Peripheral arterial disease treatment planning using noninvasive and invasive imaging methods

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ABSTRACT

With the growing prevalence and mortality of peripheral arterial disease, preoperative assessment, risk stratification, and determining the correct indication for endovascular and open surgical procedures are essential for therapeutic decision-making. The effectiveness of interventional procedures is significantly influenced by the plaque composition and calcification pattern. Therefore, the identification of patients for whom endovascular treatment is the most appropriate therapeutic solution often remains a challenge. The most commonly used imaging techniques have their own limitations and do not provide findings detailed enough for specific, personalized treatment planning. Using state-of-the-art noninvasive and invasive imaging modalities, it is now possible to obtain a view, not only of the complex vascular anatomy and plaque burden of the lower extremity arterial system, but also of complex plaque structures and various pathologic calcium distribution patterns. In the future, as these latest advancements in diagnostic methods become more widespread, we will be able to obtain more accurate views of the plaque structure and anatomic complexity to guide optimal treatment planning and device selection. We reviewed the implications of the most recent invasive and noninvasive lower extremity imaging techniques and future directions. (J Vasc Surg Cases Innov Tech 2023;9:101263.)

Keywords: Diagnostic imaging; Endovascular procedures; Future perspectives; Peripheral arterial disease; Treatment planning

Chronic peripheral arterial disease (PAD) affects >230 million people worldwide and continues to increase in prevalence.[1] Although in recent decades endovascular devices and techniques have undergone remarkable advancements,[2] conflicting reports from cohort studies on the outcomes after endovascular revascularization for PAD have resulted in a limited evidence-based approach to PAD management.[3,4] The TransAntlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease and its supplement, published in 2015, both promoted an endovascular-first approach.[5,6] Global vascular guidelines on the management of chronic limb-threatening ischemia (CLTI) introduced new aspects to the appropriate therapeutic approach.[1] These guidelines showed that bypass surgery using the great saphenous vein has similar mortality and amputation outcomes but better expected patency compared with endovascular procedures, although with low-quality evidence.[1] The results of the BEST-CLI (best endovascular vs best surgical therapy in patients with CLTI) randomized controlled study also challenges the "endovascular-first" treatment paradigm. The BEST-CLI trial showed that the incidence of a major adverse event or death for patients with CLTI was significantly lower after surgical treatment than after endovascular therapy, when a single segment greater saphenous vein was available.[7] Despite the advancements in endovascular techniques, the BEST-CLI results echo the only randomized control trial previously conducted, reported >15 years ago.[8] The BASIL (bypass vs angioplasty in severe ischaemia of the leg) studies showed that percutaneous vascular interventions (PVIs) had a significantly higher early failure rate compared with bypass surgery.[8,9] Also, the clinical outcomes after primary bypass surgery were markedly better than those for patients undergoing secondary bypass surgery after PVI.[8,9] The immediate endovascular failure rates have similarly remained stagnant at ~15% to 20% in both trials, primarily owing to the inability to successfully cross chronic total occlusions (CTOs), rather than directly related to the intervention itself. The preoperative assessment, risk stratification, and determining the correct indication for endovascular and open surgical procedures are essential for therapeutic decision-making. However, no consensus has yet been reached on how to select the patients who would benefit from PVIs. With the latest advances in imaging techniques and a review of the implications of the diverse pathologic patterns of calcium distribution on the diagnostic modalities, we can obtain a more comprehensive and accurate view of the plaque structure and anatomic complexity to guide optimal treatment planning, which could help to improve patient selection and the long-term outcomes of PVIs.[10-12] The goal of the present study was to review the most recent noninvasive and invasive lower extremity imaging modalities.

NONINVASIVE IMAGING METHODS

Color duplex ultrasound. Ultrasound with use of the Doppler mode is a well-established, noninvasive

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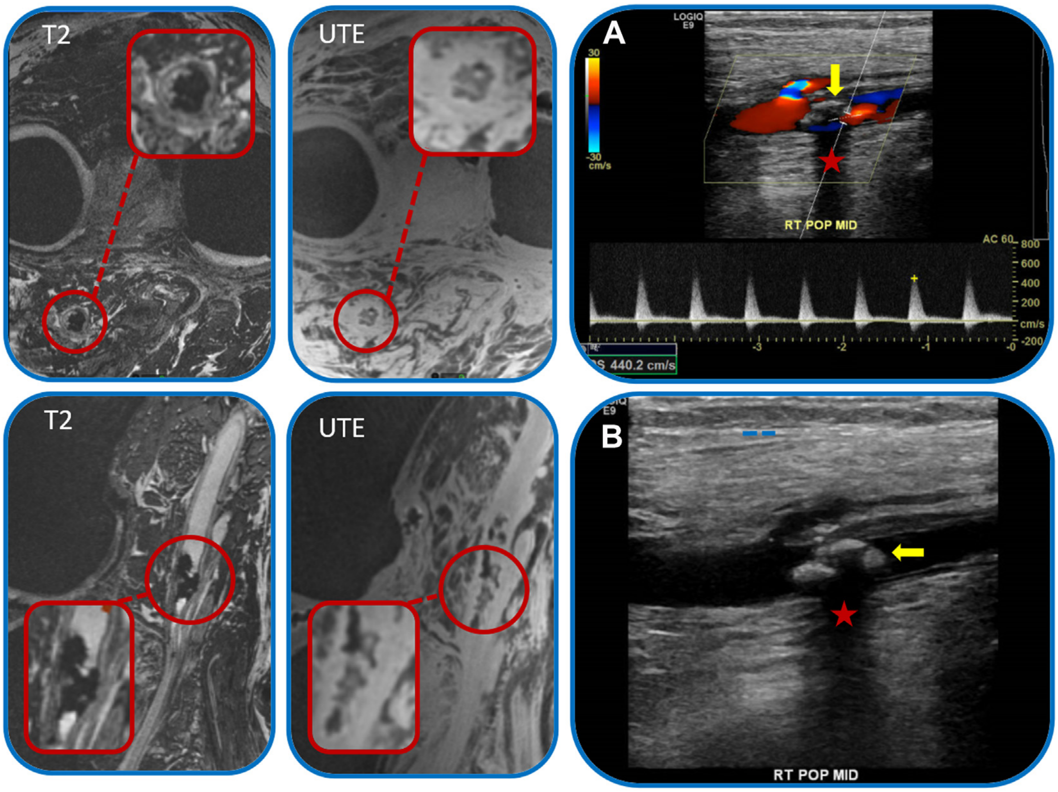

Fig 1. Comparison of 7T magnetic resonance imaging (MRI) and color duplex ultrasound examination of a middle popliteal artery segment plaque. **A,B,** Color duplex ultrasound images showing an echogenic, solid, nodular, calcified plaque (*yellow arrow*) with shadowing artifact (*red star*). Doppler ultrasound (**A**) showing significant hemodynamic stenosis (peak systolic velocity, 440 m/s). On color duplex ultrasound, detailed plaque morphology can be determined only to a very limited extent. In contrast, 7T T2 and ultrashort echo time (*UTE*) images of the same plaque show explicit plaque structure with speckled calcium as a signal void in an isointense dense collagen matrix. *MID,* Middle segment; *POP,* popliteal artery; *RT,* right.

diagnostic method to assess PAD. It can be used to determine the exact location and extent of vascular stenosis, in addition to arterial hemodynamics (Fig 1). The technique is well suited for assessing focal lesions, following up after vascular interventions, and aiding in the selection of the access approach.[13] However, diagnostic accuracy can be limited by the experience of the examining technician, patient anatomy, atypical hemodynamic patterns, and severe artifacts caused by extensive calcification. Although assessment of the carotid plaque volume, histopathologic plaque composition, and morphology has more extensive literature,[14,15] lower extremity plaque characteristics cannot be generally determined, especially in smaller below-the-knee arteries. Obtaining a comprehensive view of the whole lower extremity is time-consuming and often challenging to perform.

To achieve good long-term results after bypass surgery, in addition to good inflow and outflow arteries, the bypass graft material has an important role. The best patency and limb salvage rates are achieved with an autologous vein.[16] Duplex ultrasound, with or without color flow, is the modality of choice to assess veins for autogenous bypass grafts.[17] Thus, preoperative knowledge of variant anatomy, small venous caliber, increased wall thickness, and location of the major veins and their branches can help in planning bypass surgery procedures and might reduce the readmission and postoperative surgical site infection rates.[18]

Future directions: ultrasound-guided lower extremity interventions and ultrasound elastography. The use of ultrasound during PVIs is a well-established practice; however, its applications during PVIs have expanded. In addition to ultrasound-guided access of femoral or tibiopedal vessels, the use of this technique can aid in crossing CTOs, evaluating balloon and stent apposition, and provide ultrasound-guided closure with access closure devices.[19]

Another emerging method, ultrasound elastography, displays tissue stiffness by measuring the tissue deformation response to compression. This technique has mainly been applied in the treatment of carotid artery disease.[20,21] Arterial stiffness increases in diseased arteries with thromboembolism, soft plaque, calcified plaque, and inflammatory disease. Because the rate of this progression varies between different vascular pathologies, elastography could be useful for further evaluation. Additionally, the arterial stiffness value also depends on the plaque composition, allowing elastography to potentially differentiate between lesion types in PAD.[22,23] These expanded uses of ultrasound are growing with increasing familiarity by interventional physicians. Color duplex ultrasound, as a user-dependent technique, requires expertise to use effectively, and training programs have been adapted to address this gap in interventional imaging.

Computed tomography angiography. Computed tomography (CT) angiography (CTA) is an easily accessible imaging technique that can evaluate lower extremity arteries from the abdominal region to the feet in a single scan, assisting in the evaluation of disease distribution and vascular morphology.[24] Most research on CTA has focused on the characteristics of atherosclerotic plaques of coronary arteries.[25,26] It has been used in different studies to determine the plaque composition, dividing the plaque area into soft, intermediate/fibrous, and calcified components.[27] On lower extremity arteries, Patel et al[28] showed that the burden of calcified plaque, but not soft or fibrocalcific plaque, is related to restenosis, reintervention, and amputation-free survival. Itoga et al[29] found that although longer lengths of occlusion on preoperative CTA is associated with technical failure, on multivariable analysis, 100% calcification remained the only significant predictor of technical failure of endovascular revascularization of occlusions in the superficial femoral artery—popliteal artery region. He et al,[30] studying femoropopliteal segments on preoperative CTA images, showed that a high calcified plaque burden and excessive stent oversizing were associated with unfavorable outcomes after stent angioplasty. A detailed characterization of plaques can be made difficult by so-called blooming artifacts caused by beam hardening artifacts of extensive calcification. CTA also requires the use of ionizing radiation and iodinated contrast material, which can be an additional limiting factor. However, CTA remains one of the most widely used imaging methods for endovascular treatment planning owing to its easy availability and short examination times.

Future directions: dual-energy CTA and photon counting CT. Although CTA can be of great help in choosing an appropriate therapeutic solution, small vessel diameters, high-grade wall calcifications, and poor contrast attenuation—especially in the infrapopliteal region—still represent diagnostic challenges. Dual-energy CTA, also known as spectral CT, uses two separate energy spectra of X-rays, offers much more detailed tissue imaging, and possesses high sensitivity for detecting significant stenoses.[31,32] However, the method still requires ionizing radiation and is less common than single-energy CTA.[33] Photon counting CT (PCCT) is a new CT technology that uses a direct conversion X-ray detector, where incident X-ray photon energies are directly recorded as electrical signals. Compared with energy-integrating detector CT, PCCT provides data at high spatial resolution, without electronic noise, with an improved contrast/noise ratio, at a lower radiation dose, and with intrinsic spectral information.[34] To date, the data are available mainly for coronary atherosclerosis

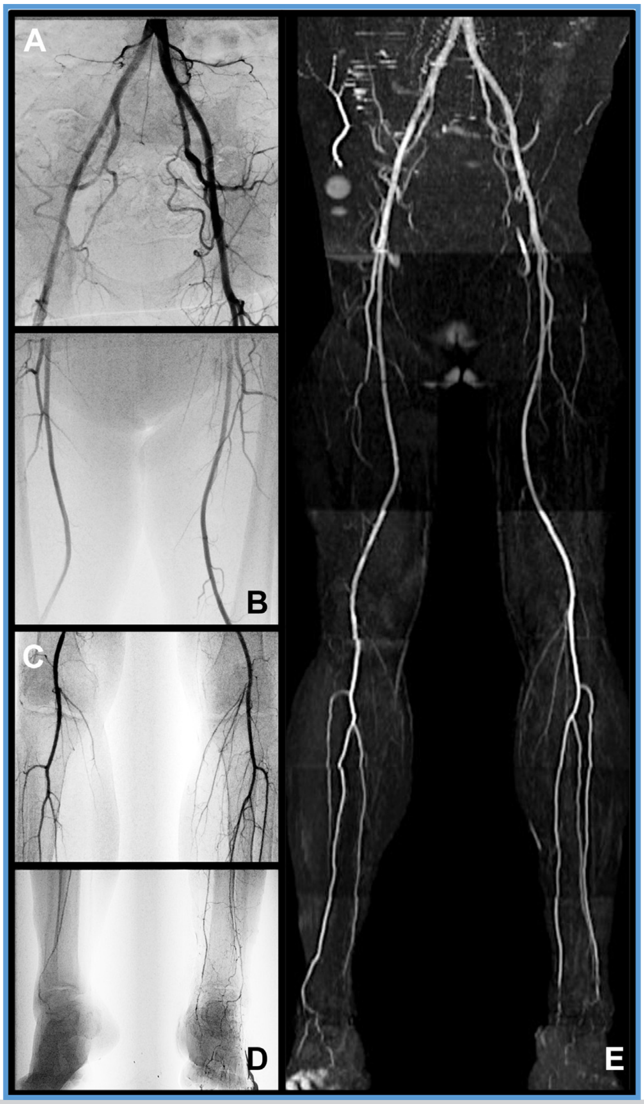

Fig 2. Conventional angiography using iodinated contrast material (**A-D**) compared with noncontrast quiescent-interval single-shot magnetic resonance angiography (**E**). The latter promising technique allows the entire lower extremity arterial system to be mapped without the use of contrast material.

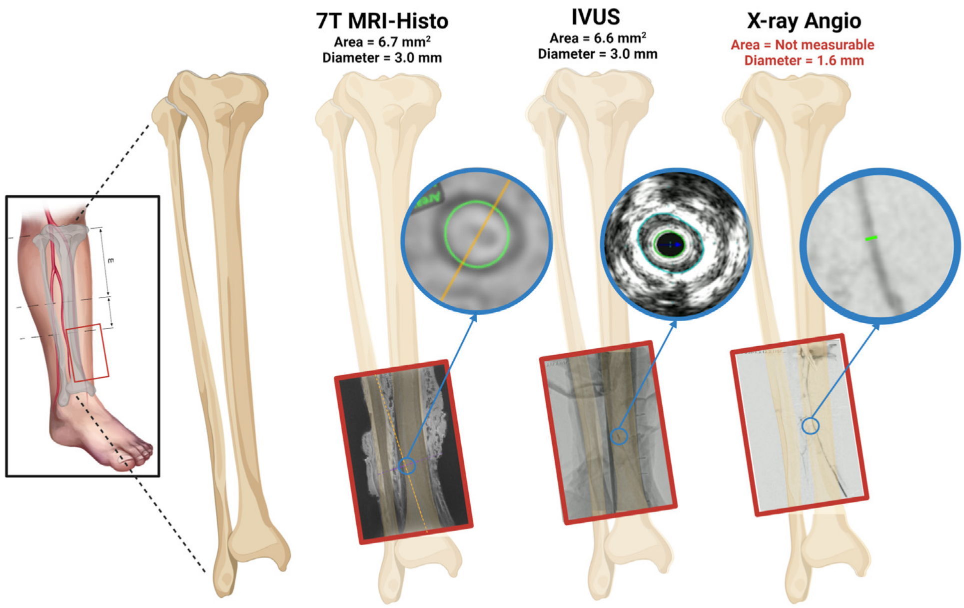

Fig 3. 7T magnetic resonance imaging histology (*MRI-Histo*) of anterior tibial artery. Bony landmarks of the tibia and fibula can be used for image registration, as illustrated. Concentric calcium (*green outline*) is detectable on both 7T MRI-Histo and intravascular ultrasound (IVUS) images showing similar area and diameter measurements of the reference vessel. The area is not measurable on angiographic images, and assessment of the vessel wall is particularly limited. The diameters shown illustrate how each modality can be used to determine the optimal stent and balloon size for endovascular interventions.

and plaques using this technique.[35,36] However, the reduced blooming artifacts might allow for improved visualization of fibrotic and lipid-rich plaque components and in-stent stenoses with the ultra-high-resolution mode of PCCT.[37] In the future, it could also help in planning lower extremity revascularization.[38,39]

Magnetic resonance imaging. Contrast-enhanced magnetic resonance angiography (MRA) has been shown to be a highly reliable technique to depict the presence and extent of arterial narrowing in patients with intermittent claudication and CLTI.[40-42] However, concerns have been raised regarding gadolinium-based contrast agents as a potential cause of nephrogenic systemic fibrosis in patients with renal dysfunction (especially if the glomerular filtration rate is <30 mL/min),[43,44] although an argument has been presented that gadolinium can be used safely in this patient population.[45] In the past decades, significant improvements have been made in nonenhanced MRA of the peripheral arteries. Modern magnetic resonance imaging (MRI) sequences, such as quiescent-interval single-shot MRA, have shown promising results and provide nearly flow-independent imaging to evaluate occlusive below-the-knee arteries without the need for contrast materials[46] (Fig 2). Although some MRI techniques might allow for limited assessment of calcifications, with the use of techniques such as "black-blood" spin-echo sequences, lower extremity plaque morphology and even detailed morphology of calcified lesions can be visualized.[47,48] These sequences attenuate the signal of blood and can provide high-quality cross-sectional images of plaques and vessel walls; thus, lesions that would be more difficult to cross during PVI can be identified using a preprocedural MRI approach. Recent studies have shown that the MRI characteristics of PAD lesions can identify patients with lesions more difficult to cross with a guidewire and at a higher risk of endovascular failure.[49] These MRI features correlate with the guidewire puncture forces for CTOs, an important aspect of determining the ability to cross such lesions, classifying plaques as "soft" (ie, loose fibrous tissue, microchannels, fat, thrombus), "hard" (ie, dense collagen, speckled calcium), or calcified (nodular calcium).[50] Current data show that using ultrashort echo time sequences, lesions composed of dense collagen and calcium can be easily identified (Fig 1).[51]

INVASIVE IMAGING METHODS

Digital subtraction angiography

Despite the inherent invasive nature and significant limitations, digital subtraction angiography (DSA) remains the gold standard for imaging of PAD. In addition to the ability to assess lumen patency, the presence of collateralization, and the quality of flow, the dual diagnostic and therapeutic role of DSA imaging is unique. The major limitations of DSA include the limited two-dimensional perspective, the need for radiation, the requirement for nephrotoxic contrast, an inability to

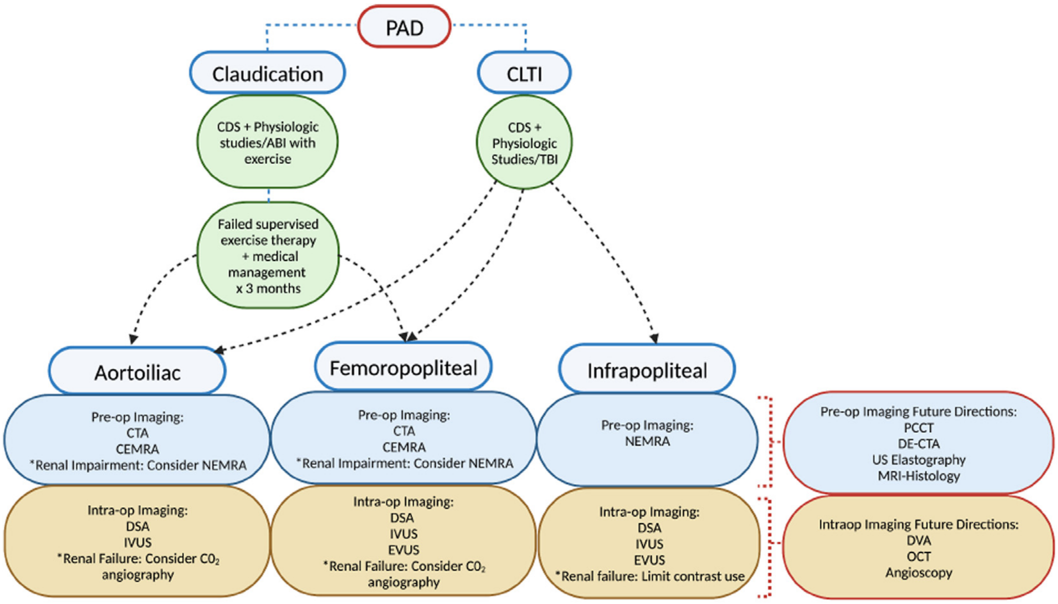

Fig 4. Decision-making algorithm for diagnostic imaging modalities in peripheral arterial disease (PAD). *ABI,* Ankle brachial index; *CDS,* color duplex ultrasound; *CEMRA,* contrast-enhanced magnetic resonance angiography; *CLTI,* chronic limb-threatening ischemia; *CO_2,* carbon dioxide; *CTA,* computed tomography angiography; *DE-CTA,* dual-energy computed tomography angiography; *DSA,* digital subtraction angiography; *DVA,* digital variance angiography; *EVUS,* extravascular ultrasound; *IVUS,* intravascular ultrasound; *MRI,* magnetic resonance imaging; *NEMRA,* nonenhanced magnetic resonance angiography; *OCT,* optical coherence tomography; *PCCT,* photon-counting computed tomography; *TBI,* toe brachial index; *US,* ultrasound.

evaluate total occlusions or vessel wall characteristics for accurate sizing, and a susceptibility to motion artifact. However, new technologies as adjuncts to DSA and catheter-based therapies to enhance the utility of DSA have been developed. As an alternative to standard iodinated contrast media, carbon dioxide and different magnetic resonance contrast agents (eg, gadolinium) can be used; however, the image quality is most often inferior to that of conventional DSA.[52,53]

Future directions

Kinetic imaging and robotic technology. A new technique based on kinetic radiographic imaging called digital variance angiography consists of several, generally underexposed, images instead of using a single, fully exposed, image and provides better image quality and lower radiation exposure than traditional DSA.[54,55] In the past two decades, the feasibility of robotic peripheral vascular interventions and diagnostic angiography with active guide catheter control were also reported with promising achievements.[56,57] With less contrast agent and ionizing radiation exposure and increased procedural speed, these techniques might open new horizons in the diagnosis and treatment of PAD in the future.

Intravascular ultrasound. Intravascular ultrasound (IVUS) uses a transducer at the tip of a catheter to transmit sound waves, which, when reflected back to the transducer, provide a luminal-based image on the acoustic properties of the tissue. IVUS is perhaps the most widespread of the emerging intravascular imaging techniques and has been used in percutaneous interventions of the coronary arteries for decades. The technique has been increasingly adopted as an adjunct to catheter-based techniques in the peripheral arteries owing to its ability to produce detailed diagnostic information regarding the lumen size, plaque morphology, degree of stenosis, and residual lumen area[58,59] (Fig 3). Although IVUS was originally used most frequently for intervention planning, including stent and balloon sizing, postintervention assessments, and identification of intimal dissection, IVUS has also shown promising results in predicting the histopathologic characteristics of plaques. Virtual histology IVUS, first described in the coronary arteries, has been evaluated in the carotid arteries via the CAPITAL (carotid artery plaque virtual histology evaluation) study.[60] However, few studies have evaluated virtual histology IVUS for determining the histopathologic plaque composition and morphology in the peripheral arterial system. The limitations of IVUS include its requirement for intraluminal access and having a wire across the lesion, which is the primary mode of immediate endovascular technical failure.[7,8] Furthermore, it is a side-looking device and cannot assess total occlusions or vessels <2 mm. Compared with optical coherence tomography (OCT) and MRI, IVUS images contain more artifact and lower frame rates and are inherently user dependent.[58,59]

Table. Advantages, disadvantages, and approximate cost of imaging methods for treatment planning

Imaging modality	Advantages	Disadvantages	Approximate cost (USD)
Noninvasive modalities			
Color duplex ultrasound	Noninvasive; nonionizing; no need for contrast material; provides hemodynamic information; good for follow-up	Operator dependent; limited field of view; longer examination time; limited assessment of calcified vessels	$900.00 (unilateral); $1100.00 (bilateral)
Computed tomography angiography	Noninvasive; affordable; high availability; high spatial resolution; fast; 3D imaging data postprocessing also possible	Ionizing radiation; requires iodinated contrast material; limited assessment of calcified and infrapopliteal vessels	$1600.00
Dual-energy computed tomography	High spatial resolution; good image quality in crural region; allows for more detailed tissue imaging	Ionizing radiation; requires specialized hardware; limited accessibility	NA
Photon-counting computed tomography	High spatial resolution; great contrast/noise ratio; lower radiation ratio; intrinsic spectral information; reduced blooming artifacts	Ionizing radiation; limited accessibility	NA
Magnetic resonance imaging	Noninvasive; no need for contrast material; 3D image reconstruction; high resolution; outstanding soft tissue contrast for evaluating plaque; flow-independent assessment of below-the-knee vessels; can provide hemodynamic information; gadolinium-based contrast material more tolerable for patients with impaired renal function	Longer acquisition time; more expensive than computed tomography; some techniques might allow for limited assessment for calcifications; claustrophobia; non-MRI conditional devices	$1750.00
Invasive modality			
Digital subtraction angiography	High resolution; fast	Invasive; requires iodinated contrast material; limited assessment of vessel wall	$286.00
Intravascular ultrasound	Widespread detailed diagnostic information on lumen size, vessel wall, and plaque burden	Artifacts; lower frame rate; operator dependent	$4422.50 (cost of intravascular ultrasound catheters: $600.00-$1200.00)
Optical coherence tomography	High resolution; 2D and 3D images suitable for smaller vessels	Limited penetrative depth; limited field of view; requires irrigation with saline accompanied by occlusion of inflow	NA
Angioscopy	Direct visualization of vessel wall and wall-associated structures; colored images	Evaluation of disease present on intraluminal surface; plaque volume, content, and depth not measurable; requires irrigation with saline accompanied by occlusion of inflow	NA

2D, Two-dimensional; *3D,* three-dimensional; *MRI,* magnetic resonance imaging; *NA,* not available.

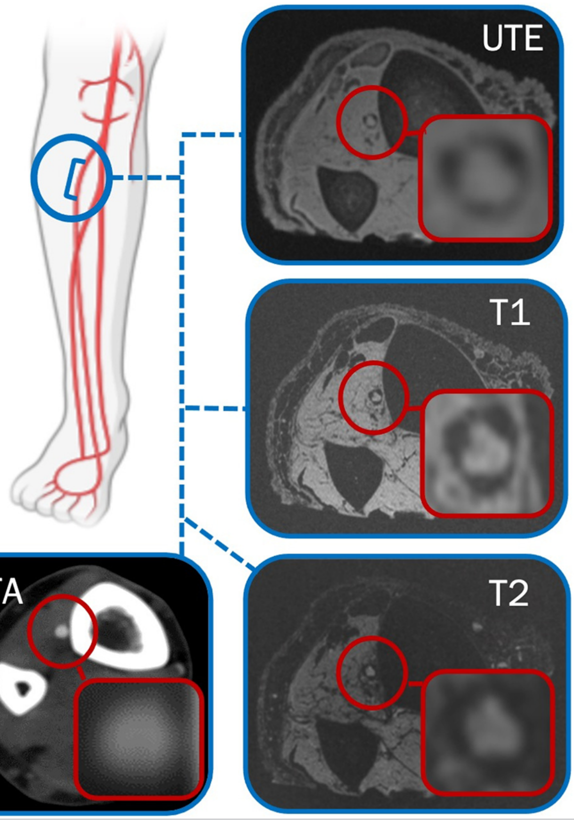

Fig 5. Anterior tibial artery plaque morphology on 7T magnetic resonance imaging (MRI) and computed tomography angiography (CTA). The 7T MRI images (ultrashort echo time [*UTE*], T1, T2) show a detailed structure of a concentric, calcified plaque with calcium as a signal void. Assessment on the CTA image is limited because of extensive calcification and consequential blooming artifact.

Optical coherence tomography. OCT is another established coronary imaging modality that is now emerging for lower extremity endovascular imaging. Compared with IVUS, OCT provides higher resolution imaging with two- and three-dimensional images. The technology uses a low-coherence light to create images from the optical scattering created from penetration of biologic tissue.[61] Like IVUS, the utility of OCT has focused mainly on luminal measurements, stent planning, and immediate feedback with direct visualization of the artery after intervention.[61] Although few studies have investigated OCT, perhaps the real utility of OCT compared with IVUS in the peripheral arterial system might be in determining plaque composition and morphology owing to the increased resolution of the images. OCT data are severely limited in the peripheral arteries; however, it has been shown to accurately demonstrate plaque composition (confirmed by histologic findings) in the coronary arteries.[62] In contrast to IVUS, OCT requires displacement of blood flow through the vessel at the time of imaging. This increases the use of contrast and/or saline and limits the use of OCT to smaller vessels (<5 mm diameter). OCT is also limited in its penetrative depth (1-3 mm) and small field of view—the reason its scope might be limited to the smaller infrapopliteal arteries in treating PAD.[61]

Angioscopy. Angioscopy was regularly used by vascular surgeons in the context of saphenous vein assessments but was largely abandoned because of the limited benefit. It is now experiencing a resurgence for lower extremity arterial disease.[63,64] Angioscopy refers to the direct visualization of the inner surface of an artery—and any associated plaque, thrombus, or calcification—using

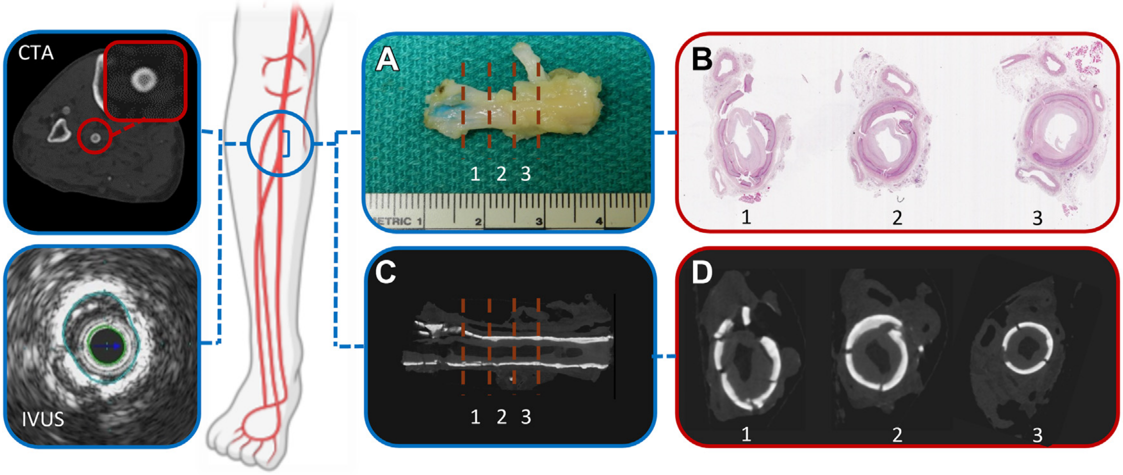

Fig 6. Detailed ex vivo plaque morphology of tibioperoneal trunk compared with preoperative computed tomography angiography (CTA) for the same patient in Fig 3. The vessel was affected by extensive, circular calcification. Assessment of the plaque was limited on in vivo CTA. On intravascular ultrasound (IVUS), ex vivo histologic samples (**A,B**), and micro-computed tomography (CT; **C,D**), we can see the explicit pattern with a concentric calcium sheet.

a small endoscope. Angioscopy is the only intravascular imaging technique that can image total occlusions and can provide color images, which adds a unique element to the characterization of a lesion and guidance for intervention. Although color differences of coronary plaques have been associated with all-cause mortality and major adverse cardiovascular events, angioscopy has not been widely adopted into use.[65] Angioscopy is limited to evaluation of disease present on the intraluminal surface; thus, evaluation of plaque volume, content, and depth might be better provided by other imaging modalities.[65]

DISCUSSION

Despite remarkable advancements in endovascular devices and techniques, endovascular procedures still have a remarkable immediate failure rate (15%-20%), and the early failure rate also remains high.[7-9] Because the main reason for this can be attributed to the challenge of effectively crossing CTOs, arterial plaque composition and calcification play a major role in the ability to intervene and the success of the intervention.[29] Invasive and noninvasive imaging methods that can accurately predict plaque characteristics have been shown to improve endovascular outcomes.[28] Several invasive and noninvasive imaging techniques have been used to evaluate lower extremity vessels as described and as illustrated in an algorithm in Fig 4. However, each has benefits and limitations to remember when making therapeutic decisions (Table).

CTA and MRA are both excellent imaging techniques for visualizing peripheral arteries, particularly in aortoiliac and femoropopliteal segments. However, in some cases, such as in severely calcified tibial vessels, blooming artifacts on CTA can obscure the vessel lumen (Figs 5 and 6). In these cases, the high resolution of MRA, which excludes calcific disease, might be better for assessing patency and noncalcific plaque or thrombus of small vessels (Fig 5). On CT scans, calcifications can be easily identified, which can affect therapeutic decision-making; however, recent gradient-echo MRI sequences can also be used for the accurate depiction and quantification of, not only vascular calcifications, but also collagen-rich fibrous plaque components in patients with PAD,[49,66] which are also challenging to treat percutaneously.[50,67] Although research on MRI plaque characterization for PAD is in its early phases, it could be used in the future to select patients and tailor device selection using a safe, noninvasive method before intervention. Additionally, by avoiding administration of contrast agents, nonenhanced MRA techniques reduce the risk of adverse reactions and offer valuable diagnostic information in various clinical scenarios. Compared with DSA alone, the use of intraluminal imaging techniques such as IVUS (Figs 3 and 6) and OCT provide more accurate measurements of luminal patency and lesion composition. Thus, these techniques have been used to accurately assess narrowing and size stents or balloons intraoperatively. However, intravascular imaging methods require physicians to cross the lesion and because that is the most common reason for endovascular treatment failure, patients with such lesions would ideally be identified before invasive procedures, making it easier to find the optimal technique and device for targeted intervention.

CONCLUSIONS

Ultimately, the choice of imaging technique for revascularization procedure planning in peripheral arteries should be patient specific owing to the complexity of the various anatomic patterns of disease, lesion characteristics, symptoms, and patient comorbidities. The use of a combination of current imaging techniques can help provide a deeper understanding of underlying diseases, thus contributing to improved procedure planning. Future innovations in imaging are required to aid patient selection and rationally guide device selection to improve the immediate and long-term success of lower extremity revascularization procedures.

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