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Orbital atherectomy for treating *de novo*, severely calcified coronary lesions: 3-year results of the pivotal ORBIT II trial☆

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ABSTRACT

Background/purpose: The presence of heavy coronary artery calcification increases the complexity of percutaneous coronary intervention (PCI) and increases the incidence of major adverse cardiac events (MACE): death, myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis. The ORBIT II (Evaluate the Safety and Efficacy of OAS in Treating Severely Calcified Coronary Lesions) trial reported low rates of procedural, 30-day, 1-year, and 2-year ischemic complications after treatment of *de novo*, severely calcified lesions with the Diamondback 360° Coronary Orbital Atherectomy System (OAS) (Cardiovascular Systems, Inc.).
Methods/materials: ORBIT II was a single-arm trial that enrolled 443 patients at 49 U.S. sites; in this study, *de novo*, severely calcified coronary lesions were treated with OAS prior to stenting. The primary safety endpoint was 30-day MACE: the composite of cardiac death, MI, and TVR (inclusive of target lesion revascularization (TLR)). The primary efficacy endpoint was procedural success: stent delivery with a residual stenosis of <50% without the occurrence of in-hospital MACE.The present analysis reports the final, 3-year follow-up results from ORBIT II.
Results: The majority of subjects (88.2%) underwent PCI with drug-eluting stents after orbital atherectomy. There were 360 (81.3%) subjects who completed the protocol-mandated 3-year visit.The overall cumulative rate of 3-year MACE was 23.5%, including cardiac death (6.7%), MI (11.2%), and TVR (10.2%). The 3-year target lesion revascularization rate was 7.8%.
Conclusions: In the final 3-year analysis of the ORBIT II trial, orbital atherectomy of severely calcified coronary lesions followed by stenting resulted in a low rate of adverse ischemic events compared with historical controls.Orbital atherectomy represents a safe and effective revascularization strategy for patients with severely calcified coronary lesions.
Summary: The ORBIT II trial enrolled 443 subjects to study orbital atherectomy followed by stenting for *de novo* severely calcified coronary lesions. The overall cumulative 3-year MACE rate was 23.5%, including cardiac death (6.7%), MI (11.2%), and TVR (10.2%); the 3-year target lesion revascularization rate was 7.8%. Orbital atherectomy of heavily calcified coronary lesions followed by stenting results in a low rate of adverse ischemic events compared with historical controls; it represents a reasonable revascularization strategy for patients with severely calcified coronary lesions.

1. Introduction

Approximately one third of patients with atherosclerosis have a significant amount of coronary artery calcification observed on angiography [1]. With intravascular ultrasound (IVUS), severe coronary artery calcification is detected in approximately 70% of patients [2]. The presence of heavily calcified coronary lesions represents advanced atherosclerosis and increases the complexity of percutaneous coronary

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intervention (PCI). Procedurally, calcium can make it difficult to deliver coronary devices, damage the drug polymer and stent platform, and limit optimal stent expansion [3]. Attempts to expand a resistant, calcified lesion with prolonged high-pressure balloon inflations may lead to complications such as ischemia, perforation, and dissection. Severe coronary calcification treated with PCI is associated with increased risk of death, myocardial infarction (MI), target vessel revascularization (TVR), and stent thrombosis [4].

Although there are several technologies to prepare calcified coronary lesions prior to stenting, such as scoring balloons and laser or rotational atherectomy (RA), the only FDA-approved device for the treatment of severely calcified lesions is orbital atherectomy [5]. The ORBIT II (Evaluate the Safety and Efficacy of OAS in Treating Severely Calcified Coronary Lesions) trial investigated the safety and efficacy of the Diamondback 360° Coronary OAS (CSI, St. Paul, Minnesota). Results revealed that OAS improved acute and 30-day outcomes for the treatment of *de novo* severely calcified coronary lesions when compared with historic control subjects [5]. Favorable results were also observed at 1- and 2-year follow-up [6,7]. We herein report the final 3-year ORBIT II results.

2. Materials and methods

2.1. Study design and population

The ORBIT II trial (ClinicalTrials.gov Identifier: NCT01092416) was a prospective, non-blinded, single-arm study conducted in 49 U.S. centers that enrolled 443 patients with severely calcified coronary lesions undergoing PCI between May 25, 2010, and November 26, 2012. The trial conformed to good clinical practice and the applicable U.S. Code of Federal Regulations. Each site received approval from its respective institutional review board and all subjects signed informed consent. The angiographic core laboratory (Cleveland Clinic Foundation, Cleveland, Ohio) performed quantitative coronary analysis and assessed for the presence of dissection or perforation.

The ORBIT II key inclusion criteria were: (1) target vessel reference diameter ≥2.5 mm and ≤4.0 mm with a stenosis ≥70% and <100% or a stenosis ≥50% and <70% with evidence of clinical ischemia *via* either positive stress test, fractional flow reserve value ≤0.8, or IVUS minimum lumen area ≤4.0 mm^2; (2) target lesion length ≤40 mm; and (3) imaging evidence of severe calcium at the lesion site based on the angiographic presence of radio-opacities noted without cardiac motion prior to contrast injection, involving both sides of the arterial wall in at least one location, total length of calcium of ≥15 mm and extending partially into the target lesion; or presence of ≥270° of calcium at one cross section *via* IVUS. The exclusion criteria included: (1) the target vessel had a stent from a previous PCI unless the stent was on a different branch than the target lesion and was implanted more than 30 days prior with no higher than 30% in-stent restenosis; (2) recent MI, defined as creatine kinase >1 times upper limit of normal (ULN) within 30 days before the index procedure; (3) chronic renal failure unless under hemodialysis, or a serum creatinine level > 2.5 mg/dL; and (4) evidence of current left ventricular ejection fraction ≤25%.

2.2. Study device

The coronary OAS modifies calcified plaque to facilitate stent delivery and to help optimize stent expansion in severely calcified arteries. The mechanism of action is differential sanding of coronary calcification: the diamond-coated crown orbits over a specialized guidewire (ViperWire, CSI, St. Paul, Minnesota), minimizing trauma to the soft, healthy vessel wall, which flexes away from the orbiting crown. The crown expands laterally with centrifugal force, up to a maximum orbit diameter specified for low (80,000 rpm) or high (120,000 rpm) speed. The pneumatic and electric OAS configurations were used [5], with a crown diameter range of 1.25 mm–2.00 mm [8–11].

2.3. Study procedure

One target lesion was treated per patient. Investigators were required to implant an FDA-approved stent after performing orbital atherectomy and were not allowed to use thrombectomy, embolic protection devices, brachytherapy, or cutting balloons. Pre-dilatation after atherectomy and post-dilatation after stenting was left to the discretion of the operator. While no medications were mandated or required, dual antiplatelet therapy was recommended [12].

2.4. Study endpoints

The primary safety endpoint was the rate of 30-day major adverse cardiac events (MACE), defined as cardiac death, MI, and TVR. MI was defined as creatine kinase-myocardial band level >3 times ULN with or without a new pathologic Q-wave. TVR was defined as repeat revascularization of the target vessel (inclusive of the target lesion) after completion of the index procedure. Patients were followed up in clinic at 30 days, and by telephone at 1, 2, and 3 years.An independent, clinical events committee adjudicated all adverse events.

The primary efficacy endpoint was defined as procedural success: stent delivery with a residual stenosis of <50% without the occurrence of an in-hospital MACE. The secondary endpoints included angiographic success, defined as success in facilitating stent delivery with a residual stenosis <50% without severe angiographic complications during the index procedure, as well as the rate of individual severe angiographic complications during the index procedure [5].

2.5. Statistical analysis

Continuous variables are expressed as mean ± standard error.The Kaplan–Meier method was used to construct survival curves for the time-to-event variables. Statistical analyses were performed with either SAS Software System (SAS Institute Inc., Cary, NC, USA) or R (R Core Team2014).

Table 1
Baseline demographic characteristics.

Average age, years, $n = 443$	71.4 ± 0.5
Male gender	286/443 (64.6)
Ethnicity	
Caucasian	390/443 (88.0)
Black or African American	25/443 (5.6)
Asian	9/443 (2.0)
Hispanic or Latino	15/443 (3.4)
Native American	1/443 (0.2)
Body mass index (kg/m^2), $n = 443$	29.4 ± 0.3
Diabetes mellitus	160/443 (36.1)
Type I	10/443 (2.3)
Type 2	150/443 (33.9)
Hypertension	406/443 (91.6)
Dyslipidemia	407/443 (91.9)
Smoking	
Current	75/443 (16.9)
Former	218/443 (49.2)
Estimated glomerular filtration rate ($mL/min/1.73\ m^2$), $n = 441$	75.8 ± 1.2
Left ventricular ejection fraction (%), $n = 437$	56.6 ± 0.5
Prior stroke/transient ischemic attack	39/443 (8.8)
Prior myocardial infarction	99/443 (22.3)
Prior percutaneous coronary revascularization	205/443 (46.3)
Prior coronary artery bypass grafting	65/443 (14.7)
NYHA classification	
No history of heart failure	28/440 (6.4)
Class I	249/440 (56.6)
Class II	161/440 (36.6)
Class III	2/440 (0.5)
Class IV	0/440 (0.0)

Values are *n*/*N* (%), mean ± standard error; NYHA = New York Heart Association.

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