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PERCUTANEOUS CORONARY INTERVENTION

Real-World Multicenter Registry of Patients with Severe Coronary Artery Calcification Undergoing Orbital Atherectomy

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***Objectives**: We evaluated the safety and efficacy of orbital atherectomy in real-world patients with severe coronary artery calcification (CAC).*
***Background**: The presence of severe CAC increases the complexity of percutaneous coronary intervention as it may impede stent delivery and optimal stent expansion. Atherectomy may be an indispensable tool for uncrossable or undilatable lesions by modifying severe CAC. Although the ORBIT I and II trials report that orbital atherectomy was safe and effective for the treatment of severe CAC, patients with kidney disease, recent myocardial infarction, long diffuse disease, severe left ventricular dysfunction, and unprotected left main disease were excluded.*
***Methods**: This retrospective study included 458 consecutive patients with severe CAC who underwent orbital atherectomy followed by stenting from October 2013 to December 2015 at 3 centers.*
***Results**: The primary endpoint of major adverse cardiac and cerebrovascular events at 30 days was 1.7%. Low rates of 30-day all-cause mortality (1.3%), myocardial infarction (1.1%), target vessel revascularization (0%), stroke (0.2%), and stent thrombosis (0.9%) were observed. Angiographic complications were low: perforation was 0.7%, dissection 0.9%, and no-reflow 0.7%. Emergency coronary artery bypass graft surgery was performed in 0.2% of patients.*
***Conclusion**: In the largest real-world study of patients who underwent orbital atherectomy, including high-risk patients who were not surgical candidates as well as those with very complex coronary anatomy, acute and short-term adverse clinical event rates were low. A randomized clinical trial is needed to identify the ideal treatment strategy for patients with severe CAC.* (J Interven Cardiol 2016;29:357–362)

Introduction

Coronary artery calcification (CAC) is a marker of advanced atherosclerosis and increases the complexity of percutaneous coronary intervention (PCI).[1] Data on PCI with drug-eluting stents in severe CAC are limited as these patients were excluded from randomized trials. Stent delivery may be difficult due to severe CAC. Furthermore, CAC may limit optimal stent expansion, impairing drug delivery, leading to increased risk of restenosis and thrombosis. Multiple, prolonged, high-pressure balloon inflations to adequately predilate a resistant lesion with severe CAC can lead to dissection, perforation, and ischemia, possibly leading to hemodynamic and electrical instability. Severe CAC is also associated with an increased risk of adverse cardiac events after PCI, including death, myocardial infarction, and repeat revascularization.[2]

Rotational atherectomy, which was first introduced in the early 1990s, modifies severely calcified plaque, thereby facilitating stent delivery and expansion.[3–9] Orbital atherectomy represents the first coronary atherectomy device in over 20 years to ablate severe CAC. The ORBIT (evaluate the safety and efficacy of

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OAS in treating severely calcified coronary lesions) II trial, which was a single arm, prospective multicenter study of 443 patients, reported that orbital atherectomy followed by stenting in patients with severe CAC resulted in excellent rates of angiographic and procedural success.[10] The favorable results were also observed at 1- and 2-year follow-up.[11,12] However, patients were excluded if they had recent myocardial infarction, chronic kidney disease, severe left ventricular systolic dysfunction (ejection fraction $\leq$25%), long diffuse disease (>40 mm lesion length), or unprotected left main coronary artery disease. Our real-world registry describes the outcomes of all-comers with severe CAC who underwent orbital atherectomy followed by stenting.

Methods

Study Population. This retrospective study included 458 consecutive patients with severe CAC who underwent orbital atherectomy between October 2013 and December 2015 at 3 centers (UCLA Medical Center, Los Angeles, CA, St. Francis Hospital, Roslyn, NY, and Northwell Health, Manhasset, NY). Severe CAC was defined by the presence of radio-opacities on fluoroscopy involving the vessel wall. The institutional review board at each site approved the review of the data.

Device Description. The coronary orbital atherectomy device (Cardiovascular Systems, Inc. [CSI], St Paul, MN) is advanced over a 0.014″ guidewire (ViperWire, CSI) while a lubricant, ViperSlide (CSI), is infused through the drive shaft to reduce friction during advancement of the device. The eccentrically mounted, 30 μ diamond-coated crown rotates over the ViperWire and laterally expands due to centrifugal force, removing calcified plaque to improve vessel compliance prior to balloon predilatation and stenting.

Procedure and Medical Treatment. Percutaneous coronary intervention was performed with standard techniques. After atherectomy, predilatation angioplasty was routinely performed. A transvenous pacemaker was inserted prior to PCI at the discretion of the operator. Orbital atherectomy was started with low speed (80,000 rpm) in all cases with subsequent high-speed (120,000 rpm) atherectomy performed at the operator's discretion. The recommended duration of each pass was 20 seconds or less. The choice of drug-eluting stent or bare-metal stent, antithrombotic therapy (heparin or bivalirudin), and the use of hemodynamic support device and intravascular imaging (intravascular ultrasound or optical coherence tomography) was left to the discretion of the operator. All of the patients received dual anti-platelet therapy for a minimum of 1 month after bare metal stenting and 12 months after drug-eluting stenting. All patients were treated with optimal medical therapy including beta-blockers, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, and statins unless contraindicated.

Study Endpoints and Clinical Follow-Up. The primary endpoint was 30-day major adverse cardiac and cerebrovascular events (MACCE), as defined as all-cause death, myocardial infarction, target vessel revascularization, and stroke. Myocardial infarction was defined as recurrent symptoms with new ST-segment elevation or re-elevation of cardiac markers to at least twice the upper limit of normal. Target vessel revascularization was defined as a repeat revascularization of the target lesion because of restenosis within the stent or in the 5 mm distal or proximal segments. Stent thrombosis was defined according to the Academic Research Consortium definition.[13] Data including patient demographics, angiographic and procedural characteristics, and clinical outcomes were collected from medical records and entered into a dedicated PCI database.

Statistical Analysis. Statistical analysis was based upon intention-to-treat and was performed with SAS version 9.1 (SAS Institute, Cary, NC). Continuous variables are expressed as means and standard deviations. Categorical variables are expressed as percentages.

Results

Baseline Clinical Characteristics. Of the 458 patients, the orbital atherectomy device could not cross the lesion in 2 patients. Another patient had the device removed as the electrocardiogram showed ST-elevation when the device was advanced to the lesion. The mean age was 74.9 ± 9.9 years, and majority of the patients were male (68.6%) (Table 1). Chronic kidney disease was present in 19.2%, and 3.7% required dialysis. The mean ejection fraction was 51.9 ± 11.3%, and severe left ventricular dysfunction (ejection fraction $\leq$25%) was present in 5.0% of patients.

Table 1. Baseline Clinical Characteristics

	N = 458
Age (years)	74.9 ± 9.9
Male gender	314 (68.6)
Diabetes mellitus	193 (42.1)
Hypertension	396 (86.4)
Hypercholesterolemia	364 (79.5)
Smoking (current or former)	21 (4.6)
Chronic kidney disease (creatinine ≥1.5 mg/dL)	88 (19.2)
Dialysis	17 (3.7)
History of myocardial infarction	71 (15.5)
Previous percutaneous coronary intervention	163 (35.6)
Previous coronary artery bypass grafting	77 (16.8)
Indication for PCI	
Myocardial infarction	51 (11.1)
Unstable angina	229 (50.0)
Elective	178 (38.9)
Mean ejection fraction (%)	51.9 ± 11.3%
Severe left ventricular systolic dysfunction (EF ≤25%)	23 (5.0)

Values are n (%) or mean ± SD. EF = ejection fraction; PCI = percutaneous coronary intervention.

Table 2. Angiographic and Procedural Characteristics

	N = 458
Location	
Left main artery	18 (3.9)
Left anterior descending artery	309 (67.4)
Left circumflex artery	63 (13.8)
Right coronary artery	136 (29.7)
Drug-eluting stent	422 (92.1)
Drug-eluting stent	422 (92.1)
Multivessel PCI	63 (13.6)
Vessels treated per case	1.2 ± 0.5
Multivessel PCI	63 (13.6)
Vessels treated per case	1.2 ± 0.5
Stent diameter (mm)	3.1 ± 0.4
Total stents used per case	2.1 ± 1.2
Total stent length (mm)	43.9 ± 24.6
Total number of passes	4.2 ± 2.7
High speed (120,000 rpm)	81 (17.7)
Total volume of contrast used (mL)	187.7 ± 91.7
Total fluoroscopy time (minutes)	21.9 ± 17.7
Maximum stent pressure (atm)	16.1 ± 4.1
Use of glycoprotein IIb/IIIa receptor antagonist	14 (3.1)
Transvenous pacemaker	27 (5.9)
Optical coherence tomography	149 (32.5)
Intravascular ultrasound	103 (22.4)
Hemodynamic support device	24 (5.2)
Intra aortic balloon device	14 (3.1)
Impella	9 (2.0)
Extracorporeal membrane oxygenation	1 (0.2)
Successful stent delivery	454 (99.1)

Values are n (%) or mean ± SE. PCI = percutaneous coronary intervention.

Baseline Angiographic and Procedural Characteristics. The number of vessels treated per case was 1.2 ± 0.5 (Table 2). The number of stents used per case was 2.1 ± 1.2, and the mean stent length was 43.9 ± 24.6 mm. Drug-eluting stents were used in 92.1% of cases. The mean number of passes was 4.2 ± 2.7 per case with high-speed (120,000 rpm) used in 14.7% of cases. A transvenous pacemaker was inserted in 5.9%, and hemodynamic support device was used in 5.2%.

Thirty-Day Clinical Outcomes. The MACCE rate at 30 days was 1.7% (Table 3). Low rates of 30-day all-cause mortality (1.3%), myocardial infarction (1.1%), target vessel revascularization (0%), and stroke (0.2%) were observed. Two of the patients who died had unprotected left main disease but died from non-PCI-related complications. Four of the 5 patients who had myocardial infarction occurred periprocedurally. The stent thrombosis rate was 0.9%. Successful stent delivery was achieved in 99.1% of patients. Emergency coronary artery bypass graft surgery was performed in 0.2%. Angiographic complications were low: perforation 0.7% (cardiac tamponade 0.7%), dissection 0.9%, and no-reflow 0.7% (Table 4).

Discussion

Orbital atherectomy represents novel technology that is safe and effective for uncrossable or undilatable lesions due to severe CAC. In the largest registry of patients with severe CAC who underwent orbital atherectomy, the rates of adverse cardiac events were

Table 3. Thirty-Day Clinical Event Rates

	N = 458
Major adverse cardiac and cerebrovascular events	8 (1.7)
Death	6 (1.3)
Myocardial infarction	5 (1.1)
Target vessel revascularization	0 (0)
Stroke	1 (0.2)
Stent thrombosis	4 (0.9)
Emergent coronary artery bypass grafting	1 (0.2)

Values are n (%).

low, despite including a sizeable number of high-risk real-world patients who would have been excluded from the ORBIT II trial.

Without adequate plaque modification of lesions with severe CAC, stent delivery and optimal stent expansion may not be feasible, which may lead to an increase in adverse clinical events. In the ROTAXUS trial, the overall strategy success rate was higher in the group treated with rotational atherectomy compared to standard therapy (92.5% vs. 83.3%, P = 0.03).[14] In patients who underwent PCI without rotational atherectomy, the rate of stent loss was 2.5%, and the crossover rate from standard therapy to atherectomy due to failure of balloon or stent delivery or suboptimal balloon expansion despite the use of a noncompliant balloon was 12.5%. Severe CAC can also scuff and damage the drug-eluting stent polymer during delivery to the lesion, possibly resulting in higher restenosis rates.[15] The 2011 American College of Cardiology/American Heart Association PCI guideline provides a class 2a (level of evidence C) recommendation for rotational atherectomy for fibrotic or heavily calcified lesions that might not be crossed by a balloon catheter or adequately dilated before stent implantation.[16] However, the guideline does not provide a recommendation for orbital atherectomy given that the ORBIT II trial was published in 2014. Successful stent delivery was high in our real-world registry (99.1%) and was similar to the results in the ORBIT II trial (97.7%).[10]

Table 4. Angiographic Complications

	N = 458
Perforation	3 (0.7)
Cardiac tamponade	3 (0.7)
Dissection	4 (0.9)
No reflow	3 (0.7)

Values are n (%).

Orbital atherectomy has different features compared with rotational atherectomy. The time and complexity for setup of rotational atherectomy may be longer as it requires a nitrogen tank. Balloons and stents can be advanced over the ViperWire to complete the PCI, whereas the 0.009″ Rotawire used for rotational atherectomy does not provide adequate support to accommodate balloons and stents and requires exchange for a workhorse wire. Rotational atherectomy may require sequential utilization of small to larger burrs which adds to the fluoroscopic and total procedural time. The mechanism of action of orbital atherectomy is differential sanding whereby calcified plaque is preferentially ablated bi-directionally to create a smooth, concentric lumen while healthy elastic tissue flexes away from the crown to minimize damage to the vessel.[10]

Our analysis included some of the most challenging patients with coronary artery disease and who otherwise would have been excluded from the ORBIT II trial. They included patients that presented in extremis with myocardial infarction and cardiogenic shock were deemed poor candidates for coronary artery bypass grafting as well as those with severe left ventricular dysfunction who had no other options except for high-risk PCI for complex coronary anatomy. Of the 18 patients who underwent PCI for left main coronary artery disease, 2 patients died, both of whom were determined to be poor candidates for surgical revascularization, from non-PCI-related causes. One patient was a 79-year-old male with heart failure with reduced ejection fraction who died from septic shock and multi-organ failure, and the other patient was a 43-year-old male who underwent emergent orbital atherectomy in the setting of cardiogenic shock after cardiac arrest at home, subsequent cardiopulmonary resuscitation and intubation, and insertion of enhanced extracorporeal membrane oxygenation for severe left ventricular dysfunction with an ejection fraction of 10% while on 4 vasopressors.

The ORBIT II trial excluded patients with severe left ventricular systolic dysfunction. Our analysis included 23 patients (5.0%) who had an ejection fraction $\leq$25%.

Hemodynamic support devices like intra-aortic balloon pump, Impella, or extracorporeal membrane oxygenation were used in 5.2% of patients. Only one study reported the outcomes of rotational atherectomy in patients with severe left ventricular dysfunction (ejection fraction <30%).[17] All 23 patients underwent successful PCI without procedure-related mortality and had no major adverse cardiac events at 30 days.

The incidence of perforation in our study was low (0.7%) and compared favorably to the results from ORBIT I (2%) and ORBIT II (1.8%) trials.[10,18] The rates of perforation in the ROTAXUS trial was 1.7% with rotational atherectomy and 0.8% with standard therapy ($P = 0.56$).[14] Two of the 3 patients who experienced perforation died in our analysis. The incidence of coronary dissection was also low (0.9%) in our analysis, and all 4 patients underwent successful stenting to treat the dissection without any sequelae.

The majority of myocardial infarction was due to periprocedural cardiac biomarker elevation, which is likely related to microparticulate debris liberated during orbital atherectomy. Distal embolization of the debris can lead to microvascular spasm and slow or no-reflow. This is possibly influenced by the length of the lesion, degree of calcification, operator technique (e.g., slow pecking movement of the burr and flushing with normal saline during atherectomy to decrease the generation of heat and increased viscosity), pretreatment with intracoronary vasodilators, the number of passes with the device, total duration of atherectomy, distal runoff for clearing the particulate debris, and other unknown factors. Orbital rotation of the eccentric crown may permit constant coronary perfusion and particulate flushing during orbital atherectomy, possibly resulting in less disturbance in coronary blood flow.

The stroke rates with orbital atherectomy were not reported in the ORBIT I and II trials. Stroke occurred in only 1 patient (0.2%) which was thought to be cardioembolic and confirmed with magnetic resonance imaging. The patient recovered with no significant neurologic deficits.

Limitations. This was a nonrandomized, retrospective study. The lack a control group for comparison necessitates the need for future correlative studies between other devices and clinical outcomes. The restenosis rate is unknown as the follow-up time was short and surveillance angiography was not performed. The data collection was during a period of time when orbital atherectomy was first commercially available, and experience with orbital atherectomy was in its infancy. A learning curve was present with this new technology. Therefore, mastery of this technology was not achieved until several cases were performed. Improved outcomes may be expected as operator experience increases. No angiographic core laboratory was used to assess the angiogram and perform quantitative coronary angiography. Clinical outcomes were not adjudicated by a clinical events committee. Periprocedural cardiac biomarkers were not obtained on all patients, thus underestimating periprocedural myocardial infarction rates. No comparison with rotational atherectomy, which has been the standard of care for the treatment of severe CAC for more than 2 decades, was made. Society of Thoracic Surgery (STS) scores were not calculated to quantify the extent of surgical risk. All cases were performed at these 3 tertiary centers with cardiothoracic surgery services. These results may not be generalizable to all medical facilities and operators. The operators in our study were experienced with rotational atherectomy and received training for orbital atherectomy. Operators were proctored for the first 6 cases by clinical specialists from CSI.

Conclusion

In the largest study of real-world patients who underwent orbital atherectomy for severe CAC, lesion modification with this essential technique facilitated stent delivery and stent expansion. Our results on all-comers mirrored the outcomes observed in the ORBIT II trial. The rate of angiographic and procedural success was high in this complex coronary lesion subset. The 30-day MACCE rates were low despite including very high-risk patients including non-surgical candidates as well as those with severe left ventricular dysfunction and those with challenging anatomy, including long, diffuse disease, and unprotected left main coronary artery disease. Randomized controlled trials are needed to determine the ideal treatment strategy for severe CAC.

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