

## DRUG ELUTING STENTS

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### Treatment of Coronary Bifurcation Lesions with Drug-Eluting Stents: Insights from the First Phase of the Prospective Multicenter German Drug-Eluting Stent Registry

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**Background:** Controversy exists about the impact of treating bifurcations on overall outcome of coronary interventions using drug-eluting stents (DES). We sought to investigate 1-year outcome of the treatment of bifurcation lesions using DES in a large “real-world” cohort.

**Methods and Results:** Among 5,126 patients enrolled in phase I of the multicenter German Drug-Eluting Stent Registry, 814 (16%) were treated for a bifurcation lesion. Patients with bifurcations were compared to those without bifurcations in terms of baseline characteristics, major adverse cardiac and cerebrovascular events (MACCE) and target vessel revascularization (TVR) at 1 year. Usage of sirolimus-eluting stents (SES) versus paclitaxel-eluting stents (PES) was also evaluated. In total, 1,021 and 5,189 stents were implanted in the bifurcation (1.25 stents/patient) and nonbifurcation (1.2 stents/patient) group, respectively, but 64.5% of bifurcation lesions were treated with a single stent. More complex lesion and procedural characteristics were observed in the bifurcation group. However, there was no difference in 1-year MACCE rates (a composite of death, myocardial infarction, and stroke) between the bifurcation group and nonbifurcation group (8.1% vs. 8.3%,  $P = 0.85$ ). Rates of TVR (11.2% vs. 10.8%,  $P = 0.75$ ) and Academic Research Consortium-defined definite stent thrombosis (0.9% vs. 0.8%,  $P = 0.67$ ) were also comparable. MACCE and TVR rates remained similar after adjustment for differences in baseline characteristics. MACCE and TVR in SES patients were 7.2% and 12.6% versus 8.7% and 10.2% in PES patients ( $P = 0.46$  and  $P = 0.30$ , respectively).

**Conclusion:** In this large multicenter registry, treatment of bifurcation lesions with DES appears effective and safe. The presence of bifurcations did not affect 1-year outcomes after DES implantation. The outcomes for SES and PES were similar. (J Intervent Cardiol 2012;25:344–352)

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## Introduction

Approximately 15–20% of percutaneous coronary intervention (PCI) procedures are performed at or adjacent to a significant division of a major epicardial coronary artery. These coronary bifurcations represent one of the most challenging lesion subsets.<sup>1</sup> In the bare metal stent (BMS) era, PCI in bifurcations was associated with lower procedural success rates and a greater restenosis rate compared to nonbifurcation lesions.<sup>2–5</sup> Although drug-eluting stents (DES) are currently preferred for treatment of bifurcation lesions in clinical practice, limited data exist about acute and long-term clinical results compared to nonbifurcation lesions. Moreover, there is uncertainty about the impact of different DES types on outcome. Finally, there is concern about an increased risk of stent thrombosis after DES implantation for bifurcation lesions.<sup>6–8</sup>

Therefore, we compared the clinical outcome of PCI for bifurcation and nonbifurcation lesions using data from phase I of the prospective multicenter German DES.DE registry. The size and quality of this real-world registry makes it possible to compare sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES), and to identify predictors of clinical events.

## Methods

**Registry Design and Study Population.** The prospective multicenter German drug-eluting stent (DES.DE) registry was initiated in October 2005 as an observational real-world registry by the Deutsche Gesellschaft für Kardiologie (DGK, German Cardiac Society), Bundesverband Niedergelassener Kardiologen (BNK, German Society of Cardiologists in Private Practice), and Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK, The Working Group of Leading Hospital Cardiologists). In phase I of the registry (October 2005–October 2006), only the 2 FDA approved DES, PES (Taxus<sup>TM</sup>, Boston Scientific Corp., Natick, MA, USA) and SES (Cypher<sup>TM</sup>, Cordis Corp., Miami Lakes, FL, USA) met the quality criteria of the registry. In all cases, the interventional strategy, including choice of stent, use of intravascular ultrasound, and the choice of periprocedural adjunctive therapy, was at the discretion of the responsible physician. Details of the registry have been described previously.<sup>9</sup> In the period between October 2005 and

October 2006, a total of 6,394 patients were enrolled in phase I of the registry. The current analysis is based on 5,126 patients who underwent PCI of one target vessel using DES. The cohort was divided into 814 (16%) patients treated for bifurcation lesions and 4,312 (84%) treated for nonbifurcation lesions. Bifurcation lesions were defined as those involving a side branch  $\geq 2$  mm in diameter by visual estimation.

**Data Collection and Follow-Up.** Data were collected via an internet platform by the Institut für Klinische Kardiovaskuläre Forschung (IKKF, Institute for Clinical Cardiovascular Research) of the German Cardiac Society. Written informed consent for processing data at the Institut für Herzinfarktforschung (IHF, Ludwigshafen) was required. Baseline clinical and angiographic characteristics, and certain procedural and clinical in-hospital events were recorded for all enrolled patients. Paper-based clinical and health quality follow-up assessments were performed at 3, 6, 9, and 12 months after initial stent placement and group allocation. IKKF forwarded corresponding questionnaires to the patients and collected all data and sent them to IHF for statistical processing. In case of an event, the IHF contacted the patient or the referring hospital for the reports. All events were verified by charts review or by direct contact with attending physicians. If patients could not be reached, the local government registration office was contacted. If patients stopped responding during follow-up, additional telephone follow-up was performed. Complete 1-year follow-up was obtained in 93.1%. Relevant events (but not routine angiography without intervention) were reviewed by a Critical Event Committee (CEC), and processed by IHF. Failure to collect detailed documentation (<1%) of a revascularization event (PCI or bypass surgery) was considered a target vessel revascularization (TVR). A query management was established for missing or unclear data. Announced source data verification was performed at 24 randomly selected hospitals, with comparison of the documented data with the hospital charts.

**Definitions.** The end-points of the registry and of the current analysis were the occurrence of TVR and major adverse cardiac and cerebrovascular events (MACCE), defined as the composite of death (cardiac and noncardiac), myocardial infarction (MI), and stroke at 1-year follow-up. Death was defined as all causes of mortality. MI was defined as ST-elevation myocardial infarction (STEMI; ST-elevation at least 1 mm in two or more limb leads or at least 2 mm in two or more contiguous precordial leads or development

of new left bundle branch block on the ECG) or non-ST-elevation myocardial infarction (NSTEMI; pathological increase of cardiac specific enzymes with CK-MB > 1.5 times of normal limits, Troponin T or I > 99th percentile of normal value). TVR was defined as a repeated procedure, either PCI or coronary artery bypass grafting (CABG), on the target vessel. Routine angiography was not part of the protocol in DES.DE for any subgroup of patients; therefore, all reinterventions are considered clinically driven. Definite stent thrombosis (presence of angiographic thrombus with a complete occlusion) was defined as proposed by the Academic Research Consortium (ARC).<sup>10</sup>

**Statistical Analysis.** Statistical analysis was performed using the SAS statistical package, version 9.1 (SAS Institute, Cary, NC, USA). Demographic characteristics, preexisting risk factors, procedure-related variables, and 1-year outcomes were summarized using mean value with standard deviation or median and interquartile range for continuous variables, and frequency and percentage for categorical variables. Differences in baseline, procedural, and angiographic characteristics, and in-hospital and follow-up data were compared between patients treated for bifurcation lesions and those treated for nonbifurcation lesions by chi-square test, whereas continuous variables were compared by Wilcoxon's rank sum test. The 1-year event-free survival rates for MACCE and TVR were analyzed using Kaplan–Meier curves and were compared using the log-rank test. P values less than 0.05 were considered significant and were results of 2-tailed tests. Stepwise multivariate logistic regression analysis was used to estimate the adjusted odds ratios with 95% confidence intervals for MACCE and TVR at 1 year. The variables entered into the multivariate models were age (>75 years), hypertension, smoking, hyperlipidemia, family history of coronary artery disease, STEMI, target vessel = left main, target vessel = left anterior descending, target vessel = bypass graft, peripheral arterial disease, vessel diameter <3 mm, lesion length >15 mm, type C lesion, stent type, and bifurcation lesion.

## Results

**Baseline Characteristics.** Of 5,126 patients treated with DES, 814 (16%) were treated for bifurcations. Patients in the bifurcation group more commonly had hypertension and hyperlipidemia, and more often

had a positive family history of coronary artery disease. Patients treated for bifurcations more often presented with stable angina compared to the nonbifurcation group (59.3% vs. 55.4%,  $P < 0.05$ ), and STEMI was a more frequent presentation in patients without bifurcation lesions (9.4% vs. 7%,  $P < 0.05$ ). Other baseline clinical characteristics were similar between both study groups as listed in Table 1.

### Angiographic and Procedural Characteristics.

A total of 1,021 stents were implanted in the bifurcation group (1.25 stent/patient) compared to 5,189 stents in the nonbifurcation group (1.20 stent/patient). Most bifurcation lesions were treated with a single stent ( $n = 520$ , 64.5%), so most side branches were not stented. Target vessel distribution was different between both groups, with the left main coronary artery and the left anterior descending artery representing a higher proportion in the bifurcation group (9.3% vs. 1.9% and 59.7% vs. 47.4%, respectively,  $P$  for both <0.0001). Of note, the left main has been reported treated more frequently than reported diseased in both study groups. This is most probably related to treatment strategies involving a left main stem that was initially evaluated as minimally diseased but eventually required treatment (e.g., ostial left anterior descending and left circumflex interventions, plaque or carina shift, dissections, etc.). Whereas type C lesions were more commonly described in the bifurcation cohort (41% vs. 25.5%,  $P < 0.0001$ ), in-stent restenosis was more frequently treated in the nonbifurcation group (16.9% vs. 13.2%,  $P < 0.01$ ). Direct stenting was more often performed in the nonbifurcation group (43.3% vs. 33.5%,  $P < 0.0001$ ). Though rotational atherectomy was used in only a few cases, significantly more patients with bifurcation lesions received a rotablation (1.2% vs. 0.4%,  $P < 0.01$ ). Glycoprotein IIb/IIIa antagonists were also more frequently given in patients treated for bifurcation lesions (20.9% vs. 15.6%,  $P < 0.001$ ). Other angiographic and procedural details are listed in Table 2.

**In-Hospital Outcome.** No statistically significant difference was found regarding death, MI, or stroke between patients treated for bifurcation or nonbifurcation lesions during their in-hospital course. The overall MACCE rate was 2.1% in bifurcations compared to 2% in nonbifurcation lesions ( $P = 0.89$ ). The occurrence of postprocedural myonecrosis defined as any elevation of cardiac biomarkers after PCI was recorded for 4,378 patients (85%), and did not differ between the bifurcation and nonbifurcation group (15.5% vs. 15.1%,

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**Table 1.** Baseline Patient Demographics and Clinical Characteristics of the Bifurcation and Nonbifurcation Group

	Bifurcation (n = 814)	Nonbifurcation (n = 4,312)	P Value
Male sex (%)	74.4	74.7	0.90
Age (years) mean ± SD	64.9 ± 10.5	65.2 ± 10.5	0.75
Body mass index (kg/m <sup>2</sup> ) median (IQR)	27.4 (25–30.1)	27.4 (24.9–30.1)	0.88
Diabetes mellitus (%)	29.5	32.1	0.14
Arterial hypertension (%)	86.6	83.3	<0.05
Hyperlipidemia (%)	83.3	79.8	<0.05
Smoking (%)	24.7	21.9	0.09
Family history of coronary artery disease (%)	42.9	34.9	<0.001
Prior myocardial infarction (%)	31.3	30.1	0.50
Prior percutaneous coronary intervention (%)	42.6	45.1	0.18
Prior CABG (%)	15.8	14.2	0.22
Prior stroke (%)	3.6	4.6	0.22
Peripheral arterial disease (%)	11.3	9.1	0.06
Atrial fibrillation (%)	8.0	8.0	0.96
Chronic heart failure (%)	15.2	15.6	0.79
Chronic kidney disease (%)	7.9	12.4	0.37
STEMI	7.0	9.4	<0.05
NSTEMI	10.0	8.1	0.08
UAP	10.5	8.6	0.09
Non-ACS	59.3	55.6	<0.05
Ejection fraction <30% (%)	3.5	3.7	0.83

ACS = acute coronary syndrome; CABG = coronary artery bypass grafting; IQR = interquartile range; NSTEMI = non-ST segment elevation myocardial infarction; SD = standard deviation; STEMI = ST segment elevation myocardial infarction; UAP = unstable angina pectoris.

P = 0.76). The need for urgent revascularization, the occurrence of renal failure requiring dialysis, and the incidence of severe bleeding were also similar in both groups. Details of in-hospital outcome are listed in Table 3.

**One-Year Outcome.** The 1-year follow-up rate was 93.7% for patients with bifurcation lesions and 93.5% for patients treated for nonbifurcation lesions. Similar to the in-hospital-outcome, no significant difference was found regarding death, MI, stroke or TVR between the 2 groups at 1-year follow-up. MACCE and TVR rates at 1 year were 8.1 and 11.2% in patients with bifurcation lesions versus 8.3 and 10.8% in patients with nonbifurcation lesions (P = 0.85 and P = 0.75, respectively). Accordingly, the Kaplan–Meier curves for survival free of MI and stroke as well as for survival free of TVR were congruent throughout the whole observation period (Fig. 1). ARC-defined definite stent thrombosis rates were nearly identical in both study groups (0.9% versus 0.8% in patients treated for bifurcation and nonbifurcation lesions, respectively, OR = 1.19, 95% CI 0.52–2.72, P = 0.67). Patients treated at bifurcations were found more adherent to clopidogrel at 1-year follow-up (60.6% vs.

55.0%, P < 0.01), but no differences in the use of aspirin (94.7% vs. 94.2%) or oral anticoagulants (7.4% vs. 8.3%) were observed. Data of the 1-year outcome are listed in Table 4. After adjustment for baseline clinical, angiographic, and procedural differences, treatment of a bifurcation was not associated with increased MACCE or TVR rates at 1 year in the multivariate analysis (adjusted OR for MACCE = 0.97, 95% CI 0.73–1.31; adjusted OR for TVR = 0.93, 95% CI 0.72–1.20).

**Sirolimus-Eluting Stents versus PES in Treatment of Bifurcation Lesions.** Patients treated for nonbifurcations more often received PES, whereas patients treated for bifurcation lesions were more commonly treated with SES, though this was not statistically significant (Table 2). The registry contains a nearly identical number of patients with bifurcation lesions treated with SES (n = 387) or PES (n = 420). Both groups of patients did not significantly differ in their clinical and procedural characteristics, except for chronic kidney disease which was more prevalent in the PES group (14.6% vs. 7.9%, P < 0.01). Overall, the type of stent used (SES vs. PES) did not impact the rates of MACCE, TVR, or definite stent thrombosis at

**Table 2.** Angiographic and Procedural Characteristics of Patients Treated for Bifurcational and Nonbifurcational Disease with Drug-Eluting Stents

	Bifurcation (n = 814)	Non-Bifurcation (n = 4312)	P Value
Vessel disease (%)			
1-vessel disease	26.8	27.4	0.72
2-vessel disease	31.2	33.4	0.23
3-vessel disease	39.1	38.6	0.80
Left main disease	2.9	0.6	<0.0001
Target vessel (%)			
Left anterior descending coronary artery	59.7	47.4	<0.0001
Left circumflex coronary artery	22.0	20.9	0.47
Right coronary artery	9.1	29.9	<0.0001
Left main coronary artery	9.3	1.9	<0.0001
Bypass graft	2.6	5.3	<0.001
Lesion class AHA/ACC (%)			
Type A	5.6	13.7	<0.0001
Type B	53.4	60.8	<0.001
Type C	41.0	25.5	<0.0001
Chronic total occlusion (%)	3.2	3.5	0.70
In-stent restenosis (%)	13.2	16.9	<0.01
Lesion length, mm, median (IQR)	15 (12–21)	15 (10–20)	0.51
Reference diameter, mm, median (IQR)	3.0 (2.5–3.0)	3.0 (2.6–3.0)	0.11
Procedural characteristics			
Number of stents implanted	1021	5189	
Sirolimus-eluting stents (%)	44.3	41.5	0.11
Paclitaxel-eluting stents (%)	51.7	55.8	<0.05
Bare metal stents (%)	4.0	2.7	<0.05
Total stent length, mm, median (IQR)	18 (13–24)	18 (13–24)	0.25
Stent diameter, mm, median (IQR)	3.0 (2.5–3.0)	3.0 (2.8–3.0)	<0.001
Direct stenting (%)	33.5	43.3	<0.0001
Post-procedural TIMI 3 flow (%)	98.1	97.8	0.50
Use of IVUS (%)	1.1	0.7	0.21
Use of rotational atherectomy (%)	1.2	0.4	<0.01
Use of GP IIb/IIIa antagonists (%)	20.9	15.6	<0.001

GP = glycoprotein; IQR = interquartile range; IVUS = intravascular ultrasound; TIMI = Thrombolysis in Myocardial Infarction. Type A lesions = discrete, concentric, nonangulated, nonostial lesions with little or no calcification or thrombus; type B lesions = tubular, eccentric, moderately angulated, ostial, bifurcated, or totally occluded (<3 months) lesions with moderate to heavy calcification or some thrombus; type C lesions = diffuse, extremely angulated, totally occluded (>3 months) lesions with inability to protect a major side branch or degenerated vein grafts.

1-year follow-up. The MACCE rate was numerically lower in the SES group (7.2% vs. 8.7%, P = 0.46), whereas the TVR rate was numerically higher in the SES group (12.6% vs. 10.2%, P = 0.3). Data comparing the 1-year outcome of patients with both types of DES used for bifurcation lesions are presented in Fig. 2.

### Discussion

The principal finding of the current analysis is that treatment of bifurcation lesions with DES is effective and safe and does not impair 1-year outcomes

compared to treatment of nonbifurcation lesions. Furthermore, the results for SES and PES were similar. DES.DE is a large multicenter German registry characterized by a high follow-up rate and an excellent data quality. The registry comprises a high number of patients with “off-label” indications, which allows meaningful assessments about subgroups not extensively studied in randomized trials. Coronary bifurcation lesions are regarded as complex interventions, because they are technically challenging and associated with more acute complications and worse long-term outcome as compared to intervention in nonbifurcation lesions.<sup>11</sup> In the BMS era, stenting of bifurcations

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**Table 3.** In-Hospital Outcome of Patients Treated for Bifurcational and Nonbifurcational Disease with Drug-Eluting Stents

	Bifurcation (n = 814)	Nonbifurcation (n = 4,312)	P Value
Death (%)	0.7	0.5	0.36
Myocardial infarction (%)	1.2	1.1	0.83
Stroke (%)	0.4	0.5	0.55
MACCE (%)	2.1	2.0	0.89
Repeat urgent revascularization (%)			
PCI	0	0.1	0.45
CABG	0.6	0.8	0.60
Repeat elective revascularization (%)			
PCI	2.1	2.8	0.26
CABG	0.4	0.7	0.28
Renal failure requiring dialysis (%)	1.7	1.4	0.41
Severe bleeding complications (%)	0.8	0.5	0.36

CABG = coronary artery bypass graft; MACCE = major adverse cardiac and cerebrovascular events; PCI = percutaneous coronary intervention.

was associated with less acute and long-term success with a remarkably high risk of in-stent restenosis at the ostium of the side branch.<sup>12</sup> A technique with 2 BMSs was inferior to a provisional single stent technique in nonrandomized studies.<sup>4,13</sup>

### Drug-Eluting Stents for Bifurcational Disease.

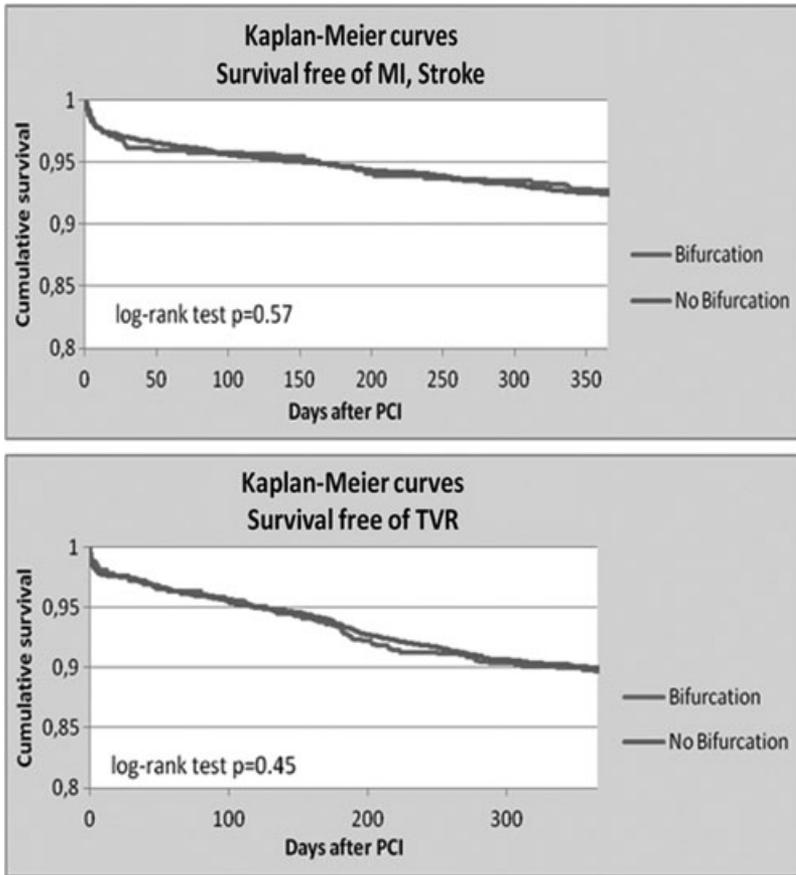
Nowadays, bifurcations are predominantly handled with DES, mainly because of the consensus of interventionists that a reduction of restenosis by DES can be translated into stenting of bifurcations. Nevertheless, bifurcations are still classified as “off-label,” and data supporting DES use in bifurcations are scarce, particularly in a real-world scenario. A subanalysis of the Stenting Coronary Arteries in NonStress/Benestent Disease (SCAND-STENT) trial comparing SES and BMS in coronary bifurcations showed that SES implantation considerably improves both angiographic and clinical outcomes compared to bare metal stenting. SES significantly reduced the restenosis rate from 28.3% to 4.9% in the main branch and from 43.4% to 14.8% in the side branches. Major adverse cardiac events (MACE) occurred in 9% with SES versus 28% with BMSs ( $P = 0.01$ ), and stent thrombosis was observed in 0% versus 9% ( $P = 0.02$ ).<sup>3</sup> The outcome of the DES-arm of the SCAND-STENT trial is remarkably similar to the results in the bifurcation cohort in this analysis of DES.DE, indicating a transferability of favorable results with DES in bifurcations into general clinical practice. Similarly, other registry studies have shown marked reductions in MACE and target lesion revascularization (TLR) rates with DES compared with historical BMS cohorts.<sup>4,5</sup>

### Bifurcations as Risk Factor for Clinical Events.

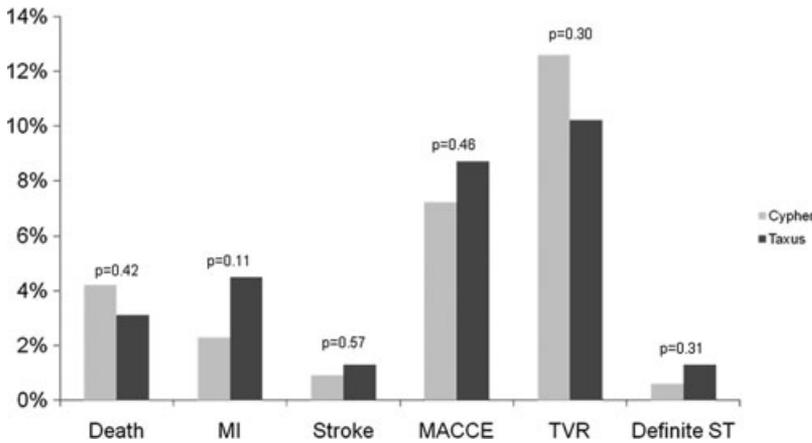
Our study suggests that PCI of a bifurcation is no

longer a risk factor for adverse events if DES are implanted. Similarly, data from the Arterial Revascularization Therapies Study (ARTS) II showed that bifurcation lesions did not affect 1-year outcomes after SES implantation when compared to nonbifurcation lesions.<sup>14</sup> This study was a nonrandomized posthoc analysis done on a total of 607 patients with multivessel coronary artery disease. These data may be underpowered to demonstrate the potential adverse impact of bifurcation lesion treatment in multivessel disease using DES because of the strong trend toward a higher incidence of MI in the bifurcation group ( $P = 0.08$ ). An extended 3-year follow-up of the ARTS II study population showed that combined definite and probable stent thrombosis was more commonly seen in bifurcations, though this did not translate into an increase in major adverse clinical events.<sup>15</sup> Our results which arise from a much larger patient population do not even show numerical increases for death, MI, or stent-thrombosis in the bifurcation cohort at 1-year follow-up.

**Stent Type and Stenting Strategy.** It is still an open question, whether there is a superior DES for bifurcation procedures. The results from the COBIS (COronary Bifurcation Stenting) registry<sup>16</sup> comparing SES and PES favored the use of SES because of better long-term outcomes primarily because of a decreased rate of TLR and TVR, with no significant difference regarding death or MI. Such an advantage for SES over PES in the treatment of bifurcations is not supported by the present comparison. Whether newer generation DES would offer similar or better efficacy is currently unknown and must await randomized controlled trials; yet, upcoming analyses from phases II and III of our registry comparing newer generation DES may further



**Figure 1.** Event-free survival at 1 year. Kaplan–Meier curves for event-free survival until 1 year of follow-up among patients with bifurcation and nonbifurcation lesions. MI = myocardial infarction; PCI = percutaneous coronary intervention; TVR = target vessel revascularization.



**Figure 2.** Cypher vs. Taxus for bifurcation lesions. Clinical outcome at 1 year for patients treated with Cypher versus Taxus stents for bifurcation lesions. MACCE = major adverse cardiac and cerebrovascular events; MI = myocardial infarction; TVR = target vessel revascularization; ST = stent thrombosis.

clarify this issue. The optimal strategy for treating coronary bifurcations also remains a debatable issue. Unfortunately, we do lack in our registry accurate data regarding the anatomical details of the bifurcation together with the procedural and technical issues. Nevertheless, having a stent-patient ratio of about 1.25 (a total of 1,021 DES were used in treatment of 814 pa-

tients with bifurcation lesions) and the fact that almost two-thirds of patients received a single stent at the bifurcation suggest that most operators proceeded with a provisional single-stent strategy. This strategy has been associated with improved outcomes compared to a routine two-stent strategy in the recently published BBC ONE and NORDIC I trials<sup>17,18</sup> partially

**Table 4.** One-Year Outcome of Patients Treated for Bifurcational and Nonbifurcational Disease with Drug-Eluting Stents

	Bifurcation (n = 757)	Nonbifurcation (n = 4,015)	P Value
Death (%)	3.7	4.1	0.58
Myocardial infarction (%)	3.4	3.3	0.89
Stroke (%)	1.1	1.2	0.86
MACCE (%)	8.1	8.3	0.85
TVR (%)	11.2	10.8	0.75
ARC-defined definite stent thrombosis (%)	0.9	0.8	0.67
Bleeding requiring blood transfusion (%)	0.8	1.1	0.49

ARC = Academic Research Consortium; MACCE = major adverse cardiac and cerebrovascular events; TVR = target vessel revascularization.

explaining the low event rate in the bifurcation group in our study.

**Study Limitations.** In general, this study has the inherent limitations of any nonrandomized multicenter registry such as residual confounding and underreporting of events, for example, stent thrombosis. Yet with enrollment of more than 5,000 patients, which were very closely monitored by 2 independent critical event committees, these problems were addressed. Concerning the issue of bifurcation stenting, some specific limitations have to be considered. First, anatomical details (e.g. medina classification) of bifurcation lesions were not documented. Second, procedural details (duration, fluoroscopy time, and amount of contrast used) were not collected. Also, technical details (number of guidewires used, stenting technique, and kissing-balloon dilatation) were not recorded. Third, no data about residual stenosis, dissections, and final TIMI flow in the side branch were documented. These missing characteristics of bifurcation lesions and side branch treatment may have had a major effect on the study findings. Finally, data at 1-year follow-up showed that patients treated for bifurcation were more adherent to their medications compared to patients treated for de novo lesions, which might have contributed to the similar long-term outcome observed in both patient cohorts.

## Conclusion

In this large cohort representing contemporary PCI practice in Germany, treatment of bifurcation lesions with DES (mostly using a single stent strategy) was

not associated with more adverse events compared with nonbifurcation lesions. No difference in outcome between patients treated with SES versus PES was observed. DES of either type seems to equalize the treatment success between patients with and without bifurcation lesions.

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## References

1. Myler RK, Shaw RE, Stertz SH, et al. Lesion morphology and coronary angioplasty: Current experience and analysis. *J Am Coll Cardiol* 1992;19:1641–1652.
2. Bernardi G, Padovani R, Morocutti G, et al. Clinical and technical determinants of the complexity of percutaneous transluminal coronary angioplasty procedures: Analysis in relation to radiation exposure parameters. *Catheter Cardiovasc Interv* 2000;51:1–9.
3. Thuesen L, Kelbaek H, Kløvgård L, et al. SCANDSTENT Investigators. Comparison of sirolimus-eluting and bare metal stents in coronary bifurcation lesions: Subgroup analysis of the Stenting Coronary Arteries in Non-Stress/Benestent Disease Trial (SCANDSTENT). *Am Heart J* 2006;152:1140–1145.
4. Yamashita T, Nishida T, Adamian MG, et al. Bifurcation lesions: Two stents versus one stent—immediate and follow-up results. *J Am Coll Cardiol* 2000;35:1145–1151.
5. Ge L, Tsagalou E, Iakovou I, et al. In-hospital and nine-month outcome of treatment of coronary bifurcational lesions with sirolimus-eluting stent. *Am J Cardiol* 2005;95:757–760.
6. Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA* 2005;293:2126–2130.
7. Ong AT, Hoye A, Aoki J, et al. Thirty-day incidence and six months clinical outcome of thrombotic stent occlusion after bare-metal, sirolimus, or paclitaxel stent implantation. *J Am Coll Cardiol* 2005;45:947–953.
8. Hoye A, Iakovou I, Ge L, et al. Long-term outcomes after stenting of bifurcation lesions with the “crush” technique: Predictors of an adverse outcome. *J Am Coll Cardiol* 2006;47:1949–1958.
9. Nienaber CA, Akin I, Schneider S, et al. DES.DE Study Group. Clinical outcomes after sirolimus-eluting, paclitaxel-eluting and bare metal stents (from the first phase of the prospective multicenter German DES.DE Registry). *Am J Cardiol* 2009;104:1362–1369.
10. Cutlip DE, Windecker S, Mehran R, et al. Academic Research Consortium. Clinical end points in coronary stent trials: A case for standard definitions. *Circulation* 2007;115:2344–2351.
11. Latib A, Colombo A. Bifurcation disease: What do we know, what should we do? *JACC Cardiovasc Interv* 2008;1: 218–226.
12. Sheiban I, Albiero R, Marsico F, et al. Immediate and long-term results of “T” stenting for bifurcation coronary lesions. *Am J Cardiol* 2000;85:1141–1144.
13. Al Suwaidi J, Yeh W, Cohen HA, et al. Immediate and one-year outcome in patients with coronary bifurcation lesions

- in the modern era (NHLBI dynamic registry). *Am J Cardiol* 2001;87:1139–1144.
14. Tsuchida K, Colombo A, Lefèvre T, et al. The clinical outcome of percutaneous treatment of bifurcation lesions in multivessel coronary artery disease with the sirolimus-eluting stent: Insights from the Arterial Revascularization Therapies Study part II (ARTS II). *Eur Heart J* 2007;28:433–442.
  15. Routledge HC, Lefèvre T, Colombo A, et al. Three-year clinical outcome of percutaneous treatment of bifurcation lesions in multivessel coronary artery disease with the sirolimus-eluting stent: Insights from the Arterial Revascularisation Therapies Study, part II (ARTS II). *EuroIntervention* 2009;5:190–196.
  16. Song YB, Hahn JY, Choi SH, et al. Sirolimus- versus paclitaxel-eluting stents for the treatment of coronary bifurcations results: From the COBIS (Coronary Bifurcation Stenting) Registry. *J Am Coll Cardiol* 2010;55:1743–1750.
  17. Hildick-Smith D, de Belder AJ, Cooter N, et al. Randomized trial of simple versus complex drug-eluting stenting for bifurcation lesions: The British Bifurcation Coronary Study: Old, new, and evolving strategies. *Circulation* 2010;121:1235–1243.
  18. Steigen TK, Maeng M, Wiseth R, et al. Nordic PCI Study Group. Randomized study on simple versus complex stenting of coronary artery bifurcation lesions: The Nordic bifurcation study. *Circulation* 2006;114:1955–1961.

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