Clinical Outcomes of Proximal Optimization Technique (POT) in Bifurcation Stenting

Short title: Impact of proximal optimization technique

Bernard Chevalier[1], Mamas A. Mamas[2,3], Thomas Hovasse[1], Muhammad Rashid[2,3], Joan Antoni Gomez[4], Manuel Pan[5], Adam Witkowski[6], James Crowley[7], Adel Aminian[8], John McDonald[9], Farzin Beygui[10], Javier Fernández Portales[11], Ariel Roguin[12], Goran Stankovic[13] on behalf of e-ULTIMASTER investigators

Author affiliations

1 Ramsay Générale de Santé, ICPS, Hôpital Jacques Cartier, Massy, France
2 Department of Cardiology, University Hospital of North Midlands, Stoke on Trent, UK
3 Keele Cardiovascular Research group, centre of prognosis research, Institute of primary care sciences, Keele University, Stoke on Trent, UK
4 Heart Disease Institute, Bellvitge University Hospital (IDIBELL), University of Barcelona, Barcelona, Spain
5 Reina Sofia Hospital, Department of Cardiology. University of Córdoba (IMIBIC). Cordoba, Spain
6 Department of Interventional Cardiology and Angiology, Institute of Cardiology, Warsaw, Poland;
7 Department of Cardiology, University Hospital Galway, Ireland
8 Centre Hospitalier Universitaire de Charleroi, Department of Cardiology, Charleroi, Belgium;
9 Department of Cardiology, Royal Blackburn Hospital, United Kingdom
10 Department of Interventional Cardiology and Cardiology Research Units, CHU Caen, France;
11 Department of Cardiology, Complejo Universitario Hospital de Caceres, Spain
12 Department of Cardiology, Hillel Yafe Medical Center, Hadera, Israel
13 Department of Cardiology, Clinical Center of Serbia, University of Belgrade, Belgrade, Serbia

Correspondence to: Dr Bernard Chevalier, ICPS, Hôpital Privé Jacques Cartier, 91300 Massy

Email: b.chevalier@angio-icps.com

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Abstract

Background: Optimal deployment of coronary stents in a bifurcation lesion remains a matter of debate.

Aims:We sought to capture the daily practice of bifurcation stenting by means of a worldwide registry and to investigate how the post-implantation deployment techniques influence the clinical outcomes.

Methods: Data from the e-ULTIMASTER registry were used to perform an analysis of 4395 patients undergoing percutaneous coronary intervention for bifurcation lesions. Inverse probability of treatment weights (IPTW) propensity score methodology was used to adjust for any baseline differences. The primary outcome of interest was target lesion failure (TLF) at 1-year (follow-up rate 96.2%).

Results: Global one-year TLF rate was low: 5.1%. Proximal optimization technique was used in 33.9 % of cases and was associated with a reduction in adjusted TLF rate [4.0 (95% confidence interval:3.0-5.1)% versus 6.0(5.1-6.9)%, p<0.01] due to a reduction of all components of this composite endpoint, except for cardiac death. Stent thrombosis was also positively impacted [0.4(0.04-0.7)% versus 1.3(0.8-1.7)%, p<0.01]. POT benefit was uniform across subgroups.

Conversely, the use of kissing balloon technique (36.5%) did not influence the adjusted TLF rate.

Conclusions: Despite a low one-year failure rate in this large bifurcation stenting cohort, proximal optimization technique was associated with a further reduction in the event rate and a uniform benefit across subgroups suggesting systematic use of this deployment technique regardless of the bifurcation anatomy and stenting technique.

Keywords: Bifurcation, one stent strategy, complex strategy, clinical outcomes, true bifurcations

Condensed Abstract

We aimed to investigate how the post-implantation deployment techniques influence the clinical outcomes of bifurcation stenting.

Data were analyzed from 4395 patients undergoing bifurcation stenting enrolled in the e-ULTIMASTER registry.

Proximal optimization technique was used in 33.9 % of cases and was associated with a reduction in adjusted 1-year TLF rate [4.0 (95% confidence interval:3.0-5.1)% versus 6.0 (5.1-6.9)p<0.01]. POT benefit was uniform across subgroups. Conversely, the use of kissing balloon technique did not influence the adjusted TLF rate.

Proximal optimization technique was associated with a further reduction in the event rate and a uniform benefit across subgroups.

Abbreviations

AHA/ACC: American College of Cardiology/American Heart Association

CABG: coronary artery bypass graft

CD: clinically driven

DES: drug-eluting stent

KBT: Kissing balloon technique

LAD: left anterior descending coronary artery

LCX: left circumflex coronary artery

MI: myocardial infarction

(N)STEMI: (non) ST-segment elevation myocardial infarction

PCI: percutaneous coronary intervention

POCE: patient-oriented composite endpoint

POT: proximal optimization technique

SS: simple strategy (one stent)

RCA: right coronary artery

ST: stent thrombosis

TLF: target lesion failure

TLR: target lesion revascularization

TVF: target vessel failure

TVMI: target vessel myocardial infarction

TVR target vessel revascularization

TS: two stent

Impact on daily practice

- This large bifurcation subgroup from a global registry using a last-generation DES shows a low one-year event rate with significant clinical improvement when a proximal optimization was performed.
- Kissing balloon technique has a more limited influence on the outcome
- The current findings suggest a benefit of proximal optimization technique irrespective of the lesion anatomy and the stenting technique, promoting its systematic use

Introduction

Bifurcation lesions remain a challenge both in terms of procedural success and long-term cardiovascular outcomes [1]. Many stenting techniques have been proposed to overcome these limitations from the early days of the bare-metal stent era until the advent of new-generation DES [2]. Most of them aim at restoring the natural bifurcation anatomy whilst conforming to a wide range of configurations in terms of diameters and angulation. Early results of the 2-stent approach prompted the European Bifurcation Club to strongly promote the provisional strategy as a one-stent strategy when acceptable, which was associated with better or neutral outcome in several randomized clinical trials and most of the meta-analyses [3].

One-stent technique and 2-stent techniques were developed in combination with two major post-dilatation methods to adjust a regular stent to the dedicated anatomy of a bifurcation : the kissing balloon technique (KBT) [4] and the proximal optimization technique (POT) [5]. Expert consensus has progressively established their respective role, emphasizing the need to respect the fractal geometry of coronary vasculature [6] Although KBT was evaluated in randomized trials [7] recommendations regarding POT have been mainly based on bench testing and small size cohort clinical studies by means of intravascular imaging [8-12].

On the basis of the e-ULTIMASTER study, we sought to evaluate post-stent implantation deployment techniques, with specific focus on POT and KBT, and their impact on the 1-year clinical outcome of a large pre-specified bifurcation subgroup of this worldwide prospective mega-registry.

Methods

Study design

e-ULTIMASTER (NCT02188355) is an all comer, single arm, prospective, multicenter registry with clinical follow-up at 3 months and 1 year. The study was conducted worldwide and enrolled patients between October 2014 and June 2018 from 378 hospitals (see supplement) in 50 countries across Europe, Asia, Africa, South America and Mexico. The primary objective of the registry was to further evaluate the safety and performance of the Ultimaster DES system (Terumo Corporation, Tokyo, Japan) in daily practice.

Study population

Inclusion criteria were broad and involved all patients ≥ 18 years old, with coronary artery disease eligible for PCI using DES according to local hospital practice and intended to be treated with the Ultimaster DES (with reference vessel diameter matching available Ultimaster DES sizes). Dual antiplatelet regimen was left to the operators' discretion. The registry was conducted in accordance with the Declaration of Helsinki and country-specific regulatory requirements. All patients signed the informed consent form reviewed and approved by the Institutional Review Board/Ethics Committee of each participating center. A Bifurcation lesion is defined as a significant stenosis in a coronary artery adjacent to and/or involving the origin of a SB that is clinically significant. Selection of patients in the bifurcation cohort was left at operator's discretion.

The study population used to analyze clinical outcomes during follow-up comprised all patients who received an Ultimaster DES upon enrolment in the e-ULTIMASTER study and (i) completed 1-year follow-up or (ii) who reached the primary endpoint target lesion failure (TLF: cardiac death, target-vessel myocardial infarction or clinically-driven target lesion revascularization) or (iii) who died during follow-up (see flowchart, Fig 1)

Study device

The Ultimaster coronary stent system is a new generation open-cell cobalt-chromium thin-strut (80µm) sirolimus-eluting stent with an abluminal biodegradable polymer coating (poly-D,L-lactic acid polycaprolactone) [13] Sirolimus is released over a 3 to 4 months period after which the polymer coating is fully degraded.

Follow-up

Follow-up was performed either via direct phone contact with the patient or during a visit of the patient to the outpatient clinic of the hospital. Measures to ensure data quality included remote and

on-site monitoring with a risk-based approach as well as close communication with the sites to reinforce the importance of complete and accurate data entry. All events composing the primary endpoint were independently adjudicated by a clinical event committee.

Outcomes and definitions

The primary outcome was target lesion failure (TLF) defined as a composite of cardiac death, myocardial infarction that could not be clearly attributed to a vessel other than the target vessel (target vessel MI) and clinically driven target lesion revascularization (CD-TLR). Secondary outcomes included any death, cardiac death, MI, TLR, target vessel revascularization (TVR), target vessel failure (TVF; a composite of cardiac death, target vessel MI and TVR), stent thrombosis and major vascular and bleeding complications.

Statistical analysis

Baseline patient, lesion and procedural characteristics are summarized using mean ± standard deviation (SD) for continuous variables and frequencies and percentages for categorical variables. Continuous variables were compared using the Wilcoxon test and categorical variables with Chi-square test. To account for differences in baseline demographics, the POT vs no POT and KBT vs no KBT comparisons were adjusted by weighting the subject by inverse propensity weights. . These propensity scores were calculated using a logistic regression model, predicting the probability of belonging to the POT or KBT group, with the baseline demographics variables as independent variables (age, gender, smoking status, renal impairment, previous MI, previous PCI, previous CABG, acute coronary syndrome, STEMI, multivessel disease, number of lesions identified and treated, treated vessel location, small vessels, long lesions, lesion type B2 or C, ostial lesions, CTO, calcification, Medina classification, one versus two stent technique, number of stents implanted, total stent length, radial access, balloon pre-dilatation, balloon post-dilatation, imaging). Propensity scores for POT versus no POT, additionally included KBT, while propensity scores for KBT versus no KBT additionally included

POT. The inverse weights were investigated for extreme values (see Supplementary Figure 1). Due to the large overlap in populations and the large sample sizes, neither the POT nor the KBT propensity score matching resulted in extreme weights (maximum weights <4).

In the propensity score weighted analyses, categorical variables were compared with a weighted Chi-square test. For time to event analysis, an inverse propensity score weighted Kaplan-Meier method was applied).. Logistic regression was used to test the interaction effect for POT or KBT separately vs. a list of predictor variables on 1-year TLF, by modelling, per predictor variable, the 1-year TLF as binary outcome, while using POT or KBT and the predictor variable as independent variables, and the interaction between POT or KBT and the predictor variable as interaction effect. Statistical analyses were performed using SAS software, version 9.4 (SAS Institute, Inc., Cary, NC, USA).

Results

At least one bifurcation lesion was treated in 4395 patients, 11.8 % of the 37,198 patients enrolled in the e-ULTIMASTER registry among whom 4230 patients (96.2%) were followed up to one year. Baseline and procedural characteristics of this bifurcation cohort are described in Table 1. More than half of the patients were treated on a true bifurcation lesion (Medina XX1: 52.2%), mainly in the LAD (68.4%) via radial access in 80.2% of cases. A double (main and side branches) vessel treatment was done in 51.8% and a double stenting was performed in 22.8% reflecting a high incidence of adoption of a provisional strategy. Details of techniques are presented in Supplement Figure 2. At one-year endpoint, TLF rate was 5.1%; each component of the composite endpoint is described in Figure 2.

POT was performed in 33.9% of cases and its use was more prevalent in left main and LAD lesions as well as in long lesions, true bifurcations, and when a two-stent technique was used (Table 2). KBT was performed in 36.5% of cases and its use was heterogeneous regarding the main baseline characteristics (Suppl Table 1). Unadjusted and adjusted (inverse propensity score weighted) outcomes according to POT and KBT use are presented in Table 3 and Suppl Table2.

Baseline characteristics of the study population after propensity weighting are described in Supplement Table 3 (POT vs no POT) and Supplement Table 4 (KBT vs no KBT). After propensity weighting, POT was associated with a reduction of TVMI [0.7 (0.2-1.1)% versus 2.0 (1.5-2.6)%, p=0.001], CD-TLR [1.9 (1.2-2.6)% versus 3.6 (2.9-4.3)%, p<0.01], stent thrombosis [0.4% versus 1.3%, p <0.01] with a strong impact on TLF [4.0 (3.0-5.1)% versus 6.0 (5.1-6.9)%, p<0.01]. POT benefit was consistent across the subgroups (p for interaction=NS) with regards to major angiographic and procedural features (Fig 3). The difference was established early, during the first month and maintained during the first year (Central illustration)

KBT had a limited clinical impact on clinical outcomes with a reduction in TVMI after propensity weighting [1.0 (0.5-1.5)% versus 1.9 (1.4-2.4)%, p=0.02] with no effect on 1-year composite endpoints TLF [4.5 (3.5-5.6)% versus 4.7 (3.9-5.5)%, p=0.77) and on stent thrombosis rates [0.9 (0.4-1.4)% versus 0.8 (0.5-1.2)%, p=0.76]; there was an interaction between KBT effect and some procedural characteristics: LM location, Medina type, stent size and persistent DAPT at one year (Suppl figure 3). Details of this analysis are presented in Supplement table 2.

Discussion

To the best of our knowledge, this is the largest bifurcation study aiming at assessing the respective impact of post-stent implantation deployment techniques, namely, proximal optimization and kissing balloon techniques. Our study shows first, a low one-year event rate in this large registry capturing the real-world practice in bifurcation stenting when using a last generation DES despite a surprisingly low rate of POT; second, a strong impact of POT on 1-year clinical outcomes which is consistent across subgroups; third, a minimal effect of KBT on outcomes.

From fractal geometry to POT

The law of conservation of mass, also known as Murray's law, established the fractal geometry [14] of artery bifurcations. A simplification of this rule, suggested by Finet et al. [15] was validated by means of quantitative angiography and intravascular ultrasound and allows the quantification of the step-up of proximal main branch reference diameter according to the distal main branch and side branch reference diameters. In order to minimize the risk of carina shift after main branch stent implantation, and the subsequent risk of side branch occlusion inducing a periprocedural myocardial infarction, a 1:1 stent diameter/distal reference diameter ratio was proposed by Darremont at the 5th European Bifurcation Club meeting [5] in combination with a 1:1 balloon post-dilatation just proximal to the carina, sized on the basis of simplified Murry's law, to eliminate undersizing, and subsequent malapposition in the proximal segment of the bifurcation and to facilitate the access to side branch by reducing strut obstruction. This concept of two diameters with a single stent allows the transformation of a regular stent in order to comply with the fractal nature of the coronary tree.

POT validation

Despite this strong rationale and the intuitive benefit, few studies have been performed to validate this strategy. This could be the reason why the POT was used only in one-third of our bifurcation registry despite strong recommendations by the various bifurcation clubs. Rigatelli et al. [16] have shown a significant improvement in terms of flow dynamics when POT is used on bench models with some 2-stent techniques. Derimay et al. emphasized the impact of balloon position to obtain the

expected effect on bench testing [10] and highlighted differences between balloon brands in terms of marker to shoulder distances.

Some studies used intravascular imaging to evaluate the potential benefit with contradictory results: Hakim et al. [8] showed that POT increased proximal stent area, as assessed by IVUS while Murasato et al. did not obtain the expected benefit on incomplete stent apposition as assessed by OCT [9]. Few clinical studies have been conducted so far. Mylotte et al. evaluated the role of POT among other modifications of the provisional strategy to improve clinical outcome [17]. Takagi et al. studied a series of 586 patients treated on left main bifurcation lesion showing a strong trend towards MACE and TLR reductions (HR 0.73 and 0.69, p=0.05 and 0.06) when POT was performed [18]. More recently, JH Yang et al. [12] in a series of 1191 bifurcation lesions with a 21.1% POT rate, showed a benefit in terms of MACE and TLR when no KBT was performed (p for interaction=0.03). Our results in a much larger cohort found an early and sustained benefit in terms of safety-stent thrombosis and target vessel myocardial infarction- and efficacy-target revascularization with no interaction with major angiographic and procedural characteristics.

Role of kissing balloon technique

In our study, KBT was not associated with a TLF benefit after propensity weighting, a result which is consistent with NORDIC III data [7] in which KBT failed to prove its impact on a provisional stenting strategy. However, the KBT subgroup experienced less target vessel myocardial infarction without any difference in terms of stent thrombosis, a finding which could be related to less side branch periprocedural obstruction with no further effect on the TLR rate. Conversely, registries data have shown a late revascularization benefit as presented in COBIS II [19] and RAIN [20]. However, guidelines [21] recommend using KBT in 2-stent techniques. A significant interaction was present with some baseline angiographic characteristics and DAPT duration but KBT effect was similar regardless of the number of stents and the deployment technique.

The question as to whether KBT and POT are complementary techniques is still a matter of debate as both techniques are implemented to reduce proximal malapposition and to further facilitate access to side branch. In our study, POT and KBT practices were more frequently associated than dissociated.

Given the low event rates, it is important to remove as much of the variability, induced by the confounding factors, as possible. For this purpose, we have performed propensity matched POT and KBT analyses. In order to more clearly identify the combined effects of POT and KBT in our study population, we performed logistic regression models where we included both POT and KBT as predictive factors of 1-year TLF (Supplement Table 5), together with their interaction effect and the covariates we used in propensity score weighting. From the multivariate model, it seems POT only ($p=0.046$), rather than KBT ($p=0.81$) or their interaction effect ($p=0.76$) is the protective factor for TLF in our study. Additionally, we also performed 2 by 2 propensity matched analyses, classifying patients by their POT and KBT status into 4 groups: (1) using POT and KBT, (2) using POT but no KBT, (3) using KBT but no POT and (4) neither POT or KBT used (Supplement Table 6). These results corroborate the results from the logistic regression models: POT is the protective factor for TLF, while KBT or the POT-KBT interaction does not seem to play a role. These data suggest that KBT cannot be a substitute for POT technique.

Limitations

First, due to the registry design, there is a potential for selection bias and under-reporting of events despite the prospective nature of the study and the specific measures undertaken to improve data quality using on and off-site monitoring. In particular, an underestimation of periprocedural MI cannot be excluded as periprocedural biomarker collection was per hospital practice. Second, vessel and lesion characteristics were assessed by operators, most commonly through visual estimation, and not measured centrally by a core lab. Third, deployment technique details are limited in terms of size selection and inflation technique. Sequence description data with regards to POT and KBT are missing, even though the latter was always performed after stenting; moreover, a small number of patients

were treated under intravascular imaging guidance *limiting the extrapolation of these results to intravascular imaging guided interventions*. Fourth, the outcomes reported are based on the use of a single new-generation stent platform for all patients; these may potentially differ with the use of different DES. Fifth, as the antiplatelet regimen nature and duration was left to the operator's discretion, interaction with deployment techniques is unknown. Finally, although we report a follow-up of one-year, coronary stents are lifelong implants and it is possible that further differences between our study groups could be observed at longer follow-up.

Conclusions

In this large prospective single-arm study with an already low one-year failure rate in the bifurcation stenting cohort, proximal optimization technique was associated with a further reduction in the event rate and a uniform benefit across subgroups reinforcing the recommendation for a systematic use of this deployment technique regardless of the bifurcation anatomy and stenting technique.

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Legends to figures:

Figure 1: Flow chart of the study population. * The 1-year follow-up population includes patients who had an event that contributed to the primary endpoint, died during follow-up or completed 1-year follow-up.

Figure 2: Unadjusted one-year clinical outcomes of all bifurcation patients (N=4230)

Figure 3: Impact of POT in major angiographic and procedural subgroups - Inverse propensity score weighted analysis

Figure 4/CENTRAL ILLUSTRATION: POT versus no POT: **Inverse propensity score weighted** Kaplan-Meier curve of target lesion failure

Tables

Table 1: Baseline patient and procedural characteristics

	Bifurcation n=4395
Patient characteristics	
Age, years	65.6±11.1 (4395)
Gender, male	76.5% (3364/4395)
Body mass index, kg/m²	27.7±4.6 (3849)
Diabetes mellitus	27.2% (1189/4366)
Current smoking	20.5% (860/4190)
Hypertension	68.8% (2886/4193)
Hypercholesterolemia	62.1% (2550/4105)
Renal impairment	9.1% (397/4368)
Previous MI	23.9% (1019/4265)
Previous PCI	30.1% (1300/4326)
Previous CABG	4.5% (194/4304)
Clinical presentation	
Silent ischemia	12.3% (539/4395)
Stable angina	39.3% (1726/4395)
Unstable angina	12.7% (556/4395)
NSTEMI	23.0% (1012/4395)
STEMI	12.7% (559/4395)
Procedural characteristics	
Radial access	80.2% (3523/4395)
Imaging use	9.3% (407/4395)
Vessel treated	
RCA	17.3% (761/4395)
Left main	12.4% (546/4395)
LAD	68.4% (3008/4395)
LCX	31.4% (1381/4395)
Graft (arterial of venous)	0.2% (9/4395)
Bifurcation type per patient	
True bifurcation	52.2% (2266/4334)
Non true bifurcation	46.2% (2004/4334)
Both	1.5% (64/4334)
Medina classification per lesion	
0.0.1	3.7% (171/4681)
0.1.0	9.1% (426/4681)
0.1.1	8.4% (394/4681)

1.0.0	8.1% (378/4681)
1.0.1	8.6% (403/4681)
1.1.0	24.9% (1165/4681)
1.1.1	37.3% (1744/4681)
Lesion characteristics	
N of lesions identified, per patient	2.1±1.1 (4395)
N of lesions treated, per patient	1.5±0.8 (4394)
CTO	3.8% (165/4395)
Long lesions	42.6% (1871/4395)
Procedure characteristics	
N of study stents implanted per patient	1.9±1.1 (4393)
Length of implanted study stents per patient, mm	36.1±22.5 (4385)

Data are reported for all lesions of 4395 patients with at least 1 bifurcation lesion and are mean ± standard deviation for continuous variable with or % (n) for categorical variables. The number of patients with available data is indicated in brackets. Renal impairment: defined as estimated glomerular filtration rate <60ml/min/1.73m^2. Lesion characteristics at index procedure are reported.

CABG: coronary artery bypass graft; CTO: chronic total occlusion; LAD: left anterior descending artery; LCX: left circumflex; MI: myocardial infarction; (N)STEMI: (non-) ST elevated myocardial infarction; PCI: percutaneous coronary intervention; RCA: right coronary artery.

Table 2: Baseline patient characteristics according to use of POT- unadjusted

	POT n=1453	No POT n=2828	P-value
Patient characteristics			
Age, years	65.9 ±11.1 (1453)	65.4 ±11.1 (2828)	0.18
Gender, male	76.1% (1105/1453)	76.3% (2157/2828)	0.87
Geographical region			<0.001
Europe	80.9% (1176/1453)	73.9% (2,089/2828)	
Asia	8.1% (117/1453)	14.0% (396/2828)	
Africa/Middle East	5.6% (81/1453)	7.2% (203/2828)	
South America/Mexico	5.4% (79/1453)	5.0% (140/2828)	
Body mass index, kg/m²	27.8 ±4.6 (1280)	27.6 ±4.6 (2462)	0.38
Diabetes mellitus	26.2% (378/1443)	28.0% (786/2810)	0.22
Current smoking	21.0% (257/1224)	24.5% (590/2407)	0.02
Hypertension	71.2% (988/1387)	67.5% (1822/2699)	0.01
Hypercholesterolemia	63.3% (862/1362)	61.5% (1622/2639)	0.26
Renal impairment	9.1% (132/1444)	9.2% (258/2814)	0.98
Previous MI	25.0% (349/1397)	23.6% (652/2760)	0.33
Previous PCI	32.7% (467/1429)	28.8% (803/2789)	0.01
Previous CABG	4.7% (67/1417)	4.1% (114/2778)	0.35
Clinical presentation			
Silent ischemia	32.7% (467/1429)	28.8% (803/2789)	0.01
Stable angina	4.7% (67/1417)	4.1% (114/2778)	0.35
Unstable angina	12.5% (182/1453)	12.2% (344/2826)	0.74
NSTEMI	41.8% (608/1453)	38.0% (1073/2826)	0.01
STEMI	13.2% (192/1453)	12.4% (349/2826)	0.42
Vessel treated			
RCA	14.5% (211/1453)	18.6% (525/2828)	0.001
Left main	16.2% (236/1453)	10.2% (287/2828)	<0.001
LAD	70.3% (1021/1453)	67.3% (1904/2828)	0.05
LCX	26.4% (384/1453)	33.1% (935/2828)	<0.001
Graft (arterial of venous)	0.1% (1/1453)	0.3% (8/2828)	0.15
Lesion characteristics			
N of lesions identified, per patient	2.0 ±1.1 (1453)	2.1 ±1.1 (2828)	0.91
N of lesions treated, per patient	1.4 ±0.7 (1452)	1.5 ±0.8 (2828)	0.04
Long lesions	47.2% (685/1451)	40.3% (1140/2826)	<0.001
True bifurcation	58.8% (854/1453)	50.3% (1421/2828)	<0.001
Two-stent technique	28.0% (407/1453)	19.7% (556/2828)	<0.001
Type of two-stent technique			
T-stenting	6.5% (95/1453)	5.0% (140/2828)	0.03

V-stenting	0.4% (7/1453)	2.3% (66/2828)	<0.001
Kissing stents	1.4% (20/1453)	2.2% (62/2828)	0.07
Crush	4.8% (70/1453)	2.8% (79/2828)	<0.001
Culotte	4.2% (61/1453)	1.9% (55/2828)	<0.001
TAP or other	10.5% (153/1453)	5.4% (152/2828)	<0.001
KBT	45.2% (657/1453)	32.6% (923/2828)	<0.001
Procedure characteristics			
N of study stents implanted per patient	1.9 ±1.03 (1452)	1.9 ±1.1 (2828)	0.58
Length of implanted study stents per patient, mm	29.4 ±15.62 (1887)	26.5 ±14.5 (3693)	<0.001

Data are reported for 4281 patients with at least 1 bifurcation lesion (114 patients were excluded from this comparison because of lack of information on POT).

Data are mean ± standard deviation for continuous variable with or % (n) for categorical variables. The number of patients with available data is indicated in brackets.

Renal impairment: defined as estimated glomerular filtration rate <60ml/min/1.73m^2. Lesion characteristics at index procedure are reported.

CABG: coronary artery bypass graft; KBT: kissing balloon technique LAD: left anterior descending artery; LCX: left circumflex MI: myocardial infarction; (N)STEMI: (non-) ST elevated myocardial infarction; PCI: percutaneous coronary intervention; POT: proximal optimization technique; RCA: right coronary artery.

Table 3: One-year clinical outcomes according to use of proximal optimization technique (POT)

	Unadjusted			Adjusted by inverse propensity score weighting		
	POT n=1398	No POT n=2729	P-value	POT n=1398	No POT n=2729	P-value
Primary outcome						
Target lesion failure	3.9% (3.0-5.1) (55/1398)	5.7% (4.9-6.7) (156/2729)	0.01	4.0% (3.0-5.1) (56/1398)	6.0% (5.1-6.9) (164/2729)	0.01
Cardiac death	1.9% (1.2-2.7) (26/1398)	1.9% (1.4-2.5) (51/2729)	0.98	1.9% (1.2-2.6) (26/1398)	2.0% (1.5-2.6) (55/2729)	0.72
Target vessel MI	0.6% (0.3-1.2) (9/1398)	1.9% (1.4-2.5) (51/2729)	<0.01	0.7% (0.2-1.1) (9/1398)	2.0% (1.5-2.6) (55/2729)	0.001
Clinically driven TLR	1.8% (1.2-2.6) (25/1398)	3.4% (2.8-4.2) (94/2729)	<0.01	1.9% (1.2-2.6) (26/1398)	3.6% (2.9-4.3) (97/2729)	<0.01
Secondary outcomes						
All-cause death	2.9% (2.1-3.9) (40/1398)	2.8% (2.2-3.5) (77/2729)	0.94	2.9% (2.4-3.8) (41/1398)	3.2% (2.6-3.9) (88/2729)	0.60
All MI	1.0% (0.6-1.7) (14/1398)	2.3% (1.8-2.9) (63/2729)	<0.01	1.0% (0.5-1.5) (14/1398)	2.5% (1.9-3.1) (67/2729)	<0.01
Revascularizations						
TVR	3.1% (2.2-4.1) (43/1398)	4.8% (4.1-5.7) (132/2729)	<0.01	3.2% (2.3-4.1) (45/1398)	5.1% (4.2-5.9) (138/2729)	0.01
TV non-TLR	1.4% (0.8-2.1) (19/1398)	1.5% (1.1-2.0) (41/2729)	0.72	1.4% (0.8-2.0) (19/1398)	1.5% (1.0-1.9) (40/2729)	0.79
TLR	1.9% (1.2-2.7) (26/1398)	3.6% (3.0-4.4) (99/2729)	<0.01	2.0% (1.2-2.7) (27/1398)	3.8% (3.1-4.5) (103/2729)	<0.01
Clinically driven revascularizations						

	Unadjusted			Adjusted by inverse propensity score weighting		
	POT n=1398	No POT n=2729	P-value	POT n=1398	No POT n=2729	P-value
TVR	3.0% (2.2-4.0) (42/1398)	4.6% (3.9-5.5) (126/2729)	0.01	3.1% (2.2-4.1) (44/1398)	4.8% (4.0-5.6) (131/2729)	0.01
TV non-TLR	1.4% (0.8-2.1) (19/1398)	1.4% (1.0-2.0) (39/2729)	0.86	1.4% (0.8-2.0) (19/1398)	1.4% (1.0-1.9) (38/2729)	0.93
Target vessel failure	5.2% (4.1-6.4) (72/1398)	6.6% (5.7-7.6) (181/2729)	0.06	5.3% (4.1-6.5) (74/1398)	6.9% (6.0-7.9) (189/2729)	0.04
Stent thrombosis						
Definite	0.3% (0.08-0.7) (4/1398)	0.8% (0.5-1.2) (21/2729)	0.06	0.3% (0.02-0.6) (4/1398)	0.7% (0.4-1.1) (20/2729)	0.09
Probable	0.1% (0.0-0.4) (1/1398)	0.4% (0.2-0.8) (12/2729)	0.05	0.04% (0.0-0.1) (1/1398)	0.5% (0.3-0.8) (14/2729)	0.01
Definite/probable	0.4% (0.1-0.8) (5/1398)	1.2% (0.8-1.7) (33/2729)	0.01	0.4% (0.04-0.7) (5/1398)	1.3% (0.8-1.7) (34/2729)	<0.01
Possible	0.9% (0.4-1.5) (12/1398)	0.8% (0.5-1.3) (23/2729)	0.96	1.0% (0.4-1.5) (13/1398)	0.8% (0.5-1.2) (23/2729)	0.74
All bleedings	3.0% (2.2-4.0) (42/1398)	2.2% (1.7-2.9) (61/2729)	0.13	3.0% (2.1 to 3.9) (42/1398)	2.3% (1.7-2.8) (62/2729)	0.14
Bleeding BARC type 1 to 2	2.1% (1.4-3.0) (29/1398)	1.4% (1.0-1.9) (38/2729)	0.10	2.2% (1.4-2.9) (30/1398)	1.4% (1.0-1.9) (39/2729)	0.08
Bleeding BARC type 3 to 5	0.8% (0.4-1.4) (11/1398)	1.0% (0.6-1.4) (26/2729)	0.59	0.7% (0.3-1.1) (10/1398)	1.0% (0.6-1.4) (27/2729)	0.35

Events are reported as % with 95% confidence interval (number of patients with event/total number of patients) in the patient population that reached 1-year follow-up, died during follow-up or who had event that contributed to the primary endpoint (n=4230 patients with at least 1 bifurcation lesion). Out of 4230 patients, 103 patients were excluded from this comparison because of lack of information on POT).

Target lesion failure: composite of cardiac death, TV-MI or clinically driven TLR. Target vessel failure: composite of cardiac death, TV-MI or clinically driven TVR

BARC: Bleeding Academic Research Consortium; MI: myocardial infarction; POT: proximal optimization technique; TLR: target lesion revascularization; TV non-TL: target vessel, non-target lesion, revascularization; TVR: target vessel revascularization

Figure 1: Flow chart of the study population. * The 1-year follow-up population includes patients who had an event that contributed to the primary endpoint, died during follow-up or completed 1-year follow-up.

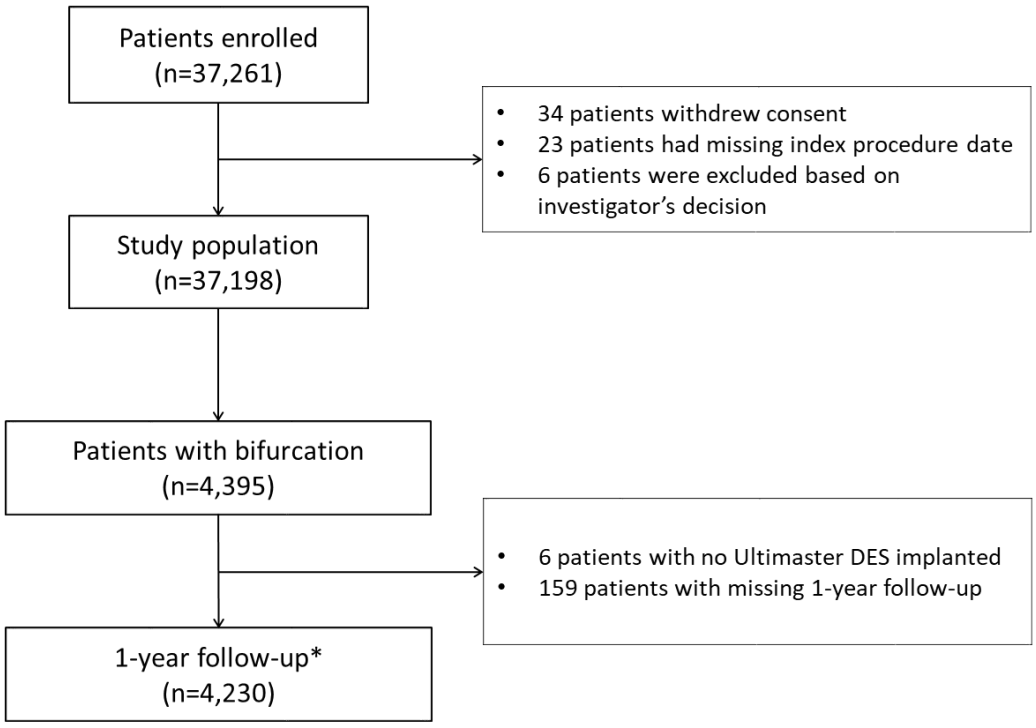


Figure 2: Unadjusted one-year clinical outcomes of all bifurcation patients (N=4230)

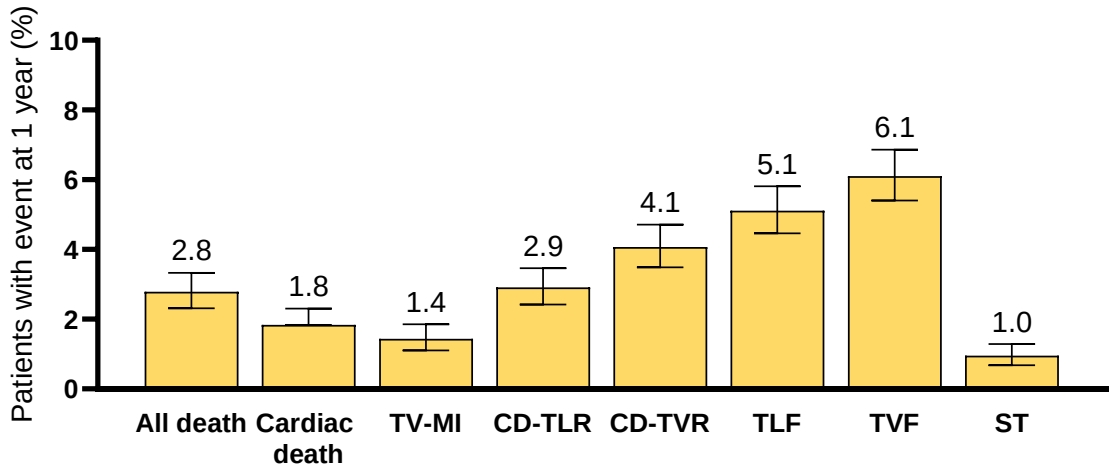
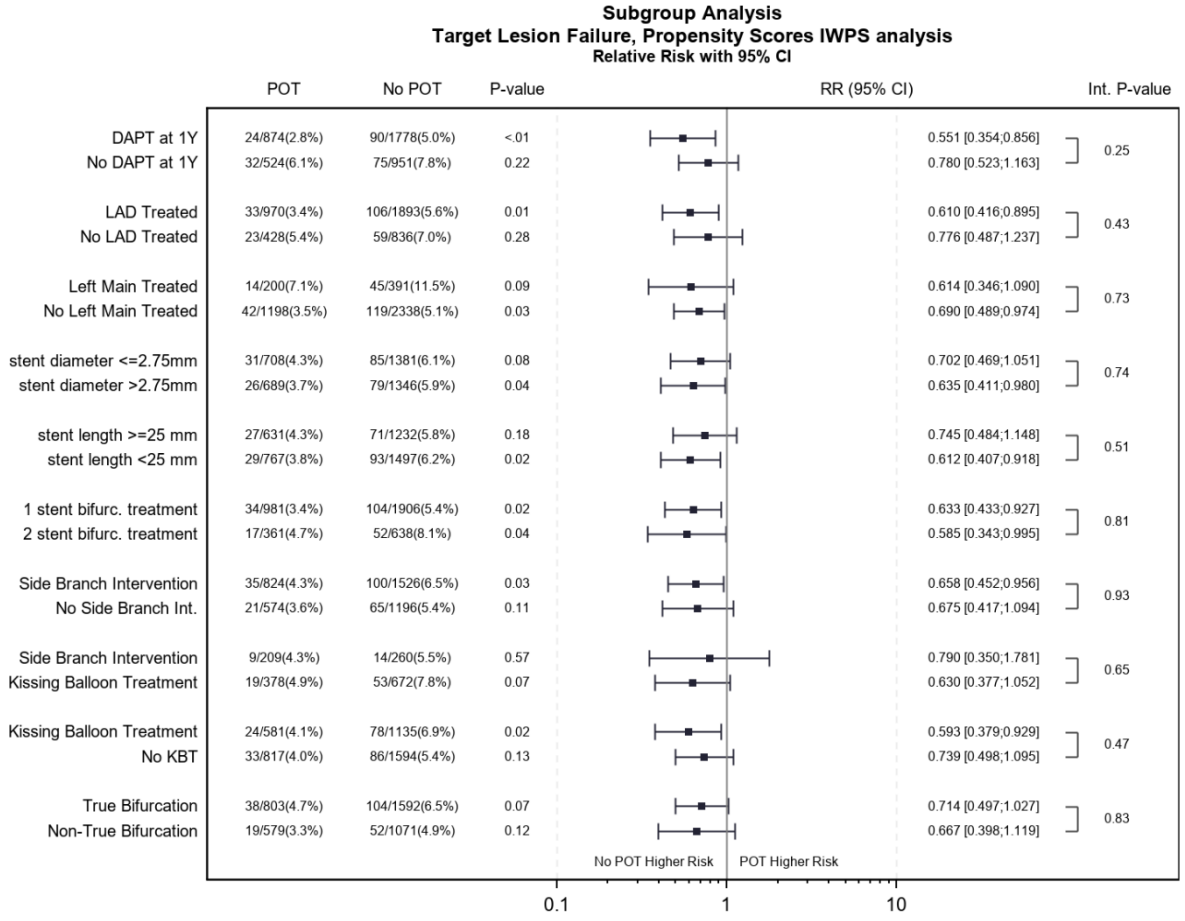
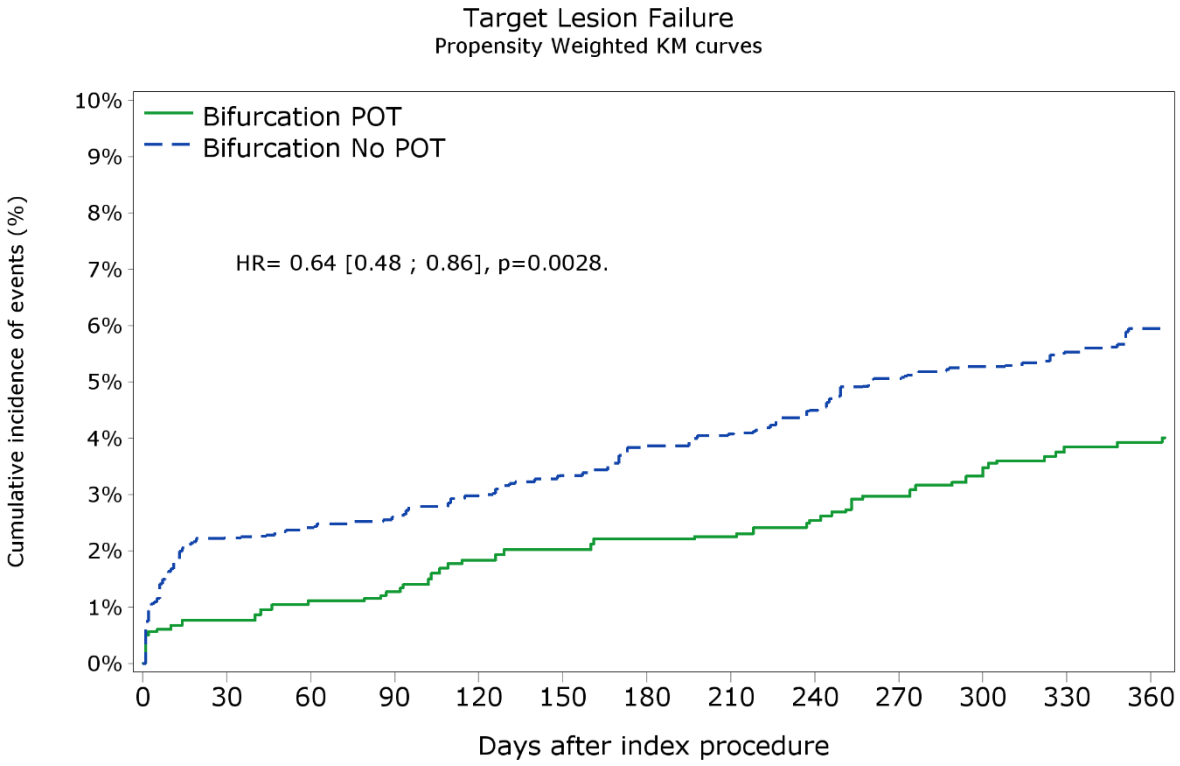


Figure 3: Impact of POT in major angiographic and procedural subgroups - Inverse propensity score weighted analysis



Central Illustration POT versus no POT: Inverse propensity score weighted Kaplan-Meier estimates of target lesion failure according to POT



Number at Risk (Unweighted)					
POT	1453	1400	1362	1347	1297
No POT	2828	2716	2621	2576	2482

Suppl Table 1: Baseline patient characteristics according to use of KBT - unadjusted

	KBT n=1583	No KBT n=2757	P-value
Patient characteristics			
Age, years	65.7±11.1 (1583)	65.5±11.1 (2757)	0.88
Gender, male	75.2% (1191/1583)	77.2% (2127/2757)	0.15
Geographical region			<0.001
Europe	65.1% (1031/1583)	83.2% (2294/2757)	
Asia	18.2% (288/1583)	8.1% (224/2757)	
Africa/Middle East	8.5% (135/1583)	5.4% (148/2757)	
South America/Mexico	8.2% (129/1583)	3.3% (91/2757)	
Body mass index, kg/m²	27.3±4.6 (1349)	27.9±4.6 (2456)	<0.001
Diabetes mellitus	28.0% (442/1577)	26.7% (730/2734)	0.35
Current smoking	18.1% (273/1512)	22.1% (579/2625)	0.24
Hypertension	71.9% (1089/1515)	67.2% (1765/2627)	<0.01
Hypercholesterolemia	63.5% (942/1484)	61.5% (1584/2575)	0.21
Renal impairment	10.6% (166/1574)	8.2% (225/2740)	0.01
Previous MI	25.5% (388/1521)	23.1% (621/2691)	0.08
Previous PCI	34.1% (531/1556)	27.8% (755/2716)	<0.001
Previous CABG	3.8% (59/1544)	4.9% (132/2707)	0.11
Clinical presentation			
Silent ischemia	11.9% (188/1583)	12.4% (341/2757)	0.63
Stable angina	43.9% (695/1583)	36.6% (1010/2757)	<0.001
Unstable angina	12.8% (203/1583)	12.6% (348/2757)	0.85
NSTEMI	20.5% (325/1583)	24.4% (672/2757)	<0.01
STEMI	10.8% (171/1583)	13.9% (384/2757)	<0.01
Vessel treated			
RCA	14.0% (221/1583)	19.1% (526/2757)	<0.001
Left main	19.3% (306/1583)	8.20% (226/2757)	<0.001
LAD	67.9% (1075/1583)	68.5% (1889/2757)	0.68
LCX	29.1% (461/1583)	32.2% (887/2757)	0.04
Graft (arterial of venous)	0.1% (1/1583)	0.3% (8/2757)	0.11
Lesion characteristics			
N of lesions identified, per patient	2.1±1.1 (1583)	2.1±1.15 (2757)	0.59
N of lesions treated, per patient	1.5±0.8 (1583)	1.5±0.7 (2756)	<0.01
Long lesions	47.5% (752/1583)	39.6% (1093/2757)	<0.001
True bifurcation	68.8% (1089/1583)	43.7% (1206/2757)	<0.001
Two-stent technique	43.8% (693/1583)	10.3% (284/2757)	<0.001
Type of two-stent technique			
T-stenting	9.0% (143/1583)	3.4% (94/2757)	<0.001

	KBT n=1583	No KBT n=2757	P-value
V-stenting	2.5% (40/1583)	1.1% (31/2757)	<0.001
Kissing stents	4.6% (72/1583)	0.4% (11/2757)	<0.001
Crush	7.5% (119/1583)	1.7% (32/2757)	<0.001
Culotte	7.1% (111/1583)	0.3% (9/2757)	<0.001
TAP or other	13.2% (209/1583)	3.6% (100/2757)	<0.001
POT	42.0% (664/1583)	29.9% (825/2757)	<0.001
Procedure characteristics			
N of study stents implanted per patient	2.1±1.1 (1583)	1.8±1.0 (2756)	<0.001
Length of implanted study stents per patient, mm	40.5±24.8 (1578)	33.4±20.5 (2754)	<0.001

Data are reported for 4340 patients with at least 1 bifurcation lesion (55 patients were excluded from this comparison because of lack of information on KBT).

Data are mean ± standard deviation for continuous variable with or % (n) for categorical variables. The number of patients with available data is indicated in brackets.

Renal impairment: defined as estimated glomerular filtration rate <60ml/min/1.73m^2. Lesion characteristics at index procedure are reported.

CABG: coronary artery bypass graft;; KBT: kissing balloon technique; LAD: left anterior descending artery; LCX: left circumflex; MI: myocardial infarction; (N)STEMI: (non-) ST elevated myocardial infarction; PCI: percutaneous coronary intervention; POT: proximal optimization technique; RCA: right coronary artery.

Suppl Table 2: One-year clinical outcomes according to use of KBT

	Unadjusted			Adjusted by inverse propensity score weighting		
	KBT n=1517	No KBT n=2663	P-value	KBT n=1517	No KBT n=2663	P-value
Primary outcome						
Target lesion failure	5.5% (4.4-6.7) (83/1517)	4.7% (4.0-5.6) (126/2663)	0.29	4.5% (3.5-5.6) (69/1517)	4.7% (3.9-5.5) (126/2663)	0.77
Cardiac death	2.2% (1.6-3.1) (34/1517)	1.6% (1.2-2.2) (43/2663)	0.15	1.8% (1.1-2.5) (27/1517)	1.6% (1.1-2.1) (42/2663)	0.60
Target vessel MI	1.1% (0.6-1.7) (16/1517)	1.6% (1.1-2.1) (42/2663)	0.17	1.0% (0.5-1.5) (15/1517)	1.9% (1.4-2.4) (50/2663)	0.02
Clinically driven TLR	2.8% (2.1-3.8) (43/1517)	2.8% (2.2-3.5) (74/2663)	0.92	2.4% (1.7-3.2) (37/1517)	2.7% (2.1-3.3) (71/2663)	0.62
Secondary outcomes						
All-cause death	3.4% (2.5-4.4) (51/1517)	2.4% (1.9-3.1) (65/2663)	0.08	2.7% (1.9-3.5) (41/1517)	2.7% (2.1-3.3) (71/2663)	0.92
All MI	1.7% (1.1-2.4) (25/1517)	2.0% (1.5-2.6) (52/2663)	0.48	1.6% (0.9-2.2) (23/1517)	2.2% (1.7-2.8) (59/2663)	0.14
Revascularizations						
TVR	4.2% (3.3-5.4) (64/1517)	4.1% (3.4-5.0) (110/2663)	0.89	3.7% (2.7-4.6) (56/1517)	4.0% (3.3-4.8) (107/2663)	0.60
TV non-TLR	1.3% (0.8-2.0) (19/1517)	1.5% (1.1-2.0) (40/2663)	0.51	1.2% (0.7-1.8) (18/1517)	1.4% (1.0-1.9) (38/2663)	0.53
TLR	3.0% (2.2-4.0) (46/1517)	2.9% (2.3-3.6) (78/2663)	0.85	2.6% (1.8-3.4) (39/1517)	2.8% (2.2-3.4) (75/2663)	0.64

	Unadjusted			Adjusted by inverse propensity score weighting		
	KBT n=1517	No KBT n=2663	P-value	KBT n=1517	No KBT n=2663	P-value
Clinically driven revascularizations						
TVR	4.0% (3.1-5.1) (61/1517)	3.9% (3.2-4.8) (105/2663)	0.90	3.6% (2.6-4.5) (54/1517)	3.9% (3.2-4.6) (104/2663)	0.60
TV non-TLR	1.3% (0.8-2.0) (19/1517)	1.4% (1.0-2.0) (38/2663)	0.64	1.2% (0.7-1.8) (18/1517)	1.4% (1.0-1.9) (38/2663)	0.57
Target vessel failure	6.4% (5.2-7.7) (97/1517)	5.8% (4.9-6.7) (154/2663)	0.42	5.5% (4.4-6.7) (84/1517)	5.9% (5.0-6.7) (156/2663)	0.66
Stent thrombosis						
Definite	0.7% (0.3-1.2) (10/1517)	0.6% (0.3-0.9) (15/2663)	0.70	0.7% (0.3-1.1) (11/1517)	0.6% (0.3-0.9) (16/2663)	0.65
Probable	0.3% (0.1-0.8) (5/1517)	0.3% (0.1-0.6) (8/2663)	0.87	0.2% (0.0-0.5) (3/1517)	0.3% (0.1-0.4) (7/2663)	0.89
Definite/probable	1.0% (0.6-1.6) (15/1517)	0.9% (0.6-1.3) (23/2663)	0.68	0.9% (0.4-1.4) (14/1517)	0.8% (0.5-1.2) (22/2663)	0.76
Possible	1.1% (0.6-1.7) (16/1517)	0.7% (0.4-1.1) (19/2663)	0.24	0.8% (0.4-1.3) (13/1517)	0.6% (0.3-0.9) (16/2663)	0.37
All bleedings	2.4% (1.7-3.3) (36/1517)	2.6% (2.0-3.3) (69/2663)	0.67	2.4% (1.7-3.2) (37/1517)	2.3% (1.7-2.9) (61/2663)	0.78
Bleeding BARC type 1 to 2	1.5% (0.9-2.2) (22/1517)	1.8% (1.3-2.3) (47/2663)	0.44	1.7% (1.1-2.3) (26/1517)	1.5% (1.1-2.0) (41/2663)	0.69
Bleeding BARC type 3 to 5	0.9% (0.5-1.5) (14/1517)	0.9% (0.6-1.3) (23/2663)	0.84	0.8% (0.3-1.2) (11/1517)	0.8% (0.4-1.1) (20/2663)	0.96

Events are reported as % with 95% confidence interval (number of patients with event/total number of patients) in the patient population that reached 1-year follow-up, died during follow-up or who had event that contributed to the primary endpoint (n=4230 patients with at least 1 bifurcation lesion). Out of 4230 patients, 50 patients were excluded from this comparison because of lack of information on KBT).

Target lesion failure: composite of cardiac death, TV-MI or clinically driven TLR. Target vessel failure: composite of cardiac death, TV-MI or clinically driven TVR
BARC: Bleeding Academic Research Consortium; MI: myocardial infarction; TLR: target lesion revascularization; TV non-TL: target vessel, non-target lesion, revascularization; TVR: target vessel revascularization

Table 3 Suppl: Baseline patient characteristics according to use of POT - inverse propensity score weighted

	POT n=1398	No POT n=2729	P-value
Patient characteristics			
Age, years	65.9±11.1 (1398)	65.9±11.1 (2729)	0.99
Gender, male	75.7% (1.058/1398)	75.7% (2.065/2729)	0.99
Body mass index, kg/m²	27.8±4.56 (1233)	27.8±4.7 (2378)	0.80
Diabetes mellitus	26.2% (364/1388)	28.4% (770/2711)	0.14
Current smoking	19.5% (260/1331)	19.4% (508/2620)	0.90
Hypertension	71.1% (947/1333)	69.0% (1.796/2602)	0.18
Hypercholesterolemia	63.0% (824/1308)	62.0% (1.577/2544)	0.54
Renal impairment	8.9% (124/1389)	8.9% (242/2720)	0.98
Previous MI	24.9% (335/1345)	24.7% (654/2650)	0.88
Previous PCI	31.3% (429/1373)	31.2% (838/2691)	0.93
Previous CABG	4.6% (63/1361)	4.6% (122/2681)	0.95
Clinical presentation			
Silent ischemia	12.6 % (175/1398)	13.0% (354/2729)	0.71
Stable angina	40.3% (563/1398)	39.8% (1.085/2729)	0.75
Unstable angina	13.4% (187/1398)	12.1% (330/2729)	0.24
NSTEMI	22.4% (308/1398)	23.3% (636/2729)	0.36
STEMI	11.8% (165/1398)	11.8% (321/2729)	0.99
Vessel treated			
RCA	15.1% (211/1398)	17.4% (474/2729)	0.06
Left main	14.3% (200/1398)	14.3% (391/2729)	0.14
LAD	69.4% (970/1398)	69.4% (1.893/2729)	0.99
LCX	27.5% (385/1398)	30.4% (830/2729)	0.05
Graft (arterial of venous)	0.06% (1/1398)	0.3% (8/2729)	0.14
Lesion characteristics			
N of lesions identified, per patient	2.1±1.15 (1398)	2.1±1.1 (2729)	0.99
N of lesions treated, per patient	1.4±0.7 (1398)	1.5±0.8 (2729)	0.04
Long lesions	45.1% (631/1398)	45.1% (1.232/2729)	0.99
True bifurcation	56.6% (791/1398)	54.9% (1.499/2729)	0.31
Two-stent technique	26.1% (365/1398)	24.0% (656/2729)	0.14
KBT	41.6% (581/1398)	41.6% (1.135/2729)	0.99
Procedure characteristics			
N of study stents implanted per patient	1.9±1.0 (1398)	2.0±1.1 (2729)	0.04
Length of implanted study stents per patient, mm	37.3±22.8 (1397)	37.3±23.0 (2728)	0.99

Data are mean ± standard deviation for continuous variable with or % (n) for categorical variables. The number of patients with available data is indicated in brackets.

Renal impairment: defined as estimated glomerular filtration rate <60ml/min/1.73m². Lesion characteristics at index procedure are reported.
CABG: coronary artery bypass graft;; KBT: kissing balloon technique LAD: left anterior descending artery; LCX: left circumflex; MI: myocardial infarction; (N)STEMI: (non-) ST elevated myocardial infarction; PCI: percutaneous coronary intervention; POT: proximal optimization technique; RCA: right coronary artery.

Table 4 Suppl: Baseline patient characteristics according to use of KBT - inverse propensity score weighted

	KBT n=1517	No KBT n=2663	P-value
Patient characteristics			
Age, years	65.5±10.9 (1517)	65.5±11.1 (2663)	0.99
Gender, male	76.5% (1160/1517)	76.5% (2037/2663)	0.99
Body mass index, kg/m²	27.4±4.5 (1297)	27.9±4.56 (2371)	<0.001
Diabetes mellitus	28.0% (423/1513)	28.2% (745/2643)	0.89
Current smoking	19.6% (283/1445)	19.7% (496/2522)	0.93
Hypertension	70.2% (1019/1452)	67.9% (1729/2546)	0.13
Hypercholesterolemia	63.4% (897/1414)	61.6% (1535/2494)	0.25
Renal impairment	8.7% (131/1506)	8.7% (230/2650)	0.98
Previous MI	24.0% (353/1468)	23.9% (619/2592)	0.92
Previous PCI	30.5% (456/1494)	30.5% (800/2626)	0.98
Previous CABG	4.3% (64/1483)	4.3% (112/2620)	0.97
Clinical presentation			
Silent ischemia	13.5% (205/1517)	12.2% (325/2663)	0.21
Stable angina	39.4% (598/1517)	40.7% (1084/2663)	0.41
Unstable angina	13.0% (198/1517)	11.9% (316/2663)	0.28
NSTEMI	21.9% (332/1517)	23.1% (614/2663)	0.40
STEMI	12.1% (183/1517)	12.1% (322/2663)	0.99
Vessel treated			
RCA	14.6% (221/1517)	17.9% (475/2663)	0.006
Left main	13.6% (206/1517)	13.6% (362/2663)	0.99
LAD	69.6% (1056/1517)	69.6% (1854/2663)	0.99
LCX	29.4% (446/1517)	31.6% (841/2663)	0.14
Graft (arterial of venous)	0.05% (1/1517)	0.3% (8/2663)	0.08
Lesion characteristics			
N of lesions identified, per patient	2.1±1.1 (1517)	2.1±1.1 (2663)	0.99
N of lesions treated, per patient	1.5±0.8 (1517)	1.5±0.8 (2663)	0.39
Long lesions	43.6% (661/1517)	43.6% (1160/2663)	0.99
True bifurcation	61.2% (929/1517)	53.2% (1418/2663)	<0.001
Two-stent technique	27.5% (417/1517)	20.9% (557/2663)	<0.001
POT	37.7% (572/1517)	37.7% (1004/2663)	0.99
Procedure characteristics			
N of study stents implanted per patient	1.9±1.1 (1517)	1.9±1.1 (2663)	0.82
Length of implanted study stents per patient, mm	36.6±22.4 (1515)	36.6±23.4 (2663)	0.99

Data are mean ± standard deviation for continuous variable with or % (n) for categorical variables. The number of patients with available data is indicated in brackets.

Renal impairment: defined as estimated glomerular filtration rate <60ml/min/1.73m². Lesion characteristics at index procedure are reported.

CABG: coronary artery bypass graft;; KBT: kissing balloon technique LAD: left anterior descending artery; LCX: left circumflex; MI: myocardial infarction; (N)STEMI: (non-) ST elevated myocardial infarction; PCI: percutaneous coronary intervention; POT: proximal optimization technique; RCA: right coronary artery.

Table 5 Suppl: Multivariate logistic regression of 1-year TLF

	Odds ratio	95% confidence interval	P-value
Use of POT	0.65	0.43 to 0.99	0.046
Use of KBT	0.96	0.68 to 1.36	0.81
Use of POT and KBT (interaction effect)	1.11	0.59 to 2.07	0.76
Age	1.02	1.17 to 2.07	0.003
Current Smoker	1.42	0.99 to 2.21	0.053
Renal impairment	1.77	1.02 to 2.12	0.038
Previous PCI	1.56	1.23 to 2.56	0.002
History of MI	1.48	1.07 to 2.29	0.021
Number of Lesion Identified	1.25	1.006 to 1.03	0.005
Left main treated	1.47	0.99 to 2.02	0.055
Imaging	1.57	0.29 to 1.04	0.064

Table 6 Suppl: One-year clinical outcomes according to use of POT and KBT - inverse propensity score weighted

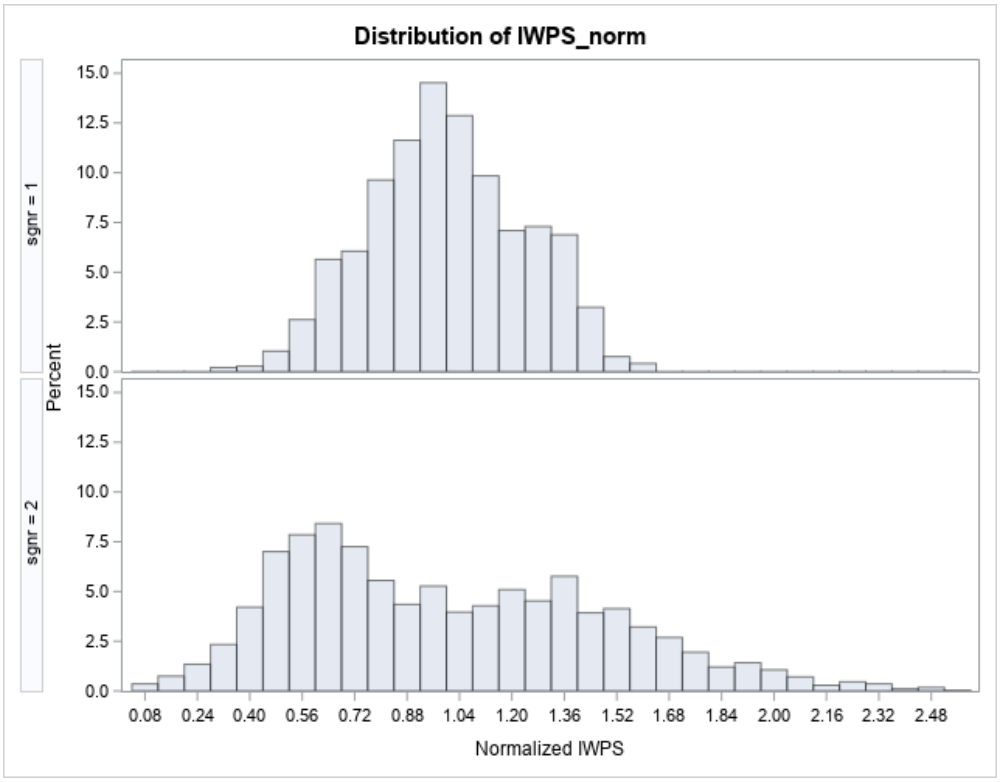
	POT and KBT n=627	POT and No KBT n=762	No POT and KBT n=864	No POT and no KBT n=1848	P-value
Primary outcome					
Target lesion failure	3.6% (22/627)	3.8% (29/762)	5.0% (43/864)	5.7% (105/1848)	0.09
Cardiac death	2.3% (14/627)	1.6% (12/762)	1.7% (15/864)	2.2% (41/1848)	0.60
Target vessel MI	0.2% (1/627)	0.9% (7/762)	1.6% (14/864)	2.5% (47/1848)	<0.001
Clinically driven TLR	1.3% (8/627)	1.6% (13/762)	2.7% (23/864)	3.4% (64/1848)	0.007
Secondary outcomes					
All-cause death	3.5% (22/627)	2.2% (17/762)	2.7% (23/864)	3.8% (71/1848)	0.13
All MI	0.4% (3/627)	1.0% (7/762)	2.2% (19/864)	2.89% (53/1848)	<0.001
Revascularizations					
TVR	2.7% (17/627)	3.4% (26/762)	3.8% (33/864)	4.6% (85/1848)	0.14
TV non-TLR	1.6% (10/627)	1.8% (14/762)	1.1% (9/864)	1.3% (25/1848)	0.56
TLR	1.3% (8/627)	1.6% (13/762)	2.8% (24/864)	3.6% (66/1848)	0.004
Clinically driven revascularizations					
TVR	2.7% (17/627)	3.4% (26/762)	3.7% (32/864)	4.5% (83/1848)	0.19
TV non-TLR	1.6% (10/627)	1.8% (14/762)	1.1% (9/864)	1.3% (24/1848)	0.53
Target vessel failure	5.0% (31/627)	5.6% (42/762)	5.8% (50/864)	6.5% (121/1848)	0.50
Stent thrombosis					
Definite	0.3% (2/627)	0.0% (0/762)	0.8% (7/864)	1.0% (18/1848)	0.03
Probable	0.0% (0/627)	0.0% (0/762)	0.4% (3/864)	0.4% (6/1848)	0.16
Definite/probable	0.3% (2/627)	0.0% (0/762)	1.2% (10/864)	1.3% (25/1848)	0.004
Possible	0.8% (5/627)	0.7% (5/762)	0.9% (8/864)	0.8% (14/1848)	0.95
All bleedings	3.10% (19/627)	2.88% (22/762)	2.1% (18/864)	2.1% (39/1848)	0.35
Bleeding BARC type 1 to 2	1.8% (11/627)	2.4% (18/762)	1.6% (14/864)	1.1% (20/1848)	0.09

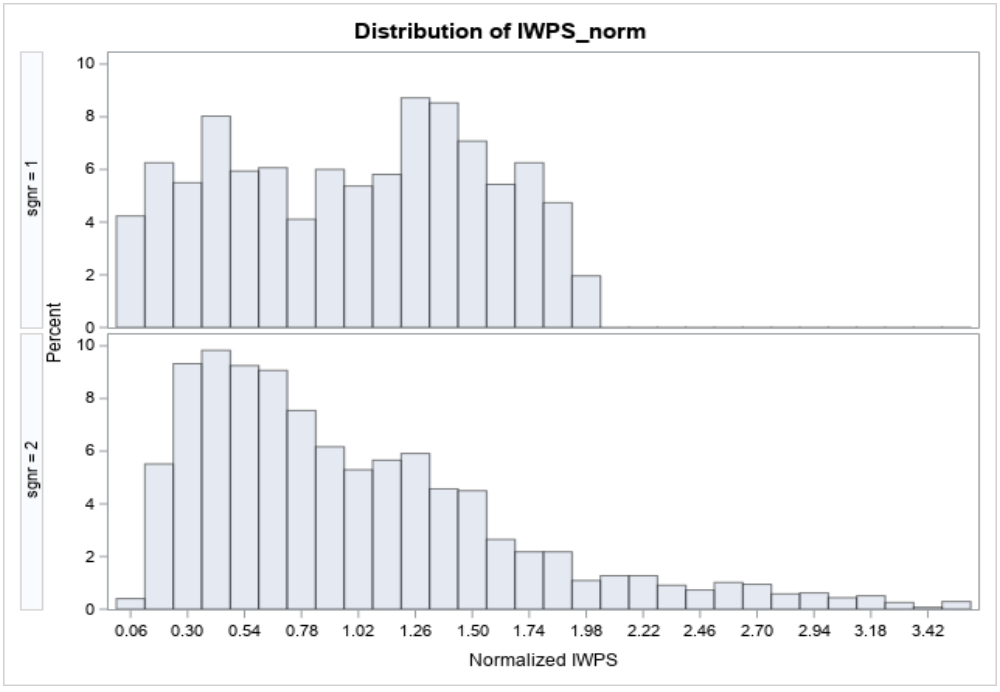
	POT and KBT n=627	POT and No KBT n=762	No POT and KBT n=864	No POT and no KBT n=1848	P-value
Bleeding BARC type 3 to 5	1.4% (9/627)	0.2% (2/762)	0.5% (4/864)	1.2% (23/1848)	0.03

Events are reported as % (n) in the patient population that reached 1-year follow-up, died during follow-up or who had event that contributed to the primary endpoint (n=4230 patients with at least 1 bifurcation lesion). Out of 4230 patients 129 patients were excluded from this comparison because of lack of information on POT or KBT.

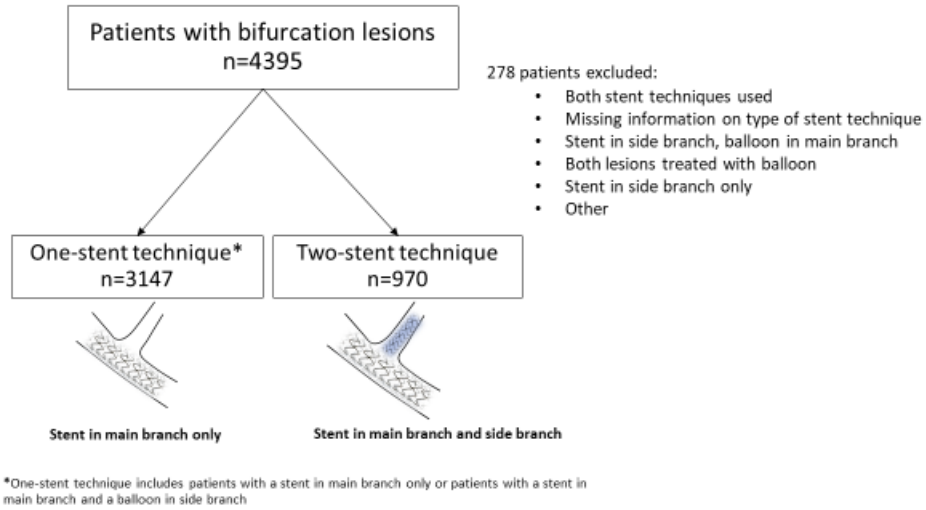
Target lesion failure: composite of cardiac death, TV-MI or clinically driven TLR. Target vessel failure: composite of cardiac death, TV-MI or clinically driven TVR

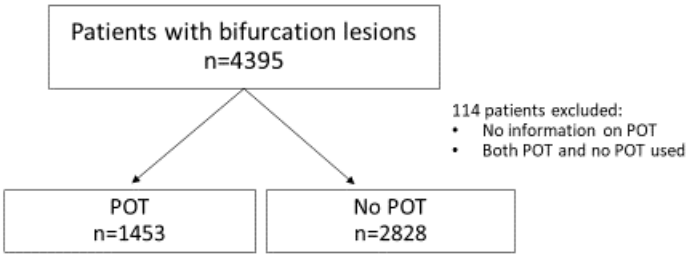
BARC: Bleeding Academic Research Consortium; MI: myocardial infarction; TLR: target lesion revascularization; TV non-TL: target vessel, non-target lesion, revascularization; TVR: target vessel revascularization

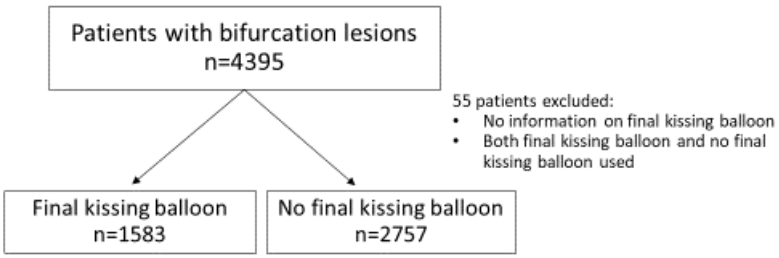




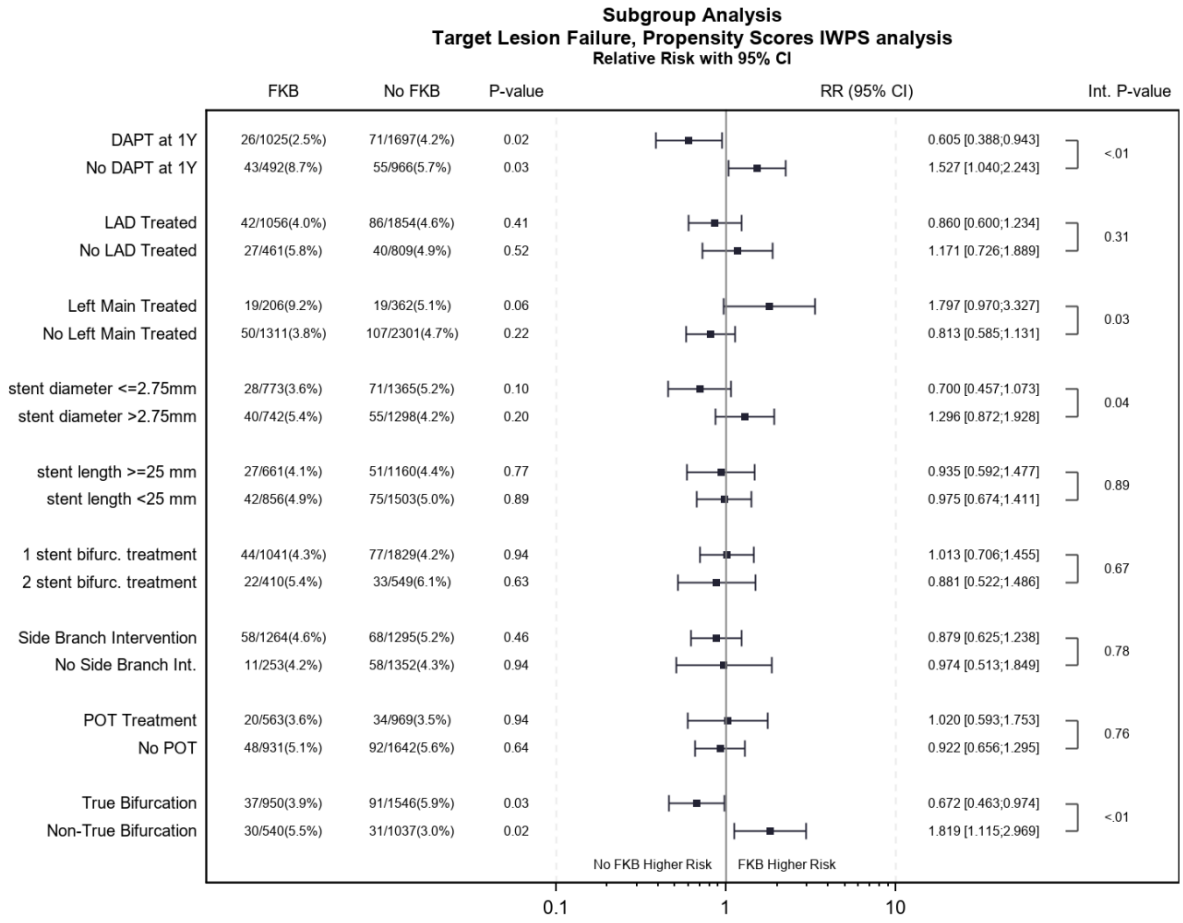
Suppl Figure 1: Distribution of the inverse weights for POT vs POT (A) and KBT vs no KBT (B)







Suppl Figure 2: Overview of bifurcation subgroups



Suppl Figure 3: Impact of KBT in major angiographic and procedural subgroups