ROUNDTABLE DISCUSSION

The Challenges of Extreme Femoropopliteal Calcification

Global perspectives on the current landscape for the treatment of extreme calcification.

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Dr. Gray: We are all familiar with some of the recently established classifications for calcification in the femoropopliteal segment (Peripheral Arterial Calcium Scoring Scale [PACSS], Peripheral Academic Research Consortium [PARC]), which are useful especially in research endeavors, but today we are talking about real-world extreme calcification. How do you define this category? On length, bulkiness/thickness, location (eg, ostial, Hunter's canal, popliteal), or some combination?

Prof. Brodmann: Without a doubt, established classifications for calcium are useful and have helped define calcified lesions in the recent trials, which was a big step forward to distinguish if drug-eluting technologies were working and in what kind of lesions.

However, in a real-world setting, we have to deal more and more with the "worst of the worst" calcium that we have not seen before. On angiographic view, it might appear simply as circumferential calcium, but when you want to bring different devices through such calcified lesions, it can be tricky and sometimes impossible.

Dr. Khashram: Tools to classify the presence and degree of calcification have been useful in research and in highlighting the relationship between severe calcifications and the worse outcomes. The Global Limb Anatomic Staging System also classifies calcification of > 50% of a lesion to be worthy of a step up in grade in its staging system, signifying the importance of this lesion characteristic. But, in the real world, classifying calcium in the femoropopliteal segment is not widely adopted. Perhaps the most useful categories to consider are the length of lesion, stenotic versus occlusive calcified plaques, and the involvement of more than one level.

Dr. Schmidt: Indeed, even the highest grade of calcification from the PACSS and PARC classification does not capture very well what we consider as an extremely calcified lesion. Whereas the highest grades (PACSS-5 or PARC-4) are often—even for drug-coated balloon (DCB) studies—exclusion criteria, the immediate reaction encountering extremely calcified lesions is that an endovascular recanalization with "standard devices" such as DCB, atherectomy, or laser-cut, nitinol stents will not work and inclusion into studies is unrealistic.

The density, thickness, and bulkiness of the calcification is especially a characteristic that is not well captured by the common classification attempts. For example, a one-sided calcification, which would be graded quite low in PACSS and PARC, but that is thick in diameter and appears dense on fluoroscopy can certainly be more difficult to treat than thinner calcifications on both sides, which falls into a higher PACSS and PARC class.

Another pattern of calcification that is, for my understanding, not well characterized in PACSS and PARC is double-sided calcification, which is considered to be the same as circumferential calcification but is often not the case. Typical intimal calcification, bulky or not and bilateral or not, must be distinguished from the certainly less frequent pattern of truly circumferential, medial, and sometimes also extreme calcification.

For choosing the appropriate endovascular tools, density and thickness of the calcification is of highest importance; length of the calcification also has influence on the treatment strategy (atherectomy is less effective, cumbersome, and complications are more frequent). Whether the location is proximal, mid, or as most often in the Hunter's canal or popliteal is of less importance. Only truly ostial, proximal extreme calcification is problematic and may require a surgical or hybrid approach.

Prof. Zeller: In my definition, extreme calcification is characterized by its bulkiness and thickness, not essentially by its extension in length. In particular, eccentric calcified plaques with a thickness of sometimes even 10 mm are challenging because they do not respond to lithotripsy nor nondirectional atherectomy devices.

Dr. Gray: What is your initial therapeutic approach in extreme calcification? Are you confident enough in your assessment that you will skip percutaneous transluminal angioplasty (PTA) altogether and move to something else?

Dr. Khashram: In a successful recanalization, PTA is still useful in identifying lesion responsiveness and to allow for size matching and vessel preparation. However, the outcomes of PTA alone are generally poor, which is why we have better options. Calcium debulking is a good option to consider prior to scaffolding, particularly in lesions where we know primary stenting or PTA do poorly.

Dr. Schmidt: Recoil forces in extremely calcified lesions are pronounced. It is very rare that balloon angioplasty will yield satisfactory results, no matter whether plain old balloon angioplasty (POBA), scoring or cutting balloons, or high-pressure balloons are used. Similarly, this applies to atherectomy. However, these techniques are not skipped but used aggressively, mainly POBA and high-pressure balloon angioplasty, for vessel preparation to eventually proceed to stenting.

Prof. Zeller: PTA in the sense of POBA or even DCB angioplasty under these conditions is not an option. Treatment options include directional atherectomy followed by DCB or stent implantation or vessel preparation with lithotripsy followed by high-pressure balloon angioplasty and stent implantation, usually with an interwoven stent like Supera (Abbott). In extreme cases, it may be necessary to rupture the artery followed by stent graft insertion (pave-and-crack technique).

Prof. Brodmann: PTA alone is not suitable in these lesions because the balloons can rupture and there is insufficient lumen gain, among other potential issues. Therefore, now my first approach is with calcium modifying tools such as intravascular lithotripsy (IVL).

Dr. Gray: When it comes to atherectomy devices, what are your top two (in rank order) devices? Given that we lack comparative data between devices, what features make these your choices?

Dr. Schmidt: The Jetstream atherectomy system (Boston Scientific Corporation) is the device we most frequently use in severe calcium. However, only in cases

of circumferential calcification and only if intraluminal or central guidewire passage could be established. But, as mentioned previously, the situation of eccentric, bulky calcified plaque, where guidewire passage is always subintimal or at least not through the center of the calcification is much more frequent, then Jetstream atherectomy is no-option. In this situation, only if the disease is rather focal and not too extensive in length, we choose directional atherectomy. Because many extremely calcified lesions are complex also due to their length, directional atherectomy is our second choice in terms of numbers. Filter protection is absolutely mandatory.

Prof. Zeller: For eccentric lesions, directional atherectomy (HawkOne, Medtronic) is the most suitable device. For concentric lesions, in particular below the knee, orbital atherectomy (Diamondback 360, Cardiovascular Systems, Inc.) or Rotablator (Boston Scientific Corporation) are the most useful atherectomy tools.

Prof. Brodmann: On a daily basis, we use the HawkOne directional atherectomy system and the Phoenix atherectomy system (Philips). With regard to alternative technologies, we have used and know the Diamondback 360 peripheral orbital atherectomy system as well as the Auryon laser atherectomy system (AngioDynamics, Inc.)

Dr. Khashram: There are now several devices available on the market, but further comparative studies are needed to establish which device is best suited for each specific lesion. My preference is directional atherectomy and for that I use the HawkOne device. I particularly appreciate the ability to direct where I see is the most appropriate area to focus on and have found it useful in vessel preparation. I have also found great utility with rotational atherectomy, particularly below the knee where lesions can be very difficult to cross.

Dr. Gray: When treating extreme calcification, will you work hard not to implant a stent, or is your anticipation that you will need to? For either answer, why?

Prof. Zeller: In short lesions, I try to avoid stenting if possible, using directional atherectomy as the first choice. For longer calcified lesions, stenting is very likely, and for longer-term interventional success, appropriate vessel preparation is key to allow maximal stent expansion.

Prof. Brodmann: I try to avoid stenting due to inadequate wall attachment, as well as the issue of stent fracture that is always in the back of my mind.

Dr. Khashram: Generally, the outcomes of stents in extreme calcifications are poor if the vessel is not adequately prepped and debulked. My preference is not to implant a stent except in flow-limiting dissections or recoil. An interwoven nitinol stent (Supera) has performed well in these lesions, considering that the most important factor is vessel preparation for this device. I have also found aggressive predilatation to be crucial.

Dr. Schmidt: My proposal is a definition of extreme calcification that should include that a satisfactory result without stenting cannot be achieved. Any attempts to follow this strategy are time-consuming (atherectomy, prolonged ballooning, use of different specialty balloons) and prolongs the procedure, which are usually already long due to its complexity.

In extreme femoropopliteal calcification, we will work hard to be able to implant stents, specifically the Supera interwoven nitinol stent. At our institute, this treatment is somewhat standardized.

After guidewire passage, stepwise POBA is performed to prepare for a Supera stent implantation with a diameter according to the reference vessel diameter. Using this method, perforation is not infrequent, especially in areas with very thick calcific burden. Local anesthesia applied along the whole calcified segment, like tumescent anesthesia before vein ablations, is performed in practically all cases. If perforation occurs or is anticipated, a Viabahn stent (Gore & Associates) implantation is often necessary before vessel preparation can proceed for a Supera stent implantation. This "pave-and-crack" technique is usually not planned but is considered as a safety net. We described this technique in detail some years ago.[1] Certainly, the detour technique is an alternative to our concept.[2]

Dr. Gray: Do you lower your expectations for the quality of the angiographic outcome in extreme calcification? If so, what is your new "standard" for a successful procedure?

Prof. Brodmann: Yes, I definitely lower my expectations. Right now, I go for a technology that I believe is a game changer, and in my mind, it currently is IVL, which has excellent data.

Dr. Khashram: On some occasions, it can be difficult to assess how much endovascular therapy is required to heal a wound. In our unit, we have been utilizing a novel assessment of foot perfusion referred to as pedal acceleration time (PAT) that doesn't seem to be affected by calcified inflow. This is a technique that involves

measuring the acceleration time in pedal arteries using duplex ultrasound. However, I do have an altered level of acceptance when it comes to angiographic results for heavily calcified lesions. In those cases, I pay close attention to the postoperative hemodynamic status, specifically PAT, and reintervene as required.

Dr. Schmidt: The expectation to the final angiographic result should be even higher than for less severe calcifications. Significant recoil is less frequent in less calcium, and residual stenosis after an implantation of a standard stent might resolve over time due to the chronic outward force of the stent. This chance of late improvement is certainly diminished in extreme calcification. Residual stenosis is a risk factor for restenosis. In this regard, we also think that implanting a relatively small Supera stent—because it requires less aggressive pretreatment, which then appears undersized compared to the reference vessel diameter—should be avoided. We cannot substantiate this yet with data, but our impression is that achieving an optimal angiographic result with similar vessel diameters within the calcific area compared to the reference vessel is optimal for long-term patency.

Prof. Zeller: Treatment success means at least a < 30% residual stenosis. This threshold is independent of lesion morphology. In particular for calcified lesions, my colleagues from Leipzig, Germany, could nicely show that incomplete stent expansion is a predictor for restenosis.[3]

Dr. Gray: With the advent of IVL, have you changed your treatment paradigm? Do you use more or less atherectomy or more or less stents? Is there a greater expectation of the angiographic result?

Dr. Schmidt: IVL is certainly one of the most interesting recent developments in the endovascular field. Whether it can be used as a stand-alone treatment for extremely calcified lesions or should rather be considered as an effective method for vessel preparation before stenting remains an open question. The recently published DISRUPT PAD III trial showing superior results for IVL compared to standard balloon treatment in terms of residual stenosis in calcified femoropopliteal lesions may not be sufficient to answer this question.[4] Because it was possible to achieve results with residual stenosis ≤ 30% in 48.1% and with stenting necessary only in 18.3% in the control arm, calcification was potentially not that extreme. Several other questions remain to be answered such as the comparison of the effectiveness of IVL in eccentric-calcified compared to circumferentially calcified lesions. It is certainly possible that less atherectomy will be performed, lowering the risk of peripheral embolization. Potentially fewer perforations may occur during vessel preparation, lowering the need for covered stents. Finally, it might be possible to create larger diameters, improving the angiographic result and potentially increasing the patency rates in these complex lesions.

Dr. Khashram: IVL has been the "game changer" in the heavy calcified lesions, and in our institution (like others using IVL), it has reduced the use for atherectomy and stent device insertion in calcified lesions. The debulking of the lesion and luminal gain achieved demonstrated on angiography has changed the treatment paradigm to avoiding stents and treating with antiproliferative therapy.

Prof. Zeller: IVL simply represents an additional interventional tool to overcome the challenge of calcium. I already explained my anatomic preferences for the different treatment tools. What may have changed since the introduction of IVL is most likely the expectation of the angiographic result.

Prof. Brodmann: Yes, I definitely do less atherectomy, as well as use fewer stents. I also have greater expectations for the angiographic result, and we see it in daily practice and from our long-term experience with IVL.

Dr. Gray: Do you believe the value of antiproliferative therapies is the same, better, or worse than in nonextreme calcification? Does your answer affect your use of antiproliferatives in this lesion class? When you have a recurrence in this lesions class, how do you approach it?

Prof. Zeller: The answer is that nobody knows. As long as no specific data for the medical treatment of severely calcified atherosclerosis exist, the same medical treatment algorithm should be applied as for nonextreme calcific vascular disease.

Prof. Brodmann: Antiproliferative therapy and severe calcium is for sure a challenge, and we know this in detail from scientific work, particularly the article by Fanelli et al.[5] Therefore, it is so crucial to modify the calcium, not for vessel expansion only, but also for better drug uptake. IVL has shown that it can be helpful in these circumstances.

Dr. Khashram: I think the results of antiproliferative therapy are worse in patients with severe calcification

as drug delivery is hindered, and this has been shown in several studies. A recurrence in this lesion class should prompt the use of antiproliferative therapy, as the treatment is designed to reduce recurrence associated with neointimal hyperplasia.

Dr. Schmidt: The platform of all current drug-eluting stents (DESs) for the femoropopliteal segment are laser-cut nitinol stents, and therefore, due to their inferior crush-resistive force, these stents are not optimal devices for extreme calcification. Whether recoil or inferior uptake of the drug into the arterial wall using DCBs in severe calcification is the main reason for inferior results is not completely understood. DCBs may be used in combination with lithotripsy, atherectomy, or Supera stents. In our lab, recanalization of extremely calcified femoropopliteal lesions often ends in a combination of different strategies and devices. Often, calcification does not affect the whole length of the lesion; proximal and distal areas may be optimally treated by additional DES implantation or DCB PTA.

In case of recurrence, it is important to try to clarify the underlying mechanism. If recoil due to calcification is likely, more aggressive final treatment as described previously should be performed. In case of intimal hyperplasia, it is no different than any other restenosis treatment since calcification will never be found within the stent. Restenosis within Supera stents may be extremely resistant to balloon angioplasty and atherectomy before DCB treatment can be essential.

Dr. Gray: Does your tolerance for surgical intervention change in these lesions? Before or after initial therapeutic attempt? Does your counseling to patients change?

Dr. Khashram: As mentioned earlier, personalizing treatment for patients is paramount in this vulnerable group. The general outcomes and survival of peripheral artery disease are worse than many oncologic conditions. Yet they are usually undertreated medically and often present late for treatment. In chronic limb-threatening ischemia and diabetic foot patients with long arterial lesions, particularly in the presence of major tissue loss, an open surgical revascularization or a hybrid approach with foot surgery is perhaps the most durable and efficient option. However, this may come with some morbidity and depends on existing institutional experience and logistics.

This decision-making algorithm should consider patient comorbidities and life expectancy, presence of suitable conduit, complexity of arterial disease, and assessment of foot function. This is then used to counsel the patients and develop a shared understanding of the treatment plan. Other factors that may need to be considered are experience of centers, resources, and costs of therapy. These are all real-world issues that should be considered and require a multidisciplinary dedicated limb salvage team.

Dr. Schmidt: Except in the case of extreme calcification in proximity to the femoral bifurcation—where we certainly tend to perform hybrid procedures more frequently compared to less calcified lesions—we have not changed our tolerance to surgical interventions and counseling of patients. Severe calcification of the anastomotic area may be a challenge for the surgeon. Additionally, the high success rate, low complication rate, and satisfactory patency rate justifies an endovascular-first approach also in extremely calcified lesions.

Prof. Brodmann: No, not right away from the beginning. An endovascular-first approach is my first choice, and if not successful, then I discuss surgery with the patient.

Prof. Zeller: My tolerance for recommending surgery in extreme calcification is lower—after having tried the endovascular option!

Dr. Gray: What future developments, if any, do you see on the horizon for extreme superficial femoral artery calcium management?

Prof. Brodmann: Severe calcium is one important focus for developing new treatment tools. We will see guidewires that will allow us to cross calcified lesions easier and hopefully intraluminally. We will see atherectomy devices that can specifically address calcium above and below the knee. And we will see followers of the IVL technology grow.

Dr. Khashram: With improvement in patients' life expectancy, this is an area of ongoing revolution and progress. Lower-profile debulking/atherectomy devices in conjunction with improved ways of delivering antiproliferative drug into the vessel wall are potential areas of further refinement. Clinical data from BEST-CLI, BASIL-2, and BASIL-3 might provide further level 1 evidence to assist in clinical decision-making in this complex patient group and provide the most durable revascularization to meet the patient needs.

Prof. Zeller: To date, I don't see a new specific tool on the horizon. It is more combining currently available tools such as atherectomy, lithotripsy, high-pressure balloons, and dedicated calcium stents, even if this combination therapy will increase the treatment costs significantly.

Prof. Schmidt: As mentioned before, IVL could play a role in extreme calcification and may facilitate the treatment significantly. New atherectomy devices like the Bycross system (Plusmedica) must prove their effectiveness and potentially superiority to other devices in calcified lesions. ■

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