Advances in stent technology and cardiology training have led to broader adoption of percutaneous coronary intervention (PCI) in increasingly complex patients, yet calcific disease continues to hamper outcomes. Atherectomy is now widely available regionally, but practice heterogeneity and variability in the access to and utilization of technology dedicated toward vessel preparation in calcified coronary artery disease (CAD) persist. This article reviews the available data to guide our learning curve on orbital atherectomy (OA) as it applies to this space, identifies gaps in current knowledge, and suggests future studies that may impact practice patterns.

IMPLICATIONS OF CALCIFIC DISEASE IN OUTCOMES OF PCI

Advances in stent design and operator experience have reduced in-stent complications, with definite or probable stent thrombosis in less than 1% of the non–acute coronary syndrome population at 2 years and in approximately 1% of all cases in the Medicare population, yet 10% of PCI in the National Cardiovascular Data Registry was performed for in-stent restenosis (ISR). ISR can be challenging to manage and is associated with a major adverse cardiac event (MACE) rate of approximately 30% in less than 1 year. This is why adequate vessel preparation is so critical. In a pooled analysis from randomized trials using contemporary drug-eluting stents (DESs), moderate-to-severe calcium was a major predictor of target lesion failure between 30 days to 1 year, observed at a rate of 2.1%. Although the rate of probable or definite stent thrombosis at 1 year was fortunately only 0.6% in the same pooled analysis, other studies have implicated severe calcification as a significant risk factor, likely linked to stent underexpansion. Limitations in practice for calcium management are numerous; among them are operator training and experience with atherectomy and concerns about time and cost. Lack of definitive data is also cited in the face of these other concerns for those who have not adopted atherectomy in their practice.

ATHERECTOMY: DATA, TRIALS, AND TRIBULATIONS

The constant conundrum facing the interventional cardiologist regarding device selection is a balance of risks and benefits of applying a technology. Of course, device utilization is impacted by operator training in best practices, but case selection, complication management, and practice environment all color that risk-benefit assessment. Additionally, our practice patterns emphasize the short-term outcomes for the patient, and a lack of disease-based registries or consistent definitions in disease characteristics such as calcium burden make the application of data more complicated than the surface layer of results. In the case of atherectomy, successful stent implantation may be possible without additional calcium modification, but the question remains: do we improve long-term patient outcomes in cases of...
calcific disease with atherectomy? Unfortunately, these questions may never be fully answered in randomized trials as those who stand to gain the most from device therapies are often not enrolled when the operator does not see equipoise, and crossover to the intervention arm clouds results. Despite these limitations, several trials have identified the relative efficacy and safety profile of atherectomy use, and this article focuses on the recent data exhibiting clinical outcomes after OA (Table 1).

Rotational atherectomy (RA) was early to the market and used in the first studies evaluating atherectomy as an adjunct to PCI in calcific CAD. The ROTAXUS trial randomized patients to DES implantation with or without the aid of RA but failed to show a clinical benefit with regard to early restenosis or clinical outcomes at 2 years. A more recent follow-up trial that randomized 500 patients to RA versus cutting/scoring balloon as vessel preparation demonstrated improved procedural success with RA, but again clinical events were not significantly different nor were they powered for detection in this analysis. Notably, there was 16% crossover, and while patients with severe calcification were included, the core laboratory found that 25% of cases fit criteria for moderate calcification. These early trials are important in emphasizing key characteristics for interventional trials—challenges with anatomic definitions, crossover to the interventional strategy, and power to detect clinical events in stable ischemic heart disease patients and the current DES platforms.

OA is the more recent addition to the market (Diamondback 360® Coronary Orbital System, Cardiovascular Systems, Inc.), and is thus building on a different mechanism of action, using centrifugal forces and orbital motion of the burr to fracture calcium and perform differential sanding.

**Table 1. Data Overview of Studies Evaluating Coronary Atherectomy**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>N</th>
<th>Dissection (%)</th>
<th>Perforation (%)</th>
<th>Slow Flow/ No Reflow (%)</th>
<th>30-Day TVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORBIT II</td>
<td>2014</td>
<td>443</td>
<td>3.4*</td>
<td>1.8</td>
<td>0.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Lee et al</td>
<td>2016</td>
<td>458</td>
<td>0.9</td>
<td>0.7</td>
<td>0.7</td>
<td>0.0</td>
</tr>
<tr>
<td>COAP-PCI</td>
<td>2018</td>
<td>273 OAS</td>
<td>1.3*</td>
<td>0.4</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Kolfman et al</td>
<td>2018</td>
<td>67</td>
<td>7.5</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Chambers et al</td>
<td>2018</td>
<td>78</td>
<td>–</td>
<td>–</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Desai et al</td>
<td>2018</td>
<td>40</td>
<td>0.0</td>
<td>2.5</td>
<td>2.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Whitbeck et al</td>
<td>2018</td>
<td>70</td>
<td>0.0†</td>
<td>1.4</td>
<td>1.4</td>
<td>Only acute (up to discharge) MACE rates were reported</td>
</tr>
<tr>
<td>Okamoto et al</td>
<td>2019</td>
<td>184</td>
<td>1.6</td>
<td>1.6</td>
<td>2.2</td>
<td>–</td>
</tr>
<tr>
<td>COAST</td>
<td>2020</td>
<td>100</td>
<td>2.0*</td>
<td>2.0</td>
<td>2.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Abbreviations: MACE, major adverse cardiac event; TVR, target vessel revascularization.

*Type C-F significant or severe dissections.
†There was no severe dissection, but 4.3% type A dissections.
cross-sectional imaging. The efficacy endpoint of stent implantation with < 50% residual stenosis after stent implantation and freedom from in-hospital MACE was met in 88.9% of participants, with successful stent delivery and < 50% stenosis in 97.7% of cases and low rates of in-hospital Q-wave myocardial infarction (MI) (0.7%), cardiac death (0.2%), and target vessel revascularization (TVR) (0.7%). Follow-up at 3 years was completed in 360 (81.3%) patients, demonstrating a cumulative event rate of MACE of 23.5%, cardiac death of 6.7%, MI of 11.2%, and TVR of 10.2%. Target lesion revascularization at 3 years was 7.8%, as compared with 13.8% and 16.7% in the ROTAXUS trial in the RA and control treatment arms, respectively.9,18,19,25 In contrast with current practice for many operators, the minority of lesions were treated with angioplasty after OA prior to stent placement (still only up to 42% in ORBIT II), whereas 52% had postdilatation after stent placement.9 In total, these data indicate OA may improve management of severely calcific disease with an acceptable safety profile in a patient population that has been poorly represented in trials but are yet limited by lack of a control arm. Recognizing that multiple facets of PCI have changed over time and other patient selection factors differ across studies, these data are encouraging in that calcific CAD can and should be treated in patients with an indication for PCI.

APPLYING DATA TO THE REAL WORLD: DOES IT WORK WHERE IT REALLY COUNTS?

Given the confines of the trial setting and the often lower overall risk profile of patients, subsequent registries shed insight into understanding outcome data in the broader population with real-world use. Lee et al published a study of 458 consecutive patients with severely calcified CAD who underwent OA-assisted PCI.10 This retrospective review of 458 consecutive patients showed low rates of 30-day MACE (1.7%), with 0.9% stent thrombosis, 1.1% MI, 0% TVR, and 1.3% all-cause mortality, indicating significant overlap in these presenting events. Perforation, dissection, and no reflow were all < 1% each, indicating an acceptable safety profile in real practice, although generalizable in the context where operators are likely highly trained in device utilization and managing complications in complex PCI.

Meraj et al performed a prospective registry to evaluate outcomes related to PCI using OA versus RA in 907 patients across five tertiary care hospitals.11 OA was associated with lower rates of the primary endpoint of in-hospital MI (primary endpoint of 6.7% vs 13.8% in RA) and similar procedural safety outcomes in the 546 cases compared after propensity score matching. A recent meta-analysis of seven retrospective studies comparing rates of MI and vascular complications also noted a stronger association of periprocedural MI after RA versus OA but a lower risk of dissection or perforation.26 Although these data are subject to selection bias based on angiographic features and operator preferences despite propensity matching, they do support future study regarding the best use for OA in treating calcified CAD.

Imaging Versus Angiographic Classification of Calcification

The definition of significant calcification by angiography and variable definitions used in studies to date are significant limitations of the current data. In ORBIT II, calcification burden was defined by IVUS in only 8% of cases, with the remaining patients included on the basis of angiographic criteria. A substudy evaluating IVUS in ORBIT II found that there was a reduction in the number of stents used in those with IVUS; 3-year MACE rates were not statistically different but were higher in the no-IVUS cohort (24.2% vs 14.3% in the IVUS group; P = .26).27 As this substudy was limited to 35 patients who underwent IVUS prior to OA, this may favor lesions that were more amenable to imaging prior to OA. However, taken in the context of contemporary data supporting IVUS as a tool to improve PCI outcomes,28 it is likely that coupling intracoronary imaging with atherectomy would further improve PCI outcomes in treating calcified lesions.
Looking Ahead: What Questions Remain?

The current data have established a platform for OA in treating calcified CAD but are limited in terms of patient selection and how that applies to the operator making a rapid decision that has real consequences to the patient: should atherectomy be used in this patient? Frequently, this is not realized until a poor stent result is recognized and is much more challenging to recover (Figure 1). The evaluation of treatment strategies for severe calcific coronary arteries (OA vs angioplasty technique) prior to implantation of DES in the ECLIPSE trial will aid in answering these questions. Currently enrolling with a target of 2,000 patients, this randomized trial is comparing vessel preparation with OA and balloon pre-dilatation to that with conventional and/or systolic balloon preparation, with a primary outcome of target vessel failure at 1 year (composite of cardiac death, target vessel–related MI, or ischemia-driven revascularization). An imaging cohort using optical coherence tomography in 500 patients will also assess minimal stent area as another primary endpoint, as well as secondary outcomes of procedural and strategy success. Importantly, the study population is expanded to include acute coronary syndrome patients provided they are stabilized > 48 hours after ST-segment elevation MI and excludes patients with severe heart failure symptoms or left ventricular ejection fraction < 25%.

The ECLIPSE trial is well positioned to inform whether the practice of using OA or “vessel preparation with balloon angioplasty only” provides the best outcomes. This study far outpaces the aforementioned studies evaluating RA and OA in terms of size; the inclusion of an imaging cohort, evaluating crossover to the alternative strategy, and use of current-generation DESs will lend further insight as to how the vessel preparation strategy affects clinical and procedural outcomes.

Conclusion

Early data evaluating the safety and efficacy of OA are promising. Although patient selection and best practices for technique remain paramount for improving clinical outcomes, many cases should not be undertaken without additional calcium modification and vessel preparation, and training in these tools is imperative for the modern interventional cardiologist. Studies using better-defined classification schemes based on intracoronary imaging to define calcific burden and assess procedural outcomes will better showcase the risks and benefits of OA and further guide use of the full complement of tools aimed at treating calcific CAD.

References