Rock-Hard Chronic Thrombotic Occlusion and Its Management in Endovascular Interventions

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Abstract

Endovascular recanalization for patient with peripheral arterial disease and the end of its spectrum critical limb ischemia (CLI) has become a preferred method of revascularization due to advancement of techniques and equipment, allowing reduction of limb amputations while maintaining a minimally invasive approach compared to surgical approaches. Interventionalists have undertaken a progressively increasing complexity of diseased vessels in the hopes of providing inline unobstructed flow through occlusions for patients with claudication as well as direct flow to a nonhealing wound in patients with CLI. One of the major roadblocks encountered in lower extremity recanalization procedures is managing severely calcified chronic thrombotic occlusions which decrease luminal revascularization, ultimately increasing use of adjunctive interventions such as subintimal tracking, reentry device utilization, and stent placement. Understanding the histopathology and classification of lower extremity calcifications, imaging findings, and escalation of equipment use provides a thorough background in dealing with these specific cases.

Keywords

- interventional radiology
- peripheral arterial disease
- critical limb ischemia
- revascularization

Objectives: Upon completion of this article, the reader will be able to describe the patient selection process, techniques used, and potential complications of chronic thrombotic occlusion revascularization techniques used in the PAD/CLI patient population.

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Endovascular recanalization for patient with peripheral arterial disease (PAD) and the end of its spectrum critical limb ischemia (CLI) has become a preferred method of revascularization due to advancement of techniques and equipment, allowing reduction of limb amputations while maintaining a minimally invasive approach compared to surgical approaches.¹ In these endeavors, interventionalists have undertaken a progressively increasing complexity of diseased vessels in the hopes of providing inline unobstructed flow through occlusions for claudicants as well as direct flow to a nonhealing wound in patients with CLI. One of the major roadblocks encountered in lower extremity recanalization procedures is managing severely calcified chronic thrombotic occlusions (CTO) which decreases luminal revascularization, ultimately increasing use of adjunctive interventions such as subintimal tracking, reentry device utilization, and stent placement. Understanding the histopathology and classification of lower extremity calcifications, imaging findings, and

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escalation of equipment use provides a thorough background in dealing with these specific cases.

The presence of a CTO within the lower extremity arterial pathway creates a difficult situation that requires a strong interventional skillset. CTOs are collagenous obstructions that can have varying quantities of calcification, and much has been studied regarding the constitution and shapes of the proximal and distal caps of the occlusions, described in the Chronic Total Occlusion crossing approach based on Plaque morphology (CTOP) classification.² In the lower extremity vasculature, the two main types of calcifications are intimal atherosclerotic calcification and medial artery calcification, the latter is more common in PAD patients.³ The difference between them is related to the pathophysiology of how the calcium forms as well as the sequelae of its progression. With intimal calcifications, the process entails increasing modified lipid laden atherosclerotic plaque, which induces inflammatory pathways, ultimately causing calcium deposits to form. Regarding medial calcifications, the predominant type seen in diabetic and chronic renal failure (CRF) patients is usually the cause of the severe calcifications seen in CLI patients.⁴ In this form, calcium is deposited in the muscular layers of the artery, induced by free radicals (elevated in poorly controlled diabetic patients) or from increased calcium phosphates in CRF patients. This causes osteogenic differentiation of vascular smooth muscle cells in the medial layer that results in remodeled and thickened calcification. This hardening, which does not necessarily cause a true “stenosis,” results in less compliance and elasticity of the vessel, which subsequently can cause atherosclerosis and poor perfusion.⁵

As the calcification process continues, eventually a severely calcified CTO can form, which can require complex techniques and devices to successfully cross. In this fashion, a peripheral arterial calcium scoring system (PACSS) was posited by Rocha-Singh et al (►Fig. 1), which, based on high-intensity fluoroscopy and digital subtraction angiography (DSA), assigns a grade of 0 to 4 depending on laterality, length, and pathologic location of calcifications in the vessel.⁵ One of the goals of developing this classification system is partly to foster more

investigative studies for device usage and outcomes in severely calcified lesions. As mentioned in their article, in many studies, patients with severe calcifications are excluded, which significantly limits our understanding of the device appropriateness in these patients. Interventionalists who perform high-volume PAD interventions have been utilizing differing devices and techniques in these difficult lesions, and the technical successes are more due to individual experience rather than evidence-based data. Adoption of such a classification system helps advance expectations and iterations of devices, which can increase overall outcomes.

Noninvasive and angiographic imaging provides adequate representations of severely calcified CTOs, which assists in planning the revascularization approach and potential equipment usage. There have been thoughts that having noninvasive imaging can help the interventionalist predict the crossing strategy for CTOs. On ultrasound, the calcified echogenic CTO can demonstrate the convex or concave nature of the occlusion (►Fig. 2) proximally and distally. With computed tomography angiography (CTA), the degree of calcification and “stump” morphology as well as potential collateral pathways can be seen⁶ (►Fig. 3). Depending on quality of the study and patient habitus, there can be difficulty in seeing the distal tibial runoff vessels, particularly with heavy calcifications. With magnetic resonance angiography (MRA), using new sequence acquisitions, in addition to visualizing the CTO, plaque morphology can be elicited⁷ (►Fig. 4). Despite these advanced imaging capabilities, factors such as cost, patient tolerance, and access to MRA are not widespread. DSA provides far greater real-time information including the calcified CTO morphology, reconstitutes flow, and enables the interventionalist to enact on the findings (►Fig. 1).

Once the rock-hard CTO is evaluated, the decision tree for approach and equipment utilization has as much to do with escalation of tools as it has with experience. In most cases, the initial crossing attempt is from the ipsilateral antegrade approach, either from the up-and-over contralateral groin access or ipsilateral groin. The antegrade approach can often provide more directional support.

Proposed Fluoroscopy/DSA based Peripheral Arterial Calcification Scoring Systems (PACSS): Intimal and medial vessel wall calcification at the target lesion site as assessed by high intensity fluoroscopy and digital subtraction angiography (DSA) assessed in the AP projection.
Grade 0: No visible calcium at the target lesion site
Grade 1: unilateral calcification < 5cm; a) intimal calcification; b) medical calcification; c) mixed type
Grade 2: unilateral calcification ≥ 5cm; a) intimal calcification; b) medical calcification; c) mixed type
Grade 3: bilateral calcification < 5cm; a) intimal calcification; b) medical calcification; c) mixed type
Grade 4: bilateral calcification ≥ 5cm; a) intimal calcification; b) medical calcification; c) mixed type

Fig. 1 Table describing proposed calcification scoring system. (From Rocha-Singh et al.⁵)

Fig. 2 Ultrasound gray scale and color Doppler (a–c) images show distal calcified chronic thrombotic occlusion cap. Correlating digital subtraction angiography image confirming ultrasound image findings. (From Mustapha et al.¹⁶)

When the rock-hard CTO is encountered, there is often minimal chance of strict intraluminal passage, as most severely calcified CTOs no longer have microchannels through them which would increase chances of intraluminal passage.^{8,9} In rare occasions, luminal passage could be attained, usually with the assistance of a CTO-weighted tip guidewire, or with assistance of mechanical drilling devices. Proving complete true lumen passage requires the use of internal imaging such as intravascular ultrasound (IVUS). Often, subintimal tracking during the CTO crossing is encountered due to the preferential deflection of the guidewire from the rock-hard occlusion. Subintimal crossing is a well-utilized technique (►Fig. 5); however, the difficulty, compared to other types of CTO constituencies, is that with severely calcified vessels, crossing back into the true lumen beyond the CTO can be cumbersome. There is potential to successfully cross from the retrograde direction, which most approach from the pedal access. As mentioned earlier, use of the CTOP system may entice the interventionalist to opt for pedal access far sooner than in the past. This is due to experience showing that for certain CTOs, remaining or reentering the true lumen can be more likely in the retrograde direction.

If reentering the true lumen beyond the CTO is not successful with the catheter and guidewire technique, then a re-entry device is often employed. By targeting

either the calcified wall beyond the CTO, a balloon catheter within the true lumen caudal to the CTO, or with a micro-snare positioned in the luminal/subintimal space, successful reentry can often be attained (►Fig. 5). However, due to calcified rigidity of the vessel walls in some patients, reentry may not occur. Wire escalation at the CTO usually progresses from hydrophilic wires to weighted tip wires and then to crossing support devices. If a channel is created with a CTO wire, then often the wire can be exchanged to a routinely used hydrophilic wire for the remaining vessel navigation. Other commonly used tools for crossing the calcified CTO include devices that use high-frequency vibrations to create microchannels and can be used from the antegrade or pedal access. Other crossing devices use over-the-wire catheters with optical coherence technology (OCT) to provide real-time intravascular visualization to navigate through CTOs via spiral flutes at its proximal tip.¹⁰ Live visualization of the crossing path theoretically should aid the interventionalists in staying intraluminal through the CTO. A steep learning curve and capital costs are associated with this device, and it is also noted that dense calcifications may be one of the limitations of this system. A high-speed diamond tipped 0.017-in drilling wire that some operators choose to use in a variety of CTO locations. Audible feedback is provided from the battery-powered control unit which alerts that an occlusion is engaged. Its

Fig. 3 Coronal reformatted images from CT angiography in a diabetic patient with chronic renal failure shows diffuse heavy calcified burden.

low profile provides comfort to some in cases where recanalization does not occur.

Although many maintain the notion that a completely intraluminal course is necessary in CTOs, the presence of rock-hard complete occlusions makes achieving this less likely; however, successful revascularization with a subintimal component can achieve appropriate perfusion. The imperative is achieving unobstructed flow, that is, with no flow-limiting stenosis, dissections, or flaps. There is now a plethora of tools for calcified vessel treatment in the armamentarium of the interventionalist, which we are still learning the long-term benefits of their use. Patency rates have been demonstrated to be insignificantly affected by having subintimal paths in the revascularization whether the final intervention results in bare metal stenting or with balloon angioplasty.^{11,12} It has been described that in stenting long subintimal segments, spot stenting has more favorable patency than longer stenting.¹³ As some have utilized in the aortoiliac regions, a “Pave-and-Crack” approach can be employed in the severely calcified lower extremity vessels, in which after initial crossing, be it luminal or subintimal, self-expanding covered stent. Graft is placed followed by relining with self-expanding interwoven nitinol bare metal stent and finally with aggressive angioplasty.¹⁴ Regarding angioplasty, the Shockwave bal-

loon catheter is a repurposed technology for the lower extremities in the form of sonic waves emitted on a low-pressure balloon-mounted catheter. This is considered as a vessel pretreatment prior to final intervention with plain/drug-coated balloon (DCB) angioplasty or stenting. Long-term results of this approach are yet to be determined. In the interim, widespread use is limited due to lack of appropriate reimbursement.

Once the CTO is crossed, some atherectomy devices may have more value than others in heavily calcified revascularizations, especially if DCB angioplasty rather than deploying a scaffold. There is always concern for emboli when dealing with atherectomy, and care is to be taken with these patients who usually have poor distal runoffs. Directional atherectomy plaque excision has been commonly used for calcified lesions, with multidirectional cutting ability while packing the plaque in its nosecone. Considerations in this patient population include possible avoidance in subintimal locations and needing embolic protection. Utilization of devices that combine rotational atherectomy with active aspiration is enticing in these heavily calcified vessels when there is increased embolic concerns. The usual presence of subintimal passage in the calcified CTO population creates pause due to concern for perforations. Orbital atherectomy can be used in these rock-hard vessels, particularly in the infrapopliteal system where limited adjunctive options exist, even with subintimal segments. The low-profile and sand-like particulate that is created has yielded significant luminal gain in vessel preparation. Despite the minute emboli, aggressive spinning can result in occlusive emboli which warrants protection device usage by some operators. Additionally, patients may report pain if the nonluminal tract has reached the adventitial space, at which point atherectomy should be discontinued. Excimer laser atherectomy, which is indicated primarily for in-stent restenosis (ISR), and now increasingly being evaluated in severely calcified lesions. These and the other devices in the market need to be used with caution in this patient population, as there are inherent potential complications with any atherectomy tool.

The advent of DCB technology has caused much excitement, mainly in cases where plain balloon angioplasty would be the final intervention, or in those that prefer not to use stent scaffolds. The concern in this patient population is whether enough drug penetration occurs in the presence of severely calcified vessel walls. For this reason, many prefer vessel preparation with atherectomy prior to DCB use. Trials such as the In.Pact Global Study showed greater than 80% freedom from revascularization, which included patients with severely calcified lesions and CTOs; this outcome holds promise for options with better patency rather than simple angioplasty and not always necessitating stent placement.¹⁵ The other DCB products in circulation and trials also will hopefully provide similar findings, thus increasing choices for interventionalists. Other options for angioplasty include cutting and scoring balloons which may provide increased DCB drug penetration and stent expansion.

Fig. 4 (a–d) Images demonstrate ultra-short echo sequences being performed on MRI to identify different chronic thrombotic occlusions (CTO), plaque differentiation. Such images can help predict the amount of heavy calcifications in a CTO. (From Roy et al.⁷)

Fig. 5 (a) Image on left showing arterial layers and chronic total occlusion (orange) with antegrade guidewire entering the subintimal space. Image on right showing guidewire reentering the true lumen. (b) Outback reentry catheter positioned in the antegrade access subintimal space of the posterior tibial artery, with a microsnare in the subintimal space of the same artery from the retrograde direction; once snared, the wire is “flossed” and then intervention performed.

Fig. 6 Initial intrapopliteal images show (a) extensive calcified vessels with (b) abrupt chronic total occlusion of the distal popliteal artery. (c) Distal reconstitution of the posterior tibial artery is present. The anterior tibial or peroneal arteries are occluded.

Fig. 7 (a) Distal posterior tibial artery, common plantar, and branches are patent. (b) Antegrade attempts at recanalization encountered significant crossing difficulty due to severely calcified occlusion and subsequently was subintimal. (c) Retrograde access in the midposterior tibial artery was obtained.

Case

An 83-year-old male with past medical history of heart failure with reduced ejection fraction of 15%, severe mitral regurgitation, coronary arterial disease with two failed percutaneous coronary interventions, diabetes mellitus, end-stage renal disease, and PAD with prior third to fifth toe amputation. Patient

was admitted with osteomyelitis and a nonhealing left heel wound. The patient had a shallow ulcer of the heel with no exposed bone and was on antibiotics. Femoral and posterior tibial arteries were palpable. The anterior and posterior tibial arteries were not palpable. Monophasic tones were present at the posterior tibial artery. No tones were noted at the dorsalis pedis. Noninvasive imaging demonstrated concern for occlusion

Fig. 8 (a) After failed attempts to regain luminal wire entry from the retrograde wire, ultimately noted in the subintimal plane, a microsnare was advanced from the pedal access. (b) After successful snaring and flossing of the wire, there was difficulty in passing support catheters and balloons across the chronic thrombotic occlusion to facilitate wire exchange. Therefore, orbital atherectomy was performed over the flossed wire. (c) Balloon angioplasty using scoring balloon.

Fig. 9 (a–c) Postangioplasty, due to recalcitrant stenosis, coronary drug-eluting, balloon-expandable stents were placed along the chronic thrombotic occlusion. Completion images show inline flow through the posterior tibial artery and plantar arch.

of the popliteal artery with moderate-to-severe arterial insufficiency and noncompressible tibials. The posterior tibial artery appeared patent. The anterior tibial artery was reported as occluded. Endovascular revascularization was deemed and this Rutherford 5 patient's best option. He underwent arteriography with contralateral groin access and required retrograde access to accomplish the recanalization as described later due to rock-hard calcified CTO (► **Figs. 6–9**). After discharge and continued wound care, the patient eventually healed the wound.

Rock-hard total occlusions in lower extremity vasculature, primarily seen in diabetic and CRF patients, pose one of the most difficult challenges to the interventionalist. Understanding their mechanism of formation, utilizing a classification system, and obtaining noninvasive imaging can significantly assist planning of the intervention. When revascularization of rock-hard occlusions is undertaken, the goal should be unobstructed flow across the CTO, with the expectation of a subintimal course. Ultimate interventions including atherectomy with DCB angioplasty, stenting versus spot stenting, or angioplasty alone are the most common considerations, and are usually based on operator experience. The potential simultaneous double-lined use of covered and bare metal stents with aggressive angioplasty may provide additional arsenal to these lead pipe vessels. This focus may allow shorter procedure times, decreased radiation and cost rather than attempting an intraluminal only approach. For tibial vessel interventions, most concerning in CLI patients, apart from plain angioplasty and atherectomy (in the United States), much is left desired regarding new technology to assist patency rates with much interest in the upcoming DCB and tibial stent platforms.

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