to stent one branch or both? A meta-analysis of patients treated with drug eluting stents. *Int J Cardiol.* 2010;139:80-91.

28. Palmerini T, Della Riva D, Biondi-Zoccai G, Leon MB, Serruys PW, Smits PC, von Birgelen C, Ben-Yehuda O, Généreux P, Bruno AG, Jenkins P, Stone GW. Mortality Following Nonemergent, Uncomplicated Target Lesion Revascularization After Percutaneous Coronary Intervention: An Individual Patient Data Pooled Analysis of 21 Randomized Trials and 32,524 Patients. *JACC Cardiovasc Interv.* 2018;11:892-902.

29. Popma JJ, Mauri L, O'Shaughnessy C, Overlie P, McLaurin B, Almonacid A, Kirtane A, Leon MB. Frequency and clinical consequences associated with sidebranch occlusion during stent implantation using zotarolimus-eluting and paclitaxel-eluting coronary stents. *Circ Cardiovasc Interv.* 2009;2:133-9.

30. Lunardi M, Louvard Y, Lefèvre T, Stankovic G, Burzotta F, Kassab GS, Lassen JF, Darremont O, Garg S, Koo BK, Holm NR, Johnson TW, Pan M, Chatzizisis YS, Banning AP, Chieffo A, Dudek D, Hildick-Smith D, Garot J, Henry TD, Dangas G, Stone G, Krucoff MW, Cutlip D, Mehran R, Wijns W, Sharif F, Serruys PW, Onuma Y. Definitions and Standardized Endpoints for Treatment of Coronary Bifurcations. *EuroIntervention.* 2023;19:e807-31.

Supplementary data

Supplementary Appendix 1. Inclusion and exclusion criteria of COBIS III, RAIN and ULTRA registries.

Supplementary Table 1. Baseline features of the propensity score-matched cohorts.

Supplementary Table 2. Procedural features of the propensity score-matched cohorts.

Supplementary Table 3. Coronary stents implanted before and after PSM.

Supplementary Table 4. Standardised mean difference before and after PSM.

Supplementary Table 5. Outcome before PSM after exclusion of patients with an additional side branch stent.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-24-00471

Supplementary data

Supplementary Appendix 1. Inclusion and exclusion criteria of COBIS III, RAIN and ULTRA registries.

COBIS III registry

Inclusion criteria

The COBIS III registry (NCT03068494) enrolled 2648 consecutive patients with coronary bifurcation lesions (CBL) who underwent PCI with second-generation DES regardless of their clinical presentation. Besides informed consent, the study population included patients based on the following inclusion criteria:

- Age ≥ 19 years old
- Any type of de novo bifurcation lesion in major epicardial artery (diameter ≥ 2.5 mm): unprotected left main coronary bifurcation lesion, LAD - diagonal, LCX-OM, distal RCA bifurcation.
- Side branch or LCX reference diameter ≥ 2.3 mm and at least stentable with 2.5 mm stent
- Treated with drug-eluting stents January 2010 to December 2014.

COBIS III included patients treated with second generation DES (not prespecified).

Exclusion criteria

- Protected LM disease (previous CABG for LAD or LCX territory)
- RCA-RV branch bifurcation, branch bifurcation
- Cardiogenic Shock
- History of CPR in the same hospitalization
- Patients with severe left ventricular systolic dysfunction (ejection fraction < 30%)

Study outcomes

Primary outcome

- Target lesion failure (TLF): composite of cardiac death, myocardial infarction, or target lesion revascularization

Secondary outcomes

- Cardiac death: all deaths were considered cardiac cause unless obvious non-cardiac causes could be identified
- Myocardial infarction (MI): an elevation of creatine kinase-myocardial band or troponin level greater than the upper limit of normal with concomitant ischemic symptoms or electrocardiography findings indicative of ischemia.
- TV-MI: an MI case with evidence of myocardial necrosis in the vascular territory of a previously treated target vessel. Direct evidence of invasive angiography, electrocardiographic, or other imaging evidence such as echocardiography (e.g., newly developed regional wall motion abnormality or extension of previous abnormality) could be used to adjudicate the involvement of target vessel territory. Any types of MI related to stent thrombosis or restenosis of the target lesion was included in TVMI case, but periprocedural MI (e.g., type 4a MI associated with and occurring

within 48 hours of coronary intervention) and death with symptoms suggestive of myocardial ischemia but without direct evidence of target vessel involvement was excluded from the outcome measure of TVMI.
- Target lesion revascularization (TLR): repeat PCI of the lesion within 5 mm of the inserted stent
- Stent thrombosis (ST): the Academic Research Consortium as definite, probable, or possible

RAIN registry

Inclusion criteria

The RAIN registry (NCT03544294) enrolled 2889 consecutive patients who underwent PCI with very-thin DES on coronary bifurcations and/or ULM regardless of their clinical presentation. Besides informed consent, the study population included patients based on the following inclusion criteria:

- Age > 18 years old
- Indication to PCI
- Complex coronary lesions, namely unprotected LM or bifurcations.

The RAIN registry included patients treated with the following DES:

- Platinum-chromium coated with a durable polymer loading Everolimus with strut thickness of 81 μm for diameters 2.25-3.5 mm (Promus Element, Boston Scientific); EES 80 μm Pl-Chr.
- Cobalt-chromium coated with a durable polymer loading Everolimus with a strut thickness of 80 μm (Xience Alpine, Abbot); EES 80 μm Co-Chr.
- Cobalt-chromium coated with a biodegradable polymer loading sirolimus with strut thickness of 80 μm; (Ultimaster, Terumo Corporation); SES 80 μm Co-Chr.
- Platinum-chromium coated with a biodegradable polymer loading Everolimus with strut thickness of 74 μm for diameters 2.25-2.75 mm, 79 μm for diameters 3.00-3.50 mm, and 81 μm for the diameter of 4.0-4.5 mm; (Synergy, Boston Scientific); EES 74 μm Pl-Chr.
- Cobalt-chromium coated with a durable polymer loading Zotarolimus with a strut thickness of 81 μm for diameters (Resolute Onyx, Medtronic). ZES 81 μm Co-Ch.

Exclusion criteria

No exclusion criteria besides PCI performed on other coronary vessels.

Study outcomes

Primary outcome:

- Major Adverse Cardiac Events (MACE): composite endpoint which includes death for any cause, non-fatal myocardial infarction, target lesion revascularization (TLR), in-stent thrombosis.

Secondary outcomes

- Death: death for any cause (both cardiologic and non-cardiologic)
- Non-fatal myocardial infarction

- Target Lesion revascularization (TLR): either repeat percutaneous or surgical revascularization for a lesion anywhere within the stent or the 5-mm borders proximal or distal to the stent.
- TV-MI: an MI case with evidence of myocardial necrosis in the vascular territory of a previously treated target vessel. Direct evidence of invasive angiography, electrocardiographic, or other imaging evidence such as echocardiography (e.g., newly developed regional wall motion abnormality or extension of previous abnormality) could be used to adjudicate the involvement of target vessel territory. Any types of MI related to stent thrombosis or restenosis of the target lesion was included in TVMI case, but periprocedural MI (e.g., type 4a MI associated with and occurring within 48 hours of coronary intervention) and death with symptoms suggestive of myocardial ischemia but without direct evidence of target vessel involvement was excluded from the outcome measure of TVMI.
- Target Vessel Revascularization (TVR): any repeat PCI in the target vessel indicating the disease progression.

ULTRA registry

Inclusion criteria
The ULTRA registry (NCT05205148) enrolled 2036 consecutive patients treated with ultrathin coronary DES for coronary bifurcation lesions, left main disease, chronic total coronary occlusion and in-stent restenosis regardless of their clinical presentation. Besides informed consent, the study population included patients based on the following inclusion criteria:

- Age > 18 years old
- Unprotected LM stenosis
- Bifurcation coronary stenosis (with side branch diameter ≥ 2.5 mm)
- Chronic total coronary occlusion
- In-stent restenosis

ULTRA included patients treated with the following DES:

- Supraflex Crux (Sahajanand Medical Technologies), a sirolimus- eluting biodegradable polymer cobalt-chromium stents with a strut thickness of 60 μm.
- MiStent (Micell Technologies), a sirolimus-eluting biodegradable polymer cobalt-chromium stent with 64 μm struts.
- BioMime (Meril Life Science), a sirolimus-eluting biodegradable polymer cobalt-chromium stents with a strut thickness of 65 μm.
- Orsiro (Biotronik), a sirolimus-eluting biodegradable polymer cobalt-chromium stents with a strut thickness of 60 μm for stent diameters of 2.25−3.00 mm and 80 μm for diameters of 3.50−4.00 mm.

Exclusion criteria
There was no formal exclusion criterion other than a follow-up duration < 6 months and death during this period.

Study outcomes

Primary outcome

- Target lesion failure (TLF): composite endpoint of cardiovascular death, target vessel myocardial infarction, target lesion revascularization and definite stent thrombosis

Secondary outcomes

- All-cause death: death from any cause
- Cardiovascular death: death from cardiovascular causes
- Acute myocardial infarction (AMI): all acute myocardial infarctions excluding peri-procedural myocardial infarction
- TV-MI: an MI case with evidence of myocardial necrosis in the vascular territory of a previously treated target vessel. Direct evidence of invasive angiography, electrocardiographic, or other imaging evidence such as echocardiography (e.g., newly developed regional wall motion abnormality or extension of previous abnormality) could be used to adjudicate the involvement of target vessel territory. Any types of MI related to stent thrombosis or restenosis of the target lesion was included in TVMI case, but periprocedural MI (e.g., type 4a MI associated with and occurring within 48 hours of coronary intervention) and death with symptoms suggestive of myocardial ischemia but without direct evidence of target vessel involvement was excluded from the outcome measure of TVMI.
- Target vessel revascularization (TVR): all revascularization in a vessel treated with ultrathin DES within the index procedure
- Target lesion revascularization (TLR): coronary revascularization due to acute coronary syndrome or stable ischemic presentation due to a lesion previously treated with ultrathin drug eluting stent within the index procedure
- Definite stent thrombosis: stent thrombosis in a coronary segment previously treated with ultrathin drug eluting stent
- Major bleedings: defined according to BARC 3-5

Supplementary Table 1. Baseline features of the propensity score-matched cohorts.

	OVERALL (n=3568)	FKB (n=1784)	NO FKB (n=1784)	P VALUE
Age	66.29 ± 11.46	66.36 ± 11.44	66.22±11.46	0.71
LVEF	56.38 ± 9.39	56.01± 9.66	56.19 ± 9.53	0.25
Male	2825 (79.2)	1430 (80.2)	1395 (78.2)	0.15
Hypertension	2473 (69.3)	1284 (71.0)	1189 (69.0)	0.45
Hyperlipidemia	1964 (55.0)	1026 (57.5)	938 (55.0)	0.10
Diabetes	1216 (34.1)	627 (35.1)	589 (33.0)	0.18
- *Insulin Dependent*	41 (30.8)	15 (26.8)	26 (33.8)	0.39
Smoke	924 (25.9)	457 (25.6)	467 (26.2)	0.92
- *Previous smokers*	*892 (25.0)*	*441 (24.7)*	*451 (25.3)*	
- *Current smokers*	*32 (0.9)*	*16 (0.9)*	*16 (0.9)*	
CKD	584 (16.4)	312 (17.5)	272 (15.2)	0.07
Previous PCI	865 (24.2)	439 (24.6)	426 (23.9)	0.61
Previous CABG	131 (3.7)	69 (3.9)	62 (3.5)	0.53
Previous MI	701 (19.6)	360 (20.2)	341 (19.1)	0.42
Previous Stroke	31 (0.9)	15 (0.8)	16 (0.9)	0.86
Active Cancer	30 (0.8)	17 (1.0)	13 (0.7)	0.46
COPD	39 (1.1)	21 (1.2)	18 (1.0)	0.63
History Of Major Bleeding	4 (0.1)	2 (0.1)	2 (0.1)	1.00
Multivessel Disease	295 (8.3)	165 (9.2)	130 (7.9)	0.06
PAD	45 (1.3)	29 (1.6)	16 (0.9)	0.05
Indication to PCI				0.47
CCS	653 (18.3)	317 (18.8)	336 (18.8)	
ACS	1645 (46.1)	891 (49.9)	754 (42.3)	
- *STE-ACS*	784 (22.0)	434 (24.3)	350 (23.0)	
- *NSTE-ACS*	861 (24.1)	457 (25.6)	404 (22.6)	
Other	1270 (35.6)	576 (32.3)	694 (34)	

Legend as in table 1.

Supplementary Table 2. Procedural features of the propensity score-matched cohorts.

	OVERALL (n=3568)	FKB (n=1784)	NO FKB (n=1784)	P VALUE
Arterial Access				0.47
- *Radial*	2614 (73.3)	1369 (76.7)	1245 (74.0)	
- *Femoral*	954 (26.7)	415 (23.3)	539 (25.0)	
Intracoronary Imaging	1319 (36.9)	709 (39.7)	610 (37.1)	0.11
- *IVUS*	1296 (36.3)	694 (38.9)	602 (36.7)	
- *OCT*	23 (0.6)	15 (0.8)	8 (0.4)	
Site Of Bifurcation				0.79
- *Distal LM*	833 (23.3)	488 (24.4)	345 (23.4)	0.48
- *LAD/Diag*	1679 (47.1)	806 (45.2)	873 (48.9)	0.02
- *LCX/OM*	704 (19.7)	345 (19.3)	359 (20.1)	0.54
- *RCA/PDA-Pl*	230 (6.4)	123 (6.9)	107 (6.0)	0.27
Medina Classification				0.78
- *0.0.1.*	142 (4.0)	56 (3.1)	86 (4.8)	
- *0.1.0.*	541 (15.2)	328 (18.4)	213 (11.9)	
- *0.1.1.*	183 (5.1)	73 (4.1)	110 (6.2)	
- *1.0.0.*	404 (11.3)	171 (9.6)	233 (13.1)	
- *1.0.1.*	267 (7.5)	101 (5.7)	166 (9.3)	
- *1.1.0.*	1202 (33.7)	616 (34.5)	586 (32.8)	
- *1.1.1.*	829 (23.2)	439 (24.6)	390 (21.9)	
True Bifurcation	1279 (35.8)	613 (34.4)	666 (37.3)	0.06
Main branch length of lesion (mm)	25.15 ± 11.05	25.15 ± 11.24	25.16 ± 10.85	1.00
Side branch diameter (mm)	1.90 ± 1.09	2.05 ± 1.05	1.89 ± 1.11	0.67
Side branch length of lesion (mm)	24.08 ± 9.85	23.09 ± 9.79	24.95 ± 9.93	0.58
Severe Calcification	672 (18.8)	297 (20.4)	375 (21.0)	0.68
Rotational atherectomy	140 (3.9)	43 (4.4)	97 (5.4)	0.89
Diffuse Disease	1173 (32.9)	561 (31.4)	612 (34.3)	0.07
Cardiogenic shock on admission	3 (0.1)	1 (0.1)	2 (0.1)	0.56
Use Of MCS				0.37
- *IABP*	1 (0.0)	1 (0.1)	0 (0.0)	
- *Impella*	1 (0.0)	0 (0.0)	1 (0.1)	
Need For Inotrope/Vasopressors	6 (0.2)	2 (0.1)	4 (0.2)	0.57
Conversion to 2stent Strategy	0 (0)	0 (0)	0 (0)	
P2Y12 inhibitors				0.56
- Clopidogrel	2520 (70.6)	1243 (70.2)	1277 (71.8)	
- Ticagrelor	1025 (20.7)	526 (29.7)	499 (28.1)	
- Prasugrel	4 (0.1)	2 (0.1)	2 (0.1)	
- DAPT Duration (months)	14.61 ± 6.11	15.13 ± 6.12	14.51 ± 5.95	0.67

Legend as in table 2

Supplementary Table 3. Coronary stents implanted before and after PSM.

	FKB (n=3474)	**NO FKB (n=2133)**	**P VALUE**	**FKB (n=1784)**	**NO FKB (n=1784)**	**P VALUE**
Biomatrix	371 (11%)	78 (4%)	<0.001	91 (5%)	70 (4%)	0.45
Orsiro	453 (13%)	481 (23%)		390 (21%)	420 (23%)	
Promus	511 (15%)	248 (12%)		260 (13%)	222 (12%)	
Resolute and Resolute Onyx	841 (24%)	405 (19%)		350 (19%)	366 (21%)	
Sinergy	293 (9%)	180 (9%)		170 (9%)	145 (8%)	
Ultimaster	101 (3%)	122 (6%)		59 (3%)	110 (6%)	
Xience and Xience Alpine	729 (14%)	551 (26)		420 (23%)	430 (24%)	
Others	175 (5%)	68 (4%)		64 (4%)	31 (1%)	

FKB: final kissing balloon

Supplementary Table 4. Standardised mean difference before and after PSM.

Colonna1	SMD before	SMD after
Age	5	2
LVEF	4	3
Male	0,1	4,9
Hypertension	2,1	0,6
Hyperlipidemia	6	4
Diabetes	11	4
Smoke	4	2
CKD	20	5
Previous PCI	2	1
Previous CABG	3	2
Previous MI	2	1
Previous Stroke	1	1
Active Cancer	3	1
COPD	2	1
History Of Major Bleeding	1	1
Multivessel Disease	17	3
PAD	9	9
Indication to PCI		
CCS	15	0
ACS	14	14
Radial access	12	5
Intracoronary Imaging	15	4
Site Of Bifurcation		
Distal LM	19	2
LAD/Diag	7	6
Cx/Om	9	5
RCA/PL	6	3
Medina Classification		
0.0.1	5	2
0.1.0	4	3
0.1.1.	7	5
1.0.0	8	5
1.0.1	9	5
1.1.0	7	5
1.1.1	6	4
True Bifurcation	11	6
Main branch length of lesion (mm)	6	4
Biomatrix	26	5
Orsiro	25	5

Promus	9	3
Resolute and Resolute Onyx	12	5
Sinergy	0	3
Ultimaster	14	14
Xience and Xience Alpine	29	2
Others	5	5
Side branch diameter (mm)	4	3
Side branch length of lesion (mm)	2	2
Severe Calcification	3	2
Rotational atherectomy	2	1
Diffuse Disease	3	2
Cardiogenic shock on admission	2	1
Use Of MCS		
IABP	5	5
Impella	4	2
Need For Inotrope/Vasopressors	3	2

Legend as in table 1 and 2.

Supplementary Table 5. Outcome before PSM after exclusion of patients with an additional side branch stent.

	Crude analysis		
OUTCOMES	**FKB (n=3348)**	**No FKB (n=2114)**	**P value**
MACE	**274 (8.1%)**	**183 (8.6%)**	**0.41**
All-cause death	**133 (3.9%)**	**91 (4.3%)**	**0.29**
All MI	**63 (1.8%)**	**74 (3.5%)**	**<0.001**
TLR	**65 (1.9%)**	**51 (2.4%)**	**0.23**
ST	**23 (0.7%)**	**24 (1.1%)**	**0.06**
TV-MI	**3 (0.1%)**	**15 (0.7%)**	**<0.001**
LOCO	**67 (2.0%)**	**63 (2.9%)**	**0.011**

Legend: MACE: major adverse cardiovascular events. MI: myocardial infarction; TLR: target lesion revascularization; ST: stent thrombosis; TV-MI: target vessel myocardial infarction; LOCO: lesion-oriented composite outcomes.