

The Challenges of Calcium in Peripheral Artery Disease

Dr. Rocha-Singh discusses the available methods for calcium assessment and scoring, how calcium affects procedural success, and the goals of the VIVA calcium scoring unification initiative.

WITH KRISHNA ROCHA-SINGH, MD

How would you summarize the challenges that calcium poses in modern peripheral artery disease (PAD)?

As an interventionalist, vascular calcification, regardless of the vascular bed, is and always has been a significant challenge that defines the limits of acute procedural and device success and limits the clinical durability of the intervention. Our early experiences in endovascular approaches, particularly plain old balloon angioplasty in heavily calcified internal carotid arteries, eccentric renal artery calcification, and calcified aortoiliac and infrainguinal lesions, have borne this out. We also understand that vascular calcification is a general marker for global atherosclerotic burden and, in some studies, a marker of cardiovascular-related mortality. Calcium has been, is, and will continue to be a major challenge in cardiovascular percutaneous interventions.

What are some of the limitations to our understanding of calcium in PAD?

There has been and continues to be a growing understanding of the multiple pathways by which vascular calcification occurs. These pathways are complex, interrelated, and involve endocrine, inflammatory, hormonal, and metabolic processes. As such, vascular calcification is a very biologically active disease process and does not represent “dead tissue,” as is commonly perceived. Evolving technologies and therapies have targeted metabolic pathways that lead to vascular calcification, and it is my hope that in the future, these therapies will help us address and potentially prevent progression to severe grades of calcification.

How is calcium best identified and measured? What methods of assessment can be deceiving, and what factors can make calcium scoring difficult?

Multiple modalities have been used for noninvasive and invasive assessment of calcification in a variety of vascular beds. We are well aware of coronary artery calcium scoring using CTA and its potential to predict future cardiovascular events. In the periphery, CT and MRI are highly sensitive methods to assess the degree and extent of vascular calcification. However, both imaging modalities use contrast agents (iodinated contrast for CT and gadolinium-based contrast for MRI), which are associated with potential nephrotoxicity, and CT exposes patients to ionizing radiation. Therefore, CTA remains an important noninvasive imaging modality.

In my experience, I believe that intravascular ultrasound can best assess the degree and extent of calcium. Unfortunately, intravascular ultrasound is not widely used because it is not uniformly reimbursed and is an associated expense. As such, we have to use more practical and uniformly available modalities, which, at this time, is fluoroscopy. However, fluoroscopy underestimates the extent and location of calcification in the superficial femoral artery (SFA) and, particularly, below-the-knee tibial vessels. As a result, these discrepant modalities add to our challenge in developing uniform scoring systems and assisting the physician in assessing the extent of vascular calcification, both pre- and postintervention.

What are the calcium scoring systems in use and how do they differ?

At last count, findings on at least seven different calcium scoring systems have been published in peer-reviewed journals or disclosed as core lab scoring systems as part of investigational trials. Frequently cited calcium scales include the PARC (Peripheral Academic Research Consortium) scale and PACSS (Peripheral Arterial Calcium Scoring Scale), as well as grading scales used by angiographic core labs in the recently presented IN.PACT Global SFA registry and the ILLUMENATE trial, which used varying definitions. Additionally, Dr. Antonio Micari published his own scale, which was used in the multicenter, core lab–adjudicated assessment of the In.Pact Admiral drug-coated balloon (DCB; Medtronic) in long SFA lesions. These scales have many commonalities: they primarily look at the circumferential nature of the calcification (ie, present on both sides of the vessel wall as assessed by fluoroscopy) and the extent of the circumferential calcium as a function of total lesion length. Importantly, all of these scales are hypothetical and have not been validated by hard data endpoints.

What do we currently know about how calcium affects procedural success? What can be done to improve outcomes in patients with heavily calcified lesions?

We must understand that the present calcium scales are hypothetical and are not driven by prospective adjudicated outcome data. As a result, we are left with the general impression that higher degrees of calcification may represent a mode of failure of DCB angioplasty, as observed in the IN.PACT Global Registry Long Lesion substudy. It is my impression that higher degrees of calcium predict acute procedural failure with a balloon or a DCB, and subsequently, adjunct stenting is required to resolve significant vessel recoil or dissection. Addressing higher grades of calcium with adequate “vessel preparation” using either an adjunct balloon (eg, AngioSculpt scoring balloon, Spectranetics Corporation), cutting balloon, or an atherectomy device prior to using a definitive therapy (ie, a DCB or drug-eluting stent) represents the next challenge as these technologies are utilized in more complex lesion morphologies.

Vessel preparation in severely calcified lesions prior to DCB use appeared to improve clinical outcomes in the small registry arm of the DEFINITIVE AR trial. Directional atherectomy in severely calcified arteries prior to DCB use appeared to be safe and perhaps provide favorable patency outcomes, as defined by duplex ultrasonography at 12-month follow-up. This observation is being further evaluated in the 250-patient REALITY study, where

moderate to severely calcified SFA lesions between 8 and 25 cm in length are treated with directional atherectomy prior to use of the In.Pact Admiral DCB.

What are your thoughts on the ideal follow-up period for data collection in patients who require adjunct stenting? What do we know about the use of spot stenting versus the full metal jacket approach, and what can be learned at 30 days versus immediately post-procedure?

As previously mentioned, we only have insights from adjudicated data sets that suggest that more calcification translates into a higher rate of acute procedural failure due to vessel recoil and/or dissections, which then requires adjunct bare nitinol stenting. Although adjunct stenting represents an acute procedural failure, when evaluating patients over the long term, it does not appear that adjunct stenting impacts patency at 1 year versus a DCB alone (ie, no postprocedure stenting). However, these data are derived from small patient cohorts, and we have yet to understand whether spot stenting an area of acute recoil and/or dissection as opposed to applying a full metal jacket is the appropriate therapy in addressing acute DCB failure.

Safety data from adjudicated registries that included more severe grades of calcification would suggest that adjunct bare nitinol stenting to address the acute procedural failure of a DCB is not associated with safety concerns through 30 days (ie, subacute stent thrombosis, need for target lesion revascularization, or limb loss).

Can you tell us about the VIVA calcium scoring unification initiative to gather data on calcium severity? What are the goals of this initiative and where do we stand at initiation?

VIVA Physicians is committed to close collaboration with our industry partners, who have completed, published data on, and marketed DCBs to better understand how vascular calcification affects the acute and 30-day outcomes of this technology. In this regard, access to a robust sample of patient-level, line-item angiographic and patient demographic data is essential to best understand the impact of calcium on both acute procedural and 30-day clinical outcomes. In collaboration with our industry partners and statisticians, VIVA Physicians is looking at multiple angiographic variables—not just calcium—as well as demographic variables that may drive outcomes. We hope to gain access to over 1,000 procedural angiograms and associated 30-day outcomes to bolster with analysis

so that clinicians can be given a predictive score of procedural success and freedom from adverse events through 30 days. These data are very important to help with procedural preplanning, and we also hope to have access to 1-year clinical outcomes in the future. This effort is currently ongoing, and it is VIVA's strong hope that, with continued collaboration, this analysis will be available for podium presentation in early 2018. ■

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