



Cracking the Calcified Plaque[☆]

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It goes without saying that calcium is one of the biggest enemies of percutaneous coronary intervention (PCI). Apart from resistance to delivering wires, balloons, and stents down the artery, calcified plaques are also responsible for suboptimal results after balloon angioplasty and stenting, with extensive dissections (sometimes ending in ruptures), underexpansion of stents, malapposition of stent struts, overexpansion of the adjacent non-calcified vessel wall segments, non-circular lumen, less acute gain, and suboptimal minimal lumen areas. All of these factors undeniably influence procedural outcomes in a negative way in the short and long term. There are two types of coronary artery calcification: atherosclerotic and medial artery calcification. Atherosclerotic calcification mainly occurs in the intima and is a result of inflammation, lipid infiltration and differentiation of smooth muscle cells into an osteogenic cell type [1]. Medial artery calcification is more associated with older age, diabetes mellitus, and chronic renal insufficiency and results in stiffer arteries [1]. Although the distribution of the calcium is different between both types of coronary artery calcification, they are equally related to increased risk for cardiovascular events [2].

In this issue of *Cardiovascular Revascularization Medicine*, Y. Otaki et al. report the outcomes of a large multicenter registry with rotational atherectomy followed by durable-polymer everolimus-eluting stenting (DP-EES) [3]. The main finding of the study is that stenting with DP-EES after rotational atherectomy results in low target lesion revascularization rates, which compare favorably to the results of previous trials with first-generation paclitaxel-eluting stents (PES).

When dealing with severely calcified stenotic coronary plaques, a few things come to mind. How do we identify and classify calcified plaques, and what is the best approach to treat?

Although computed tomography angiography, intravascular ultrasound (IVUS), optical coherence tomography (OCT), and magnetic resonance angiography have been shown to be quite accurate in plaque composition characterization, the easiest and most used way to identify calcified plaques is by standard coronary angiography. In general, three degrees of coronary artery calcification can be classified: none/mild, moderate, and severe. Severe calcification is most commonly defined as radiopacities seen without cardiac motion before contrast injection, usually affecting both sides of the arterial lumen, and moderate calcification as radiopacities noted only during the cardiac cycle before contrast injection [4]. On the other hand, in the SYNTAX score, a heavily calcified lesion is defined as multiple persisting opacifications of the coronary wall in more than 1 projection surrounding the complete lumen

at the site of the stenosis [5]. Nevertheless, standard angiography can sometimes fail to detect concentric discrete rings of superficial and deep calcium-limiting PCI [4]. In those cases, IVUS or OCT can be very helpful in identifying the problem.

Treatment of severely calcified coronary lesions has always been troublesome. Medications such as statins, calcium-channel blockers, hormonal therapy, and phosphate binders have not been unequivocally shown to reduce or slow the progression of calcified plaques [6]. And interventional therapies remain associated with suboptimal end results and increased major adverse cardiovascular events rates during follow-up compared to treatment of non-calcified artery lesions.

Pre-treatment of calcified coronary artery lesions is commonly used before stenting. Cutting and scoring balloons can help improve vessel compliance and facilitate balloon angioplasty with better balloon expansion, controlled dissections, and less recoil. However, little evidence exists as to whether pre-treatment before stenting improves outcomes [6,7] and, personally, I doubt whether these devices are helpful in treating truly severe calcified lesions. The Shockwave C²™ balloon catheter (Shockwave Medical, Inc., Santa Clara, CA) is a new pre-treatment technology for calcified coronary lesions. It uses pulsatile sonic pressure waves to create fractures in the calcified plaque. Proof of concept has been established, and more studies are needed to evaluate safety and efficacy.

High-speed rotational atherectomy with the Rotablator™ (Boston Scientific, Marlborough, MA) or the Diamondback 360™ orbital catheter (Cardiovascular Systems, Inc., St. Paul, MN) does remove calcified plaque and facilitate balloon angioplasty, stent delivery, and stent expansion in severely calcified lesions. Registry studies of rotational atherectomy in severely calcified lesions show safety and favorable target lesion revascularization rates after drug-eluting stenting at follow-up. However, unfortunately, little evidence exists from randomized trials as to whether rotational atherectomy actually improves outcomes compared with balloon angioplasty before stenting. Up to now, only 2 relatively small-sized randomized controlled trials exist. In the ROTAXUS trial of 240 patients with *de novo* calcified stenoses, rotational atherectomy with PES showed no improvement in clinical outcomes over plain balloon angioplasty with PES stenting. Although higher acute gain was obtained with stenting after rotational atherectomy, late lumen loss was significantly higher at 9-month follow-up compared with balloon angioplasty and stenting [8].

Very recently, the PREPARE-CALC trial was published. In this randomized trial of 200 patients with severely calcified native lesions, rotational atherectomy was a more successful strategy than the use of scoring/cutting balloons before implanting a third-generation DES. Furthermore, the trial showed similar clinical outcomes at 9 months with similar low late lumen loss for both strategies [9].

[☆] (Invited editorial)

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In conclusion, in severely calcified coronary lesions, rotational atherectomy facilitates the success rate of the procedure, but adds little extra compared to plain, cutting, or scoring balloon angioplasty as pre-treatment for DES stenting. This is also reflected in the guidelines.

What does the Tokyo-MD PCI study add to the current knowledge? As stated above, one of the randomized trials (ROTAXUS) was done with the first-generation PES, showing increased in-stent late lumen loss after rotational atherectomy compared to balloon angioplasty at 9-month follow-up (0.44 ± 0.58 vs. 0.31 ± 0.52 , $p = 0.04$). The heat generated during high-speed rotational atherectomy probably enhances the intimal hyperplasia response after angioplasty and stenting. DP-EES is known for superiority compared to PES, and the Tokyo-MD PCI study confirms the good outcomes with DP-EES in severely calcified lesions after rotational atherectomy. In fact, after rotational atherectomy, I would use a DES with a polymer with good elastic and sustainable integrity properties and with a minimal 90-day eluting profile of a limus-analogue and a stent platform with good radial strength and conformability.

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