ORIGINAL ARTICLE

Clinical outcomes after zotarolimus and everolimus drug eluting stent implantation in coronary artery bifurcation lesions: insights from the RESOLUTE All Comers Trial

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ABSTRACT

Objective We investigated clinical outcomes after treatment of coronary bifurcation lesions with second generation drug eluting stents (DES).

Design Post hoc analysis of a randomised, multicentre, non-inferiority trial.

Setting Multicentre study.

Patients All comers study with minimal exclusion criteria.

Interventions Patients were treated with either zotarolimus or everolimus eluting stents. The patient population was divided according to treatment of bifurcation or non-bifurcation lesions and clinical outcomes were compared between groups.

Main outcomes measures Clinical outcomes within 2-year follow-up.

Results A total of 2265 patients were included in the present analysis. Two-year follow-up data were available in 2223 patients: 1838 patients in the non-bifurcation group and 385 patients in the bifurcation group. At 2-year follow-up the bifurcation and the non-bifurcation lesion groups showed no significant differences in terms of cardiac death (2.3 vs 2.1, p=0.273), target lesion failure (9.7% vs 13.8%, p=0.255), major adverse cardiac events (11.5% vs 15.1%, p=0.305), target lesion revascularisation (4.7% vs 6.0%, p=0.569), and definite or probable stent thrombosis (1.6% vs 1.8%, p=0.419).

Conclusions The use of second generation DES for the treatment of coronary bifurcation lesions was associated with similar long term mortality and clinical outcomes compared with non-bifurcation lesions.

INTRODUCTION

Percutaneous treatment of coronary artery bifurcation lesions is a recognised challenge in the field of interventional cardiology. Early experiences with balloon angioplasty were characterised by a poor success rate and a high incidence of restenosis.[1 2] The introduction of bare metal stents (BMS) improved procedural success rates, but the long term clinical outcomes remained affected by a high restenosis rate (especially at the side branch ostium), irrespective of the technique used.[3–9] First generation drug eluting stents (DES) caused a substantial reduction in main vessel restenosis, with clinical outcomes remaining poorer in bifurcation lesions compared to non-bifurcation lesions.[10–12] The advent of second generation DES, with new antiproliferative drugs, biocompatible polymer, and newer stent designs incorporating thinner stent struts,[13–15] has shown promising results and improved clinical outcomes compared with first generation DES.[16–18] However, despite the wide use of the newer generation DES, data relating to their performance in the treatment of coronary bifurcation lesions are limited.

The aim of the present study was to investigate the long term clinical outcomes after implantation of second generation DES for the treatment of coronary bifurcations within the large scale multicentre prospective randomised RESOLUTE All Comers Trial.[16]

METHODS

Study design and population

The study design of the RESOLUTE All Comers Trial has previously been described.[16] In brief, the RESOLUTE All Comers Trial is a multicentre, prospective, double-arm, randomised controlled trial with minimal exclusion criteria. Enrolled patients were older than 18 years, and had a diagnosis of chronic stable coronary artery disease or acute coronary syndromes, including ST segment elevation myocardial infarction (STEMI). Patients were eligible if they had at least one coronary lesion with percentage stenosis >50% in a vessel with a reference diameter of 2.25–4.0 mm. No restriction was applied to the total number of treated lesions, treated vessels, lesion length, or number of stents implanted. Exclusion criteria were appropriately minimal, reflecting the all comers design of the trial, namely: a known intolerance to a study drug, metal alloys, or contrast media; planned surgery within 6 months after the index procedure;

childbearing potential; and participation in another trial before reaching the primary end point.

The institutional review board at each study centre approved the study protocol and all patients provided written informed consent. Patients were randomly assigned to undergo percutaneous coronary intervention with either zotarolimus or everolimus eluting stents.

Notably, in the RESOLUTE All Comers Trial at least one off-label criterion was present in 1520 patients (66.3%).

In the present study long term (2-year) clinical outcomes were evaluated according to the treatment of coronary bifurcation lesions. The entire patient population was categorised into a 'bifurcation group' comprising patients with at least one treated coronary bifurcation, and a 'non-bifurcation group' comprising patients without any treated bifurcation. The bifurcation group was further divided according to the adopted bifurcation technique into one or two stent strategy groups.

Stent implantation procedure

Procedures were performed according to standard techniques with full lesion coverage pursued with one or multiple stent implantations. Mixture of different DES types was prohibited unless the operator was unable to insert the study stent. Unplanned revascularisation procedures required stent implantation to be performed using the same stent type as the study stent.

Unfractionated heparin at a dose of 5000 international units (IU) or 70–100 IU/kg to maintain an activated clotting time of >250 s was administered at the index procedure. Glycoprotein IIb/IIIa inhibitors were used at the physician's discretion. All patients received at least 75 mg of acetylsalicylic acid before the procedure. If the patient had received no clopidogrel during the previous 7 days, a loading dose of 300–600 mg of clopidogrel was administered.

All patients were discharged with a prescription for at least 75 mg daily of acetylsalicylic acid indefinitely and 75 mg of clopidogrel for a minimum of 6 months after the index procedure.

The choice of bifurcation lesion stent strategy (one or two stent approach) was at the operator's discretion.

Definitions

All deaths were considered cardiac unless an undisputed non-cardiac cause was present. Myocardial infarction (MI) was defined according to the extended historical protocol definition and according to the Academic Research Consortium (ARC) definitions.[19 20] An MI was defined as periprocedural when occurring within 48 h after percutaneous coronary intervention (PCI). Target lesion revascularisation (TLR) was considered clinically indicated if a diameter stenosis >70% was present, even in the absence of ischaemic signs or symptoms, or if angiography during follow-up showed a diameter stenosis >50% (as assessed by quantitative coronary angiography undertaken by an independent core laboratory) and one of the following was present: (1) presence of a positive history of recurrent angina pectoris, pre-related to the target vessel; (2) objective signs of ischaemia at rest (ECG changes) or during exercise test, presumably related to the target vessel; (3) abnormal results of any invasive functional diagnostic test. Major adverse cardiac events (MACE) included a composite of death, MI (Q wave and non-Q wave), emergent coronary artery bypass surgery, or repeat clinically indicated target lesion percutaneous or surgical revascularisation. Target lesion failure (TLF) was defined as the composite end point of death from cardiac causes, any MI (not clearly attributable to a non-target vessel), or clinically indicated TLR. Stent thrombosis was defined according to the ARC definition.[19]

A true bifurcation lesion was defined as the presence of a significant lesion in both the main and side branch; a partial bifurcation lesion was defined as the presence of a significant lesion only in one of the two branches. In the present post hoc analysis patients were allocated in the bifurcation group if at least one coronary bifurcation was treated. Patients were included in the one stent strategy group if at least one bifurcation was treated with a one stent technique and no other bifurcation was treated with a two stent approach; patients were included in the two stent technique group if at least one bifurcation was treated with a two stent technique.

Quantitative coronary angiography analyses

Quantitative coronary angiography (QCA) analyses were performed using the Coronary Angiography Analysis System (Pie Medical Imaging, Maastricht, The Netherlands). All analyses were performed by an independent core laboratory (Cardialysis, Rotterdam, The Netherlands). The following QCA parameters were computed as per one segment analysis: preprocedural reference vessel diameter (RVD) calculated with interpolated method,[21] minimal luminal diameter (MLD), percentage diameter stenosis (%DS), and acute gain (defined as postprocedural MLD minus preprocedural MLD).

Statistical analysis

Categorical variables are presented as counts and percentages and compared using Fisher's exact test. Continuous variables are presented as means±SD and compared using the Student's unpaired t test. Baseline clinical and procedural covariates showing statistically significant differences in the univariate model were considered candidate variables in the multivariate model. Patients with missing values for these covariates were not included in the analysis. Covariate adjusted comparisons were obtained by logistic regression analysis. Survival curves were constructed using Kaplan–Meier estimates and compared using the log rank test. The Cox proportional hazard model was used to compare clinical outcomes across groups. A two sided $p<0.05$ were considered statistically significant. Statistical analyses were performed by two independent dedicated statisticians using SAS V.9.2 (SAS Institute, Inc, Cary, North Carolina, USA).

RESULTS

Out of the 2292 patients enrolled in the RESOLUTE All Comers Trial, data for 2265 (99%) patients were available for the present analysis, 1873 in the non-bifurcation group and 392 in the bifurcation group.[16] Out of this population 2223 patients (98.1%) completed the 2-year follow-up, 1838 (98.1%) in the non-bifurcation group and 385 (98.2%) in the bifurcation group (table 1 and 3, figure 1).

Baseline clinical characteristics of the two groups are reported in table 1; patients in the non-bifurcation group presented more frequently with acute MI (35.3% vs 29.3%, $p=0.026$), whereas the bifurcation group had a higher number of treated lesions per patient (1.4±0.7 vs 1.8±0.9, $p<0.001$), higher SYNTAX score (13.8±8.9 vs 18.7±9.5, $p<0.001$) and a higher percentage of small vessel disease (65.2% vs 77.2%, $p<0.001$) (table 1).

Baseline lesion characteristics showed that the non-bifurcation group was characterised by a higher percentage of luminal stenosis (64.17±18.19% vs 62.26±18.28%, $p=0.015$). Vessels with treated bifurcation lesions had smaller preprocedural RVD (2.65±0.58mm vs 2.56±0.57 mm, $p<0.001$), were more frequently affected by moderate/heavy calcification

Table 1 Baseline patient clinical characteristics in the non-bifurcation and bifurcation groups

Variables	Non-bifurcation N=(1873)	Bifurcation N=(392)	p Value
Age, years	64.0±10.8 (1873)	65.0±10.8 (392)	0.107
Body mass index, kg/m^2	27.8±4.4 (1864)	27.6±4.1 (391)	0.275
Male, % (n/N)	76.6% (1434/1873)	79.1% (310/392)	0.292
Diabetes mellitus, % (n/N)	23.4% (438/1873)	22.7% (89/392)	0.793
Hypertension, % (n/N)	70.7% (1325/1873)	71.4% (280/392)	0.807
Hyperlipidaemia, % (n/N)	65.8% (1232/1873)	65.6% (257/392)	0.953
Family history of CAD, % (n/N)	36.3% (573/1579)	31.7% (108/341)	0.119
Previous MI, % (n/N)	30.1% (553/1837)	26.8% (102/380)	0.217
Previous PCI, % (n/N)	32.4% (606/1873)	30.1% (118/392)	0.405
Previous CABG, % (n/N)	9.5% (177/1873)	10.2% (40/392)	0.637
Current smoker, % (n/N)	27.2% (509/1873)	23.5% (92/392)	0.148
Index procedure prompted by:			
Unstable angina, % (n/N)	19.4% (363/1873)	18.6% (73/392)	0.778
Stable angina, % (n/N)	34.1% (639/1873)	36.7% (144/392)	0.321
Myocardial infarction, % (n/N)	35.3% (661/1873)	29.3% (115/392)	0.026
LVEF class, % (n/N)			0.993
<30%	2.2% (21/962)	2.1% (5/240)	
30–50%	29.7% (286/962)	30.0% (72/240)	
>50%	68.1% (655/962)	67.9% (163/240)	
Creatinine, μmol/l	86.6±41.0 (1830)	85.6±58.9 (384)	0.741
No. of treated lesions per patient	1.4±0.7 (1873)	1.8±0.9 (392)	<0.001
SYNTAX score	13.8±8.9 (1669)	18.7±9.5 (347)	<0.001
At least one small vessel (RVD ≤2.75 mm), % (n/N)	65.2% (1026/1573)	77.2% (271/351)	<0.001
At least one lesion length >18 mm, % (n/N)	19.1% (301/1573)	22.5% (79/351)	0.159
At least one total occlusion, % (n/N)	16.8% (314/1865)	15.6% (60/385)	0.599

CABG, coronary artery bypass graft; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RVD reference vessel diameter.

(19.7% vs 24.8%, p<0.005), and had a higher rate of ostial lesions (3.3% vs 5.2%, p=0.030) compared to non-bifurcation lesions (table 2). In the bifurcation group 24.6% (157/638) of the lesions were defined as true bifurcation lesions.

Clinical outcomes

At 2-year follow-up, adjusting for baseline clinical and procedural characteristics, both groups had similar rates of cardiac death (2.3% vs 2.1%, p=0.273), all cause death (3.5% vs 3.4%, p=0.539), MACE (11.5% vs 15.1%, p=0.305), TLR (4.7% vs 6.0%, p=0.569), TLF (9.7% vs 13.8%, p=0.255), and the composite of definite or probable stent thrombosis (1.6% vs 1.8%, p=0.419) (table 3). The bifurcation group showed a trend towards a higher rate of target vessel MI (4.0% vs 7.3%, p=0.068) (table 3). To evaluate this trend further, and given the fact that the unadjusted brute comparison between the two groups showed a numerical increase in MI (mostly periprocedural MI) and TLF in the bifurcation group (table 3), a landmark analysis for the composite end point TLF and its components (death from cardiac causes, any MI, or clinically indicated TLR) was performed at 30 days (this time point was the first for assessment of clinical end points).

TLF was increased in the first 30 days after procedure in the bifurcation group (0–30 days: HR 2.081, 95% CI 1.336 to 3.241; p<0.001) but was similar between groups from 30 to 720 days after procedure (30–720 days: HR 1.102, 95% CI 0.714 to 1.699; p=0.662) (figure 2, upper panel).

Analysing the three components of TLF, it was observed that the increased 0–30 days rate of TLF was mostly due to an increased rate of periprocedural MI, while cardiac death and TLR were similar in both groups (figure 2, lower panel).

One or two stent strategy

Among 392 patients in the bifurcation group, 310 patients were treated with a single stent technique and 82 with a two stent strategy. The baseline comparison of one stent and two stent bifurcation groups are reported in the online supplementary appendix.

At 2 years clinical follow-up, in both unadjusted and adjusted analyses a higher rate of target vessel MI and a trend towards increased TLF—mainly due to an increased number of periprocedural MIs (figure 3)—was observed in the two sent strategy group (table 4).

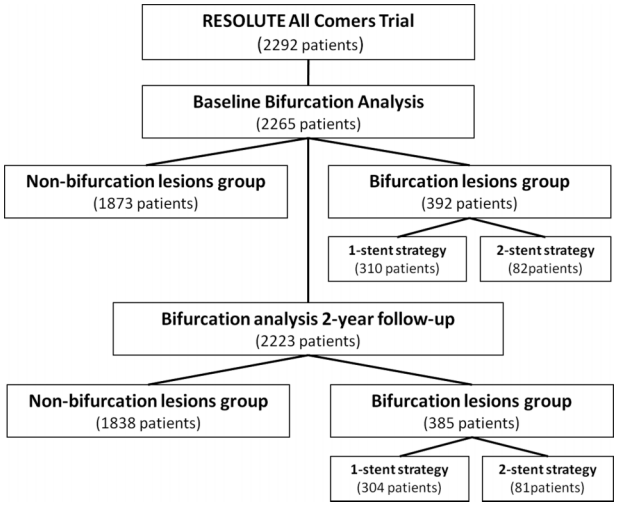

Figure 1 Flow chart of the study.

Table 2 Baseline lesion and procedural characteristics in the non-bifurcation and bifurcation groups (per lesion analysis)

Variables	Non-bifurcation N=(2635)	Bifurcation N=(687)	p Value
Lesion length, mm	12.20±7.48 (2151)	11.44±8.40 (575)	0.051
Reference vessel diameter, mm	2.65±0.58 (2151)	2.56±0.57 (575)	0.001
Minimum lumen diameter, mm	0.94±0.53 (2557)	0.96±0.52 (671)	0.429
Per cent stenosis, mm	64.17±18.19 (2557)	62.26±18.28 (671)	0.015
Thrombus, % (n/N)	5.4% (131/2409)	3.6% (23/643)	0.055
Excessive tortuosity, % (n/N)	22.3% (567/2548)	20.5% (136/665)	0.119
Moderate or heavy calcification, % (n/N)	19.7% (501/2537)	24.8% (167/674)	0.005
TIMI score of 0 or 1, % (n/N)	15.6% (406/2596)	14.0% (96/687)	0.311
RCA, % (n/N)	34.2% (902/2635)	22.4% (158/706)	<0.001
LAD, % (n/N)	37.5% (989/2635)	47.3% (334/706)	<0.001
LCX, % (n/N)	24.6% (648/2635)	25.2% (178/706)	0.731
Diffuse lesion (lesion length≥20 mm), % (n/N)	13.7% (332/2419)	15.0% (96/641)	0.406
Lesion angulation, % (n/N)	7.8% (178/2271)	8.9% (54/609)	0.402
Ostial lesion, % (n/N)	3.3% (86/2573)	5.2% (35/678)	0.030
Modified ACC/AHA lesion class, % (n/N)			<0.001
A	2.3% (61/2598)	1.3% (9/687)	
B1	24.2% (630/2598)	13.0% (89/687)	
B2	29.4% (765/2598)	24.0% (165/687)	
C	44.0% (1142/2598)	61.7% (424/687)	

ACC/AHA, American College of Cardiology/American Heart Association; LAD, left anterior descending; LCX, left circumflex; RCA, right coronary artery; TIMI, Thrombolysis In Myocardial Infarction.

DISCUSSION

The main finding of the present study is that second generation DES implantation in coronary bifurcation lesions showed similar long term mortality and overall clinical outcomes compared to non-bifurcation lesions.

First generation DES showed a high impact on intra-stent neointimal proliferation with a reduction in restenosis and need for repeated revascularisation compare to BMS.[22 23] However, these first generation devices failed to add a major gain in terms of long term mortality[24] and a major concern remained over long term safety, particularly in relation to late stent thrombosis.[25–29] Possible mechanisms underlining this phenomenon were hypothesised to be late acquired malapposition, delayed vascular healing,[30–32] and low biocompatibility of the coating polymer leading to hypersensitivity and inflammation.[33]

The second generation DES were designed to improve performances and offer possible solutions to first generation DES limitations, with novel stent design, a reduced strut thickness,

Table 3 Clinical end points at 2-year follow-up in the non-bifurcation and bifurcation groups

Variables	Non-bifurcation N=(1838)	Bifurcation N=(385)	Unadjusted p value	Adjusted p value
Death				
From any cause	3.5% (65/1838)	3.4% (13/385)	1.000	0.539
From cardiac cause	2.3% (43/1838)	2.1% (8/385)	0.853	0.273
Target vessel myocardial infarction				
Any	4.0% (74/1838)	7.3% (28/385)	0.010	0.068
Q wave	0.6% (11/1838)	1.6% (6/385)	0.097	0.121
Non-Q wave	3.5% (64/1838)	5.7% (22/385)	0.057	0.250
Clinically indicated target lesion revascularisation				
Any	4.7% (86/1838)	6.0% (23/385)	0.299	0.569
Coronary artery bypass grafting	0.8% (14/1838)	1.3% (5/385)	0.355	0.517
Percutaneous coronary intervention	4.1% (76/1838)	5.2% (20/385)	0.336	0.513
Myocardial infarction				
Any	4.8% (88/1838)	7.3% (28/385)	0.058	0.161
Periprocedural	3.4% (63/1838)	6.5% (25/385)	0.009	0.126
Major adverse cardiac events	11.5% (212/1838)	15.1% (58/385)	0.059	0.305
Target lesion failure	9.7% (178/1838)	13.8% (53/385)	0.021	0.255
Definite stent thrombosis (0–720 days)	1.1% (20/1838)	1.3% (5/385)	0.789	0.198
Probable stent thrombosis (0–720 days)	0.5% (9/1838)	0.8% (3/385)	0.447	0.793
Possible stent thrombosis (0–720 days)	1.5% (27/1838)	1.3% (5/385)	1.000	0.232
Stent thrombosis (0–720 days)				
Definite or probable	1.6% (29/1838)	1.8% (7/385)	0.661	0.419
Definite, probable or possible	3.0% (55/1838)	3.1% (12/385)	0.870	0.844

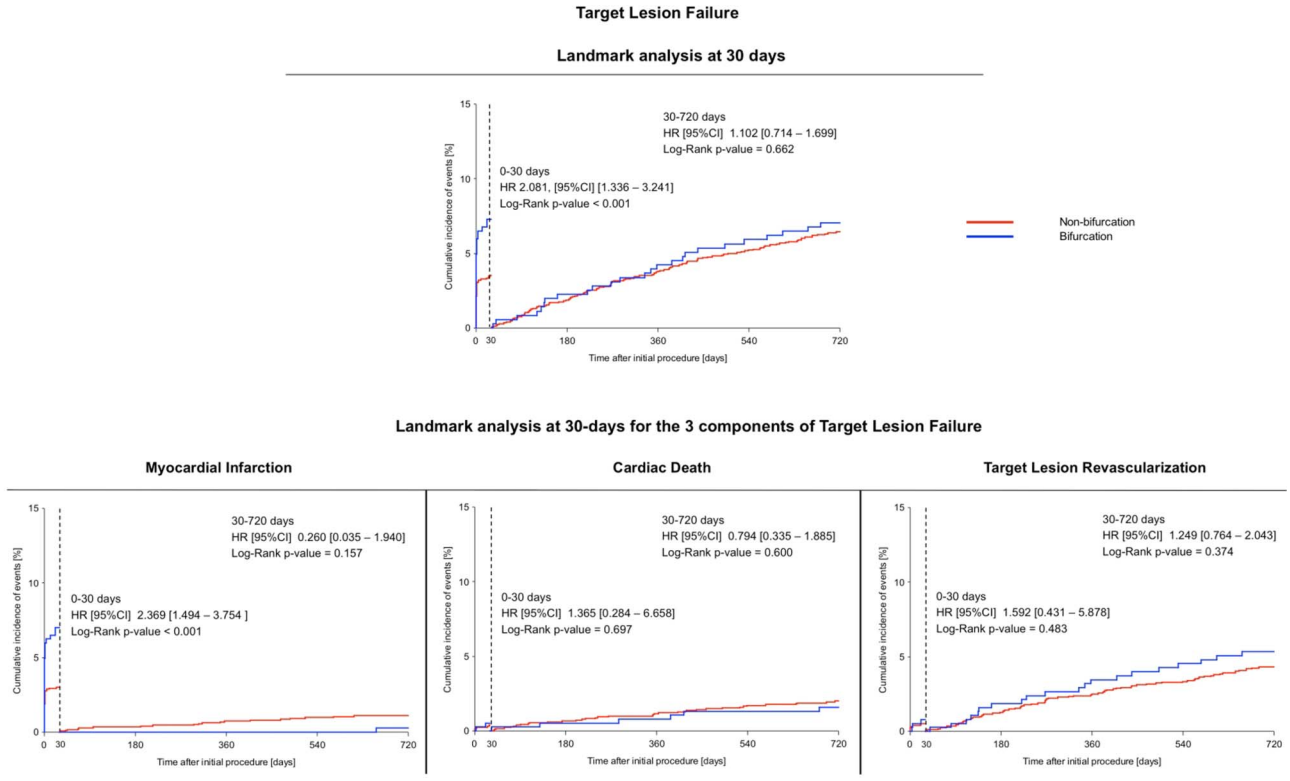

Figure 2 (Upper panel) Kaplan-Meier curves—cumulative incidence for target lesion failure: non-bifurcation group versus bifurcation group with landmark analysis at 30 days. Target lesion failure is the combined clinical outcome of cardiac death, myocardial infarction (not clearly attributable to a non-target vessel), and target lesion revascularisation. (Lower panel) Kaplan-Meier curves—landmark analysis at 30 days for myocardial infarction, cardiac death and target lesion revascularisation: non-bifurcation group versus bifurcation group. – –, unadjusted data. Access the article online to view this figure in colour.

improved polymer biocompatibility, and novel drugs.[32 34] In addition the improvement in flexibility, conformability, and deliverability were regarded as key characteristics in complex scenarios such as bifurcation lesions.[35] Preliminary clinical results suggested that second generation DES could be associated with comparable safety and superior efficacy when

Table 4 Clinical end points at 2-year follow-up in bifurcations and one or two stent strategy

Variables	One stent strategy N=(304)	Two stent strategy N=(81)	Unadjusted p value	Adjusted p value
Death				
From any cause	3.6% (11/304)	2.5% (2/81)	1.000	0.873
From cardiac cause	2.3% (7/304)	1.2% (1/81)	1.000	0.862
Target vessel myocardial infarction				
Any	5.6% (17/304)	13.6% (11/81)	0.027	0.034
Q wave	1.6% (5/304)	1.2% (1/81)	1.000	0.948
Non-Q wave	3.9% (12/304)	12.3% (10/81)	0.012	0.017
Clinically indicated target lesion revascularisation				
Any	5.6% (17/304)	7.4% (6/81)	0.597	0.505
Coronary artery bypass grafting	1.0% (3/304)	2.5% (2/81)	0.284	0.672
Percutaneous coronary intervention	5.3% (16/304)	4.9% (4/81)	1.000	0.804
Myocardial infarction				
Any	5.6% (17/304)	13.6% (11/81)	0.027	0.034
Periprocedural	4.9% (15/304)	12.3% (10/81)	0.023	0.051
Major adverse cardiac events	13.5% (41/304)	21.0% (17/81)	0.115	0.119
Target lesion failure	12.2% (37/304)	19.8% (16/81)	0.101	0.098
Definite stent thrombosis (0–720 days)	1.0% (3/304)	2.5% (2/81)	0.284	0.205
Probable stent thrombosis (0–720 days)	1.0% (3/304)	0.0% (0/81)	1.000	0.954
Possible stent thrombosis (0–720 days)	1.3% (4/304)	1.2% (1/81)	1.000	0.518
Stent thrombosis (0–720 days)				
Definite or probable	1.6% (5/304)	2.5% (2/81)	0.641	0.482
Definite, probable or possible	3.0% (9/304)	3.7% (3/81)	0.722	0.348

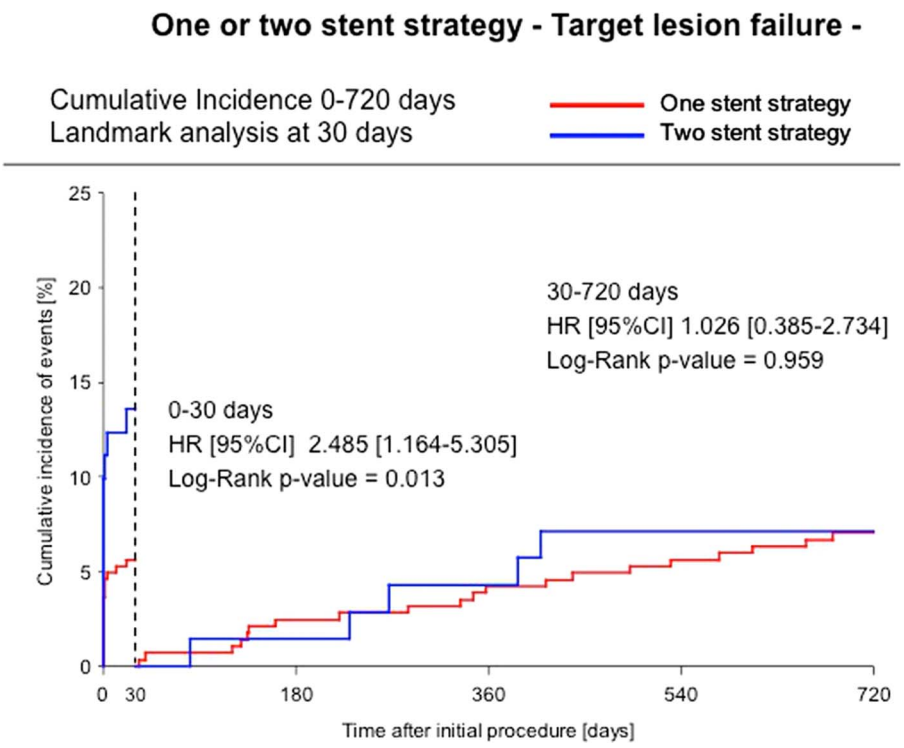

Figure 3 Kaplan-Meier curves—cumulative incidence for target lesion failure: one versus two stent strategy and landmark analysis at 30 days. – –, unadjusted data. Access the article online to view this figure in colour.

compared to first generation DES for treatment of coronary bifurcations.[36]

The RESOLUTE All Comers Trial evaluated the performance of the everolimus and zotarolimus eluting stents, that represent the paradigm of the newer generation DES with comparable clinical outcomes.[16 37] Both devices have been consistently shown to be superior to first generation DES.[17 38 39] These results constitute the background for the actual widespread use of these two novel DES in the clinical arena; however, limited data are currently available on their performance in complex lesions or specific subsets such as coronary artery bifurcation that have been classically regarded as a challenging subgroup burdened by worse clinical outcomes compared to non-bifurcation lesions. It is noteworthy that no comparison has been performed so far between bifurcated and non-bifurcated lesions treated with second generation DES.

In the present study, the cardiac and the overall long term mortality between the bifurcation and non-bifurcation groups were investigated and observed to be similar and low, as well as MACE and TLR—suggesting the possibility of an important improvement in long term hard clinical end points associated with the use of second generation DES in coronary bifurcations.

In the first generation DES era, bifurcation lesions treatment was also reported to be a key factor for increased risk of stent thrombosis.[31] Farb and colleagues described the pathological mechanisms of stent thrombosis in humans, observing that side branch ostia represent sites that could be associated with delayed vascular healing and incomplete neointimal coverage.[40] Iakovou *et al*,[41] analysing the predictors of stent thrombosis after first generation DES implantation, reported the bifurcation lesion as being an independent predictor of late stent thrombosis.

In our study, no differences were observed at any time points in terms of stent thrombosis between bifurcation and non-bifurcation lesions (table 3, figure 4). Due to the limited number of patients and events these data should be interpreted with caution and considered as hypothesis generating.

However, such seminal observation, if confirmed in larger randomised studies, could further support a possible advantage for the use of second generation DES in bifurcation lesions.

In the present analysis, the unadjusted brute comparison between the two groups showed a numerical increase in periprocedural MI in the bifurcation group (not significant after adjustment for baseline characteristics); this had no impact on mortality and the 30-day landmark analysis showed that, if not taking into consideration the periprocedural MI, the cumulative incidence of TLF and its component (death from cardiac causes,

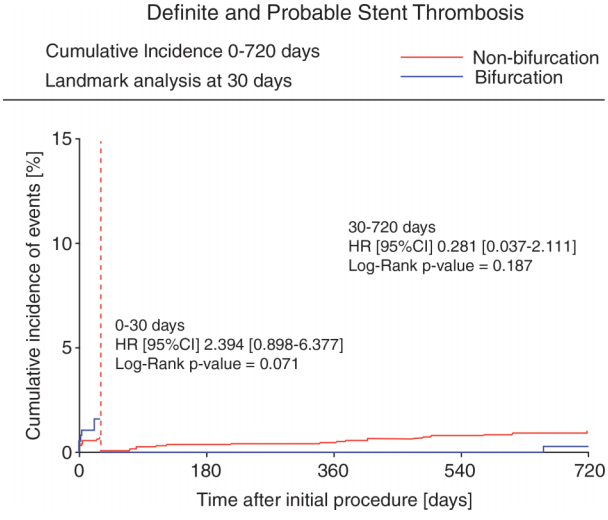

Figure 4 Kaplan-Meier curves—cumulative incidence for stent thrombosis: non-bifurcation group versus bifurcation group with landmark analysis at 30 days. Sub-acute stent thrombosis (<30 days) showed a trend towards a higher incidence in the bifurcation group. – –, unadjusted data. Access the article online to view this figure in colour.

any MI, or clinically indicated TLR) is similar between groups also in the unadjusted analysis (figure 2).

Finally, in the present study a substantial predominance of the one stent technique was observed for the treatment of bifurcation lesions (table 4, see online supplementary file). This approach is in line with the increasing amount of evidence in favour of provisional 'T' stenting for most of the bifurcation lesions.[42 43] Notably, a higher number of periprocedural MIs occurred in association with a two stent strategy. These data reflect the findings of a recently reported randomised trial comparing simple versus complex drug eluting stenting for bifurcation lesions.[44]

Comparisons between previous large studies on coronary bifurcations[42 44 45] and the present investigation are challenging due to different follow-up periods, the use of first generation DES, the absence of a non-bifurcation lesion group, different inclusion and exclusion criteria, and variable rates of one or two stent strategy. On the other hand, it should be highlighted that a recent sub-analysis of the LEADERS randomised trial, investigating clinical outcomes at 12-month follow-up in 497 patients (BES, n=258; SES, n=239), showed comparable safety between the two stents and superior BES efficacy in terms of target vessel revascularisation.

Such data may be supportive of an improvement in clinical results using second generation DES in the bifurcation setting, suggesting the stent design, polymer, and the eluted drug play an important role.

In conclusion, in the present investigation the long term mortality and overall events rates in patients treated with implantation of second generation DES in coronary artery bifurcations were low and similar to those observed in patients treated for non-bifurcation lesions.

Further larger and randomised studies are needed to confirm these preliminary observations.

Limitations

The present study represents a post hoc analysis of the RESOLUTE All Comers Trial; no formal power calculation was performed. Because of the limited number of patients, the numerical mismatch between groups, and the low event rate, caution should be made in reaching firm conclusions. QCA assessment of the bifurcation angle and the side branch diameter was not performed.

CONCLUSIONS

In the present investigation, percutaneous treatment of coronary bifurcation lesions with second generation DES was associated with similar long term mortality and clinical outcomes compared with non-bifurcation lesions.

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Competing interests Manuela Negoita and Frank van Leeuwen, who are co-authors of the present study, are employed by Medtronic; the other authors have no conflict of interest to declare.

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Heart

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