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Clinical

Direct Stenting in Patients Treated with Orbital Atherectomy: An ORBIT II Subanalysis☆,☆☆

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ABSTRACT

Background: Direct stenting offers many potential advantages in appropriately selected lesions. Coronary artery calcification increases the complexity and risk of adverse events associated with percutaneous coronary intervention. This study aimed to examine the feasibility of direct stenting after treatment with orbital atherectomy (OA).
Methods: ORBIT II was a single-arm trial enrolling 443 subjects with de novo severely calcified coronary lesions treated with OA; direct stenting was utilized in 59.0% of cases. Procedural outcomes and 3-year major adverse cardiac event (MACE) rates were compared in subjects treated with pre-stent balloon dilatation versus direct stenting after OA.
Results: Procedural success (84.2% vs. 93.3%; $p = 0.004$) was significantly higher in the direct stenting cohort. 3-year MACE occurred less frequently in the direct stenting cohort (29.9% vs. 19.1%; $p = 0.006$), driven by lower rates of myocardial infarction and target lesion revascularization. In a propensity matched analysis, procedural success and 3-year MACE rates were similar in the pre-stent balloon dilatation and direct stenting groups (85.0% vs. 91.8%; $p = 0.122$ and 28.2% vs. 19.6%; $p = 0.078$, respectively).
Conclusions: Orbital atherectomy facilitates direct stenting and is associated with high procedural success and favorable 3-year outcomes in carefully selected patients. Randomized studies are needed to assess the optimal strategy after lesion preparation with OA.

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This post-hoc analysis of the ORBIT II study examined the feasibility of direct stenting after treatment with orbital atherectomy. The results demonstrate that orbital atherectomy facilitates direct stenting and is associated with high procedural success and favorable 3-year outcomes in carefully selected patients. Using lesion preparation with orbital atherectomy and intravascular imaging may obviate the need for pre-stent balloon dilatation prior to stenting in appropriately selected patients with calcified coronary artery disease.

Abbreviations: CABG, Coronary artery bypass grafting; CAC, Coronary artery calcification; CK-MB, Creatinine kinase-myocardial band; CSI, Cardiovascular Systems, Inc.; DS, Direct stenting; IVUS, Intravascular ultrasound; LVEF, Left ventricular ejection fraction; MACE, Major adverse cardiac events; MI, Myocardial infarction; MLD, Minimum lumen diameter; OA, Orbital atherectomy; OCT, Optical coherence tomography; PCI, Percutaneous coronary intervention; RVD, Reference vessel diameter; SCAI, Society for Cardiovascular Angiography and Interventions; TLR, Target lesion revascularization; TVR, Target vessel revascularization; ULN, Upper limit of normal.

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1. Introduction

Coronary artery calcification (CAC) increases procedure complexity, and risk of peri-procedural adverse events with percutaneous coronary intervention (PCI) [1]. There is a strong association with CAC and stent underexpansion [2]. Stent underexpansion is an important independent predictor for failure of DES [3] driven by high rates of restenosis. Conventionally, balloon pre-dilatation or alternative adjunctive techniques are used in treating CAC prior to stent implantation.

Direct stenting (DS) offers many potential advantages in appropriately selected lesions and has been shown to achieve adequate stent expansion with both bare metal and drug-eluting stents [4–6]. Benefits of DS include a reduction in equipment used, procedure time, radiation time and use of contrast. As a result, DS may offer significant cost savings.

Orbital atherectomy (OA) is used for lesion preparation prior to stent implantation to modify severely calcified coronary lesions by differential ablation to change lesion compliance. The ORBIT II study evaluated the safety and efficacy of treating de novo, severely calcified lesions with OA [7–9]. Long term benefits have been demonstrated with a target lesion revascularization (TLR) rate of 7.8% at 3 years in this complex patient cohort [10].

Stent optimization is particularly important in this complex patient population. The safety and efficacy of direct stenting after treatment with Diamondback 360° Coronary Orbital Atherectomy System (CSI, St. Paul, MN) has not been previously reported. We sought to evaluate the outcomes of subjects in which direct stenting was used after treatment with the Diamondback 360° Coronary Orbital Atherectomy System Classic Crown (Cardiovascular Systems, Inc. [CSI], St. Paul, MN) compared to subjects treated with conventional angioplasty after orbital atherectomy.

2. Materials and methods

2.1. Device description

The coronary orbital atherectomy system evaluated in the ORBIT II study has been previously described [11]. A diamond-coated, 1.25 mm eccentrically mounted crown is the key feature. Moving bi-directionally over the ViperWire (CSI), differential sanding from centrifugal forces during orbit, changes the compliance of calcified plaque. The crown selectively rotates at either 80,000 rpm at low speed or 120,000 rpm at high speed. ViperSlide lubricating solution (CSI) is infused into the device during orbit, to reduce friction and heat while flushing particles of approximately 2 μm in size [12].

2.2. Study design

The multicenter, prospective, single-arm, non-randomized ORBIT II study enrolled 443 subjects with de novo, severely calcified coronary lesions from May 25, 2010 to November 26, 2012 at 49 US sites [7]. The study had Institutional Review Board approval from each participating center and all subjects provided informed consent. Severely calcified lesions were identified on fluoroscopy or intravascular ultrasound (IVUS) at the operator's discretion. Severe calcium (as determined by the investigator) was defined as the angiographic presence of radiopacities noted without cardiac motion prior to contrast injection involving both sides of the arterial wall and total length of calcium of at least 15 mm and extending partially into the target lesion, or presence of an arc of calcium ≥270° visualized with IVUS. The degree of calcification was a study inclusion criterion and therefore was reported by the Investigator, not the Angiographic Core Lab (Cleveland Clinic Foundation, Cleveland, OH). The Angiographic Core Lab reported the final minimum lumen diameter (MLD), final percentage of residual stenosis, and the presence and type of dissection and perforation. The option for treatment with direct stenting was left to operator discretion as part of the ORBIT II study protocol. Subjects were followed in clinic at 30 days post-procedure and were contacted annually by phone for 3 years post-procedure. For this post-hoc analysis, subjects with the orbital atherectomy device inserted (N = 432) were stratified into 2 groups based on PCI strategy: subjects that received balloon angioplasty after the use of orbital atherectomy, but prior to attempted implantation of a stent (pre-stent balloon dilatation group, N = 177, 41.0%) were compared with subjects where attempted stent implantation occurred immediately after the use of orbital atherectomy (DS group, N = 255, 59.0%).

2.3. Clinical outcomes

Procedural outcomes and major adverse cardiac events (MACE) through 3-year follow-up were assessed. In the ORBIT II study, procedural success was defined as successful stent delivery with <50% residual stenosis without in-hospital MACE [cardiac death, myocardial infarction (MI), and target vessel revascularization (TVR) inclusive of the target lesion]. Myocardial infarction was defined as creatinine kinase-myocardial band (CK-MB) level >3× the upper limit of normal with or without a new pathologic Q-wave. For this analysis, clinically relevant MI was defined based on the Society for Cardiovascular Angiography and Interventions (SCAI) definition of a peak CK-MB measured within 48-h of PCI ≥10× upper limit of normal (ULN) or CK-MB ≥5× ULN with Q-wave MI, or in the absence of CK-MB measurements, cardiac troponin (cTN) ≥70× ULN or cTn ≥35× ULN with Q-wave MI [13]. Angiographic success was defined as successful stent delivery with <50% residual stenosis, and without occurrence of a severe angiographic complication (type C-F dissection, perforation, persistent slow/no reflow, and abrupt vessel closure).

2.4. Statistical analysis

Continuous variables are presented as mean ± standard deviation and categorical variables are presented as proportions. Wilcoxon rank sum test and Fisher's exact test were used to compare continuous and categorical variables, respectively. MACE rates were estimated using the Kaplan-Meier method and were compared using the Cox proportional hazards model.

Propensity-score matching was used to minimize the effect of the differences in baseline demographic and lesion characteristics when comparing clinical outcomes. Subjects in the direct stenting cohort were matched using a 1:1 ratio with pre-stent balloon dilatation subjects based on propensity scores (caliper size of 0.3). The propensity scores were calculated using a logistic regression model with adjusting covariates. The list of propensity score matching covariates included: gender, age, eGFR, left ventricular ejection fraction (LVEF), history of diabetes, smoking, history of dyslipidemia, history of hypertension, history of stroke/transient ischemic attack, history of MI, history of coronary artery bypass grafting (CABG), target lesion vessel, pre-procedure target lesion length, ACC/AHA lesion classification, pre-procedure percent stenosis, and total length of calcium. Outcome analyses to compare the pre-stent balloon dilatation and direct stenting groups were performed using conditional logistic regression and conditional Cox proportional hazards regression. In the event that the conditional logistic regression models would not converge and/or the model fit was questionable, Fisher's exact tests are reported.

Logistic regression and Cox proportional hazards regression were performed to assess covariates found to introduce confounding effects on procedural success and 3-year MACE outcomes, respectively. For the propensity matched dataset, conditional logistic regression and conditional Cox proportional hazards regression were used. Covariates in the model included baseline demographic and lesion characteristics that differed significantly between the 2 groups as well as clinically relevant demographics. The baseline demographics (age, gender, Caucasian, Black or African American, eGFR, history of diabetes, current/former smoker, history of dyslipidemia, history of hypertension, history of CABG, LVEF), lesion characteristics (pre-procedure target lesion

Table 1
Baseline demographics.

	All subjects			Propensity score matched subjects		
	OA + Pre-stent balloon	OA + Direct stent	*p*-Value	OA + Pre-stent balloon	OA + Direct stent	*p*-Value
Number of subjects	N = 177[a]	N = 255[a]		N = 147	N = 147	
Male	121 (68.4)	157 (61.6)	0.154	97 (66.0)	99 (67.3)	0.902
Ethnicity			0.854			0.844
Caucasian	158 (89.3)	224 (87.8)		129 (87.8)	131 (89.1)	
Black or African American	7 (4.0)	16 (6.3)		7 (4.8)	8 (5.4)	
Asian	4 (2.3)	4 (1.6)		4 (2.7)	2 (1.4)	
Hispanic or Latino	7 (4.0)	8 (3.1)		6 (4.1)	4 (2.7)	
Native American	0 (0.0)	1 (0.4)		0 (0.0)	0 (0.0)	
Other	1 (0.6)	2 (0.8)		1 (0.7)	2 (1.4)	
Age (years)	73.0 ± 8.7	70.5 ± 10.6	0.013	72.1 ± 8.9	72.3 ± 10.5	0.837
BMI	28.9 ± 6.2	29.6 ± 5.5	0.058	29.0 ± 6.5	29.4 ± 5.2	0.164
eGFR (ml/min/1.73 m^2)	75.6 ± 27.2 (N = 176)	75.6 ± 25.8 (N = 254)	0.821	75.2 ± 27.0	76.5 ± 23.1	0.445
LVEF (%)	55.4 ± 10.4 (N = 175)	57.4 ± 8.8 (N = 251)	0.020	56.2 ± 10.2	56.4 ± 9.1	0.704
History of diabetes	64 (36.2)	91 (35.7)	0.919	53 (36.1)	52 (35.4)	>0.99
Type I	4 (6.3)	6 (6.6)	>0.99	4 (7.5)	3 (5.8)	>0.99
Type II	60 (93.8)	85 (93.4)	>0.99	49 (92.5)	49 (94.2)	>0.99
Smoking			0.111			0.986
No, never smoked	51 (28.8)	93 (36.5)		42 (28.6)	44 (29.9)	
Yes, current smoker	26 (14.7)	44 (17.3)		21 (14.3)	21 (14.3)	
Yes, former smoker	100 (56.5)	118 (46.3)		84 (57.1)	82 (55.8)	
History of dyslipidemia	164/176 (93.2)	234 (91.8)	0.713	137 (93.2)	136 (92.5)	>0.99
History of hypertension	163 (92.1)	232 (91.0)	0.730	135 (91.8)	133 (90.5)	0.838
History of stroke/TIA	12 (6.8)	27/254 (10.6)	0.232	10 (6.8)	10 (6.8)	>0.99
History of MI	38/174 (21.8)	56/253 (22.1)	>0.99	29 (19.7)	33 (22.4)	0.668
History of angina	138 (78.0)	201 (78.8)	0.905	114 (77.6)	115 (78.2)	>0.99
History of CABG	26 (14.7)	38 (14.9)	>0.99	19 (12.9)	24 (16.3)	0.510

BMI = body mass index; CABG = coronary artery bypass grafting; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; MI = myocardial infarction; OA = orbital atherectomy; TIA = transient ischemic attack.
[a] Unless otherwise indicated.

length, pre-procedure reference vessel diameter (RVD), pre-procedure MLD, ACC/AHA lesion classification, total length of calcium), and direct stenting vs. pre-stent balloon dilatation were included in the model. The entry criterion for the initial multivariable model was based on univariable models for covariates with $p < 0.20$. The criterion for inclusion in the final multivariable was based on initial multivariable model covariates with $p < 0.10$. Significant predictors of outcomes in the final multivariable model were identified at $p < 0.05$.

Data are presented before and after propensity matching. A *p*-value <0.05 was considered statistically significant. Statistical analyses were performed with either SAS software system (SAS Institute, Inc.) or R (R Core Team 2012; R Foundation for Statistical Computing).

3. Results

3.1. Baseline characteristics

There were no significant differences in terms of gender, history of diabetes, renal function, or lesion location in the direct stenting and pre-stent balloon dilatation groups; however, subjects in the pre-stent

Table 2
Vessel and lesion characteristics.

	All subjects			Propensity score matched subjects		
	OA + Pre-stent balloon	OA + Direct stent	*p*-Value	OA + Pre-stent balloon	OA + Direct stent	*p*-Value
Number of subjects	N = 177[a]	N = 255[a]		N = 147	N = 147	
Target lesion vessel			0.127			0.971
LAD	88 (49.7)	137 (53.7)		80 (54.4)	79 (53.7)	
LCX	19 (10.7)	44 (17.3)		15 (10.2)	18 (12.2)	
LM	5 (2.8)	5 (2.0)		3 (2.0)	4 (2.7)	
RCA	62 (35.0)	65 (25.5)		46 (31.3)	43 (29.3)	
Ramus	3 (1.7)	4 (1.6)		3 (2.0)	3 (2.0)	
Pre-procedure target lesion length (mm)	20.2 ± 9.5	18.0 ± 8.4	0.026	20.3 ± 9.5	19.6 ± 9.0	0.596
Pre-procedure RVD (mm)	3.15 ± 0.40	3.06 ± 0.41	0.018	3.1 ± 0.38	3.1 ± 0.40	0.297
ACC/AHA lesion classification			<0.001			0.310
B1	29 (16.4)	83 (32.5)	<0.001	27 (18.4)	30 (20.4)	0.768
B2	72 (40.7)	123 (48.2)	0.140	68 (46.3)	74 (50.3)	0.560
C	76 (42.9)	49 (19.2)	<0.001	52 (35.4)	43 (29.3)	0.319
Pre-procedure MLD (mm)	0.4 ± 0.3	0.5 ± 0.3	0.008	0.5 ± 0.3	0.5 ± 0.3	0.932
Pre-procedure percent stenosis (%)	85.9 ± 8.8	83.1 ± 8.9	0.001	84.9 ± 8.9	84.9 ± 8.4	0.945
Subjects with calcification determined by angiography only	164 (92.7)	233 (91.4)	0.721	137 (93.2)	135 (91.8)	0.825
Total length of calcium (including segmented) (mm)	30.1 ± 15.1 (N = 164)	27.3 ± 15.3 (N = 233)	0.031	29.3 ± 14.7 (N = 137)	28.4 ± 15.7 (N = 135)	0.628
Subjects with calcification determined by IVUS only	13 (7.3)	22 (8.6)	0.721	10 (6.8)	12 (8.2)	0.825
Maximum degree of calcium via IVUS (°)	301.9 ± 41.3 (N = 13)	290.9 ± 33.4 (N = 22)	0.395	308.5 ± 44.7 (N = 10)	299.2 ± 40.4 (N = 12)	0.579

ACC/AHA = American College of Cardiology/American Heart Association; IVUS = intravascular ultrasound; LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main artery; MLD = minimum lumen diameter; OA = orbital atherectomy; RCA = right coronary artery; RVD = reference vessel diameter.
[a] Unless otherwise indicated.

Table 3
Orbital atherectomy treatment parameters.

	All subjects			Propensity score matched subjects		
	OA + Pre-stent balloon	OA + Direct stent	*p*-Value	OA + Pre-stent balloon	OA + Direct stent	*p*-Value
Number of subjects	N = 177	N = 255[a]		N = 147	N = 147[a]	
OA devices used per subject	1.1 ± 0.3	1.0 ± 0.2	0.117	1.1 ± 0.3	1.0 ± 0.2	0.214
OA speed(s) used (rpm)			0.890			0.833
Low only (80,000)	36 (20.3)	57 (22.4)		33 (22.4)	28 (19.0)	
Low and high (80,000/120,000)	132 (74.6)	185 (72.5)		106 (72.1)	110 (74.8)	
High only (120,000)	9 (5.1)	13 (5.1)		8 (5.4)	9 (6.1)	
Total OA device run time (seconds)	80.8 ± 56.9	57.0 ± 32.5 (N = 254)	<0.001	81.0 ± 55.9	59.0 ± 29.1 (N = 146)	<0.001
Average individual OA device run time (seconds)	20.7 ± 5.6	18.7 ± 5.6 (N = 253)	<0.001	20.8 ± 5.7	19.0 ± 5.0 (N = 146)	0.005

OA = orbital atherectomy.
[a] Unless otherwise indicated.

balloon dilatation group were older and had lower left ventricular ejection fraction (Table 1). ACC/AHA lesion classification differed, with more Type C lesions in the pre-stent balloon dilatation group. In the pre-stent balloon dilatation cohort, there was significantly longer target lesion length, larger pre-procedure RVD and percent stenosis (Table 2).

3.2. Procedural results

Subjects treated with pre-stent balloon dilatation had increased overall OA treatment time as well as longer individual run durations (Table 3). There was a significant reduction in the number of stents used in the direct stenting group and increased maximum stent deployment pressure (Table 4). Procedure time was significantly shorter in the direct stenting group, with reduced fluoroscopy time and lower overall volume of contrast.

3.3. Procedural and angiographic success

Procedural success was significantly higher in the direct stenting cohort, driven primarily by lower in-hospital MI. Additionally, the clinically relevant MI rate (SCAI definition) was lower in the direct stenting group. As shown in Table 5, angiographic success was higher in the direct stenting cohort with a decreased incidence of the composite of severe angiographic complications. Overall, both the pre-stent balloon dilatation and direct stenting groups had low rates of severe angiographic complications, with no significant differences noted (Table 5).

3.4. Clinical outcomes

At 3-year follow-up, MACE occurred less frequently in subjects treated with direct stenting, driven primarily by lower rates of MI and TLR (Fig. 1 and Table 6).

3.5. Propensity score-matched cohort analysis

Since there were several differences in baseline demographics and lesion characteristics, propensity score matching was performed; 147 matched pairs were identified. There were no significant differences noted in terms of baseline demographics and lesion characteristics in the propensity score-matched analysis (Tables 1 and 2). As shown in Table 3, total OA device run time and average individual OA device run time was significantly shorter in the direct stenting group. The maximum stent deployment pressure was significantly higher in the direct stenting group (Table 4). Compared to the pre-stent balloon dilatation group, total procedure time and total fluoroscopy time were significantly shorter, and the total contrast volume was significantly smaller in the direct stenting group (Table 4).

Procedural success and in-hospital MACE rates were similar in the pre-stent balloon dilatation and direct stenting groups. However, the SCAI MI rate and severe angiographic complication rates were significantly lower in the direct stenting. As shown in Table 6, 3-year MACE rates were similar in the pre-stent balloon dilatation and direct stenting groups; the 3-year TLR rate was significantly lower in the direct stenting group.

Table 4
Procedural results.

	All subjects			Propensity score matched subjects		
	OA + Pre-stent balloon	OA + Direct stent	*p*-Value	OA + Pre-stent balloon	OA + Direct stent	*p*-Value
Number of subjects	N = 177[a]	N = 255[a]		N = 147[a]	N = 147[a]	
Post-OA MLD (mm)	1.2 ± 0.6	1.3 ± 0.5	<0.001	1.2 ± 0.6	1.3 ± 0.6	0.120
Post-OA residual stenosis (%)	62.9 ± 17.4	55.8 ± 16.8	<0.001	61.3 ± 17.2	58.2 ± 17.5	0.091
Subjects with stent placed	174 (98.3)	253 (99.2)	0.404	144 (98.0)	147 (100.0)	0.247
Post-OA stents used per subject	1.4 ± 0.7 (N = 174)	1.2 ± 0.4 (N = 253)	0.009	1.4 ± 0.7 (N = 144)	1.2 ± 0.5	0.247
Types of stents used in study			0.014			0.094
Bare metal stent	34/236 (14.4)	25/300 (8.3)		31/194 (16.0)	18/180 (10.0)	
Covered	2/236 (0.8)	0/300 (0.0)		1/194 (0.5)	0/180 (0.0)	
Drug eluting stent	200/236 (84.7)	275/300 (91.7)		162/194 (83.5)	162/180 (90.0)	
Maximum stent deployment pressure (atmospheres)	13.3 ± 3.4 (N = 172)	14.2 ± 3.0 (N = 253)	0.002	13.1 ± 3.3 (N = 142)	14.3 ± 2.9	<0.001
Post-stent residual stenosis (%)	7.1 ± 13.4 (N = 173)	4.9 ± 10.4 (N = 253)	0.036	7.3 ± 14.2 (N = 143)	5.8 ± 11.9	0.189
Total procedure time (minutes)	66.7 ± 33.0 (N = 176)	41.5 ± 20.4	<0.001	66.8 ± 33.6 (N = 146)	43.2 ± 21.7	<0.001
Total fluoroscopy time (minutes)	24.9 ± 14.1 (N = 176)	12.9 ± 6.3 (N = 252)	<0.001	24.8 ± 13.0 (N = 146)	13.3 ± 6.9 (N = 146)	<0.001
Total volume of contrast used (ml)	194.5 ± 87.8	157.1 ± 79.3 (N = 253)	<0.001	202.0 ± 91.0	156.4 ± 82.6 (N = 145)	<0.001
Final procedure MLD (mm)	2.9 ± 0.6 (N = 171)	2.9 ± 0.5 (N = 246)	0.340	2.9 ± 0.6 (N = 142)	2.9 ± 0.4 (N = 140)	0.439
Final procedure stenosis (%)	4.7 ± 15.6	4.2 ± 12.7 (N = 254)	0.462	4.3 ± 15.7	4.3 ± 12.0	0.195

MLD = minimum lumen diameter; OA = orbital atherectomy.
[a] Unless otherwise indicated.

Table 5
Angiographic and in-hospital results.

	All subjects			Propensity score matched subjects		
	OA + Pre-stent balloon	OA + Direct stent	*p*-Value	OA + Pre-stent balloon	OA + Direct stent	*p*-Value[a]
Number of subjects	N = 177	N = 255		N = 147	N = 147	
Procedural success	149 (84.2)	238 (93.3)	0.004	125 (85.0)	135 (91.8)	0.122
Stent delivered	172 (97.2)	253 (99.2)	0.128	142 (96.6)	147 (100.0)	0.060[b]
<50% residual stenosis	174 (98.3)	253 (99.2)	0.404	144 (98.0)	147 (100.0)	0.247[b]
In-hospital MACE	26 (14.7)	17 (6.7)	0.008	20 (13.6)	12 (8.2)	0.213
Cardiac death	0 (0.0)	1 (0.4)	>0.99	0 (0.0)	0 (0.0)	–
MI	26 (14.7)	15 (5.9)	0.003	20 (13.6)	12 (8.2)	0.162
TVR/TLR	2 (1.1)	1 (0.4)	0.570	1 (0.7)	0 (0.0)	>0.99[b]
SCAI MI	8 (4.5)	1 (0.4)	0.004	6 (4.1)	0 (0.0)	0.030[b]
Subjects meeting angiographic success criteria	157 (88.7)	243 (95.3)	0.014	129 (87.8)	141 (95.9)	0.018[b]
Subjects with severe angiographic complications	18 (10.2)	11 (4.3)	0.019	16 (10.9)	6 (4.1)	0.041
Severe dissection (Type C, D, E, and F)	7 (4.0)	6 (2.4)	0.396	7 (4.8)	4 (2.7)	0.372
Perforation	5 (2.8)	3 (1.2)	0.281	4 (2.7)	1 (0.7)	0.215
Persistent slow flow/no reflow	2 (1.1)	1 (0.4)	0.570	2 (1.4)	0 (0.0)	0.498[b]
Abrupt closure	5 (2.8)	3 (1.2)	0.281	4 (2.7)	3 (2.0)	0.706

MACE = major adverse cardiac events; MI = myocardial infarction; OA = orbital atherectomy; SCAI=Society for Cardiovascular Angiography and Interventions; TLR = target lesion revascularization; TVR = target vessel revascularization.
[a] *p*-Values from conditional logistic regression, unless otherwise noted.
[b] *p*-Value from Fisher's exact test due to lack of convergence in conditional logistic regression model.

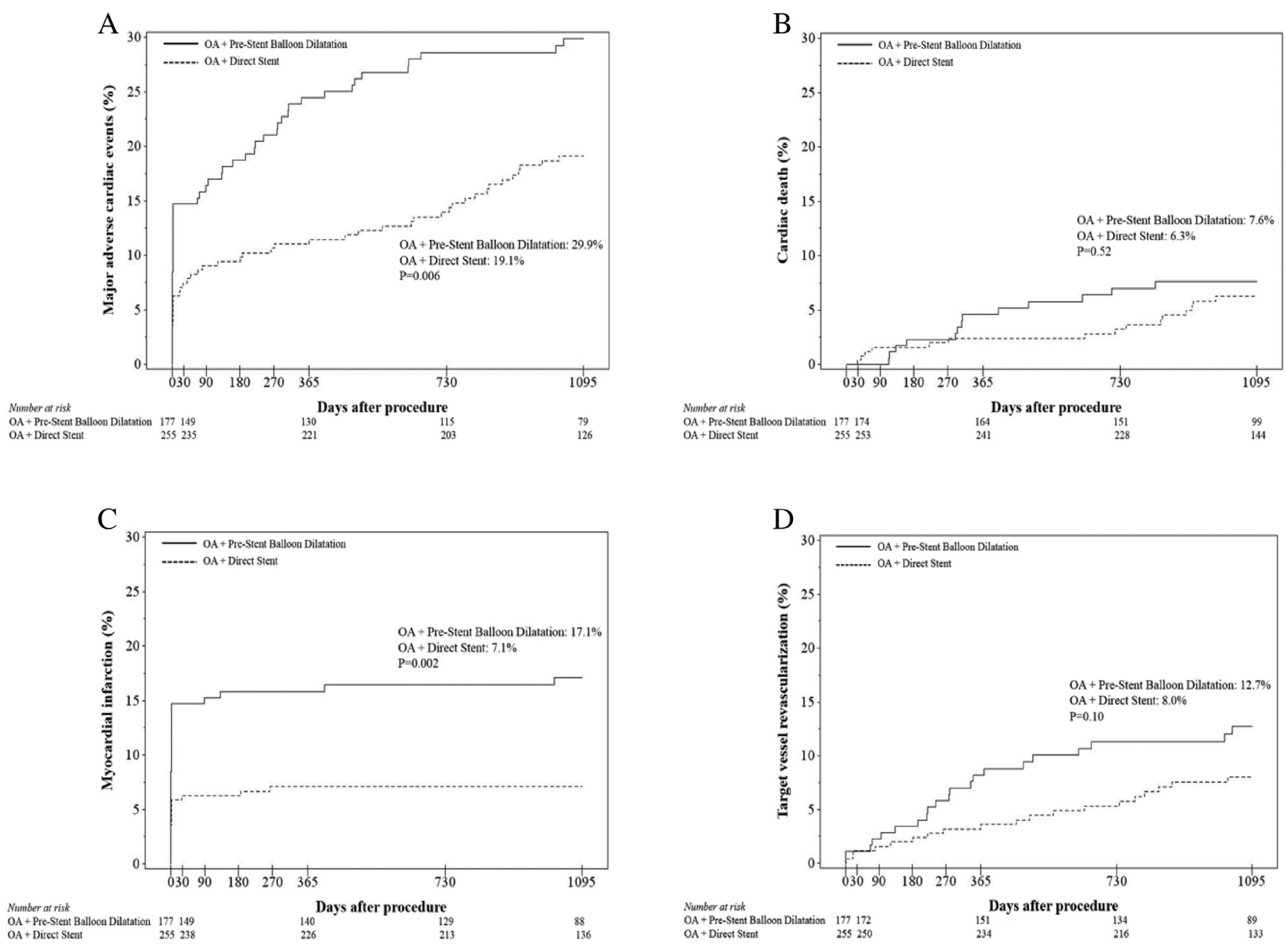

Fig. 1. Time-to-event curves through 3 years. Comparison of the cumulative event rates though 3 years in the propensity score-matched cohort analysis of ORBIT II subjects stratified into 2 groups based on PCI strategy: subjects that received balloon angioplasty after the use of orbital atherectomy, but prior to attempted implantation of a stent (Pre-Stent Balloon Dilatation group) and subjects where attempted stent implantation occurred immediately after the use of orbital atherectomy (Direct Stent group). (A) Major adverse cardiac events. (B) Target vessel revascularization. (OA = orbital atherectomy.)

Table 6
3-year major adverse cardiac events.

	All subjects			Propensity score matched subjects		
	OA + Pre-stent balloon	OA + Direct stent	*p*-Value	OA + Pre-stent balloon	OA + Direct stent	*p*-Value[a]
Number of subjects	N = 177	N = 255		N = 147	N = 147	
3-year MACE	29.9	19.1	0.006	28.2	19.6	0.078
Cardiac death	7.6	6.3	0.525	7.7	5.0	0.232
MI	17.1	7.1	0.002	15.0	9.6	0.186
Q-wave MI	2.4	0.4	0.115	1.4	0.0	>0.999
Non-Q-wave MI	14.7	6.7	0.009	13.6	9.6	0.306
TVR/TLR	12.7	8.0	0.105	12.3	8.1	0.167
TVR (non-TLR)	2.5	3.4	0.612	3.0	3.6	0.739
TLR	11.5	5.1	0.018	10.8	5.2	0.048

MACE = major adverse cardiac events; MI = myocardial infarction; OA = orbital atherectomy; TLR = target lesion revascularization; TVR = target vessel revascularization.
[a] *p*-Values from conditional Cox proportional hazards regression.

3.6. Independent predictors of procedural failure and 3-year MACE

After multivariable analysis of all subjects, pre-stent balloon dilatation was identified as an independent predictor of procedural failure and 3-year MACE (Table 7). Lesion length was also an independent predictor of procedural failure; pre-procedure RVD was identified as an independent predictor of 3-year MACE.

In the propensity-matched cohort, pre-stent balloon dilatation was not identified as a predictor of procedural failure; however, pre-stent balloon dilatation and pre-procedure RVD were identified as independent predictors of 3-year MACE. None of the covariates were identified as independent predictors of procedural failure.

4. Discussion

Currently the literature does not provide information regarding the outcomes of direct stenting (i.e. no pre-stent balloon dilatation) post-orbital atherectomy. However, prior PCI studies have shown that direct stenting results in luminal gain via vessel expansion with a potential reduction in arterial elastic recoil [14] and decrease in vessel injury [15]. Furthermore direct stenting may be associated with more even redistribution of plaque and longitudinally centered stent implantation [16]. In contrast to pre-stent balloon dilatation, when dissections occur during direct stenting, they are often immediately covered by the deployed stent. There may also be a reduction in ischemic time with the direct stenting method [4], and decreased likelihood of geographic miss which increases the risk of restenosis and target vessel revascularization [17]. In addition, direct stenting may offer procedural benefits including reductions in cost related to procedure time, radiation time, and contrast use [18]. The unique mechanism of action of OA allows for significant calcium modification and fracture which may facilitate direct stenting in selected lesions despite severe calcification [19,20].

Therefore, this post-hoc, hypothesis generating analysis of the ORBIT II study was conducted to further understand the results of direct stenting after orbital atherectomy treatment. Despite differences in outcomes in the all subject analysis, after 1:1 matching, the following outcome differences remained. Total OA device run time and average individual OA device run time was significantly shorter in the direct stenting group. This difference may be explained by unknown lesion characteristics not accounted for in the model. The maximum stent deployment pressure was significantly higher in the direct stenting group. Compared to the pre-stent balloon dilatation group, total procedure time and total fluoroscopy time were significantly shorter, and the total contrast volume was significantly smaller in the direct stenting group. Procedural success and in-hospital MACE rates were similar in the pre-stent balloon dilatation and direct stenting groups. However, the SCAI MI rate and severe angiographic complication rates were significantly lower in the direct stenting cohort. The 3-year MACE rates were similar in the pre-stent balloon dilatation and direct stenting groups; however, 3-year TLR rate was significantly lower in the direct stenting cohort.

Important differences in ACC/AHA lesion classification existed between groups, and operator selection bias had an inherent role in treatment strategy selected. Direct stenting should not be used in all patients after treatment with orbital atherectomy. Further intravascular imaging based studies must delineate predictors for which patients can benefit from direct stenting and who requires additional treatment. Our findings however demonstrate that in select calcified lesions that have been treated with orbital atherectomy, direct stenting can be safely performed with favorable long-term outcomes.

The importance of intravascular imaging with IVUS or optical coherence tomography (OCT) is magnified in patients with severely calcified lesions undergoing direct stenting after orbital atherectomy. The potential harm of implanting an underexpanded stent exceeds the benefit of a direct stenting strategy, and therefore DS should not be used in all lesions following OA. Prior to stent implantation, IVUS or OCT imaging

Table 7
Independent predictors of procedural failure and 3-year MACE.

Procedural failure	All subjects				Propensity score matched subjects			
	Unadjusted odds ratio (95% CI)	*p*-Value	Adjusted odds ratio (95% CI)	*p*-Value	Unadjusted odds ratio (95% CI)	*p*-Value	Adjusted odds ratio (95% CI)	*p*-Value
Direct stenting vs. pre-stent balloon dilatation	0.38 [0.20, 0.72]	0.003	0.39 [0.20, 0.75]	0.005	0.55 [0.27, 1.10]	0.091	0.55 [0.27, 1.10]	0.091
Lesion length (per 1 mm increase)	1.04 [1.01, 1.08]	0.009	1.04 [1.00, 1.07]	0.026	1.03 [0.97, 1.08]	0.333	–	–
3-year MACE	Unadjusted hazard ratio (95% CI)	*p*-Value	Adjusted hazard ratio (95% CI)	*p*-Value	Unadjusted hazard ratio (95% CI)	*p*-Value	Adjusted hazard ratio (95% CI)	*p*-Value
Direct stenting vs. pre-stent balloon dilatation	0.57 [0.39, 0.85]	0.006	0.54 [0.36, 0.80]	0.002	0.63 [0.38, 1.05]	0.078	0.56 [0.32, 0.99]	0.046
Pre-procedure RVD (per 1 mm increase)	0.56 [0.34, 0.94]	0.027	0.50 [0.30, 0.85]	0.010	0.32 [0.11, 0.98]	0.046	0.26 [0.08, 0.87]	0.029

CI = confidence interval; RVD = reference vessel diameter.

can help determine which patients are optimal candidates for direct stenting and to ensure lesion preparation is complete. Certain calcium-related lesion characteristics increase the risk of stent underexpansion including calcium deposits with a maximum angle >180°, thickness >0.5 mm, and length >5 mm [21]. Using an OCT-based calcium scoring system can help identify lesions that may benefit from plaque modification prior to stenting versus balloon pre-dilatation alone [21]. Assessment of calcium thickness plays a key role in predicting when calcium fracture is likely to be achieved during balloon inflation [22]. Features including calcium fracture following atherectomy and thickness of calcium can be easily identified with intravascular imaging, impacting further treatment decisions. Post-stenting IVUS or OCT intravascular imaging can confirm optimal stent expansion has been attained and assess if post-dilatation is necessary.

4.1. Study limitations

This post-hoc analysis was not powered to evaluate the effects of direct stenting when treating lesions with orbital atherectomy. Use of direct stenting was at the operator's discretion and patient selection bias is a major study limitation. Despite propensity-score matching and multivariable analysis, other unmeasurable confounders may exist. The use of baseline IVUS was assessed, however utilization of intravascular imaging following orbital atherectomy and post-stenting was not tracked. Future studies are needed to determine the morphological features of which patients are most likely to benefit from direct stenting after orbital atherectomy and in whom it should be avoided. Clearly, more complex lesions with greater calcification may require pre-stent balloon dilatation; however, this analysis is the first to demonstrate that in certain severely calcified lesions, direct stenting can be safely performed after lesion preparation with orbital atherectomy and with excellent long-term outcomes.

5. Conclusion

This subanalysis of the ORBIT II study suggests that direct stenting after orbital atherectomy is feasible and safe in select patients with severely calcified lesions. Furthermore, in appropriately selected patients, this strategy is associated with favorable procedural and long-term clinical outcomes. Using lesion preparation with orbital atherectomy and intravascular imaging may obviate the need for pre-stent balloon dilatation prior to stenting in appropriately selected patients with calcified coronary artery disease. It is imperative that future intravascular imaging studies help delineate which patients can benefit from direct stenting, and more importantly, which patients should not be treated with direct stenting after orbital atherectomy treatment.

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