Arterial imaging in patients with lower extremity ischemia and diabetes mellitus

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Precise, comprehensive imaging of the arterial circulation is the cornerstone of successful revascularization of the ischemic extremity in patients with diabetes mellitus. Arterial imaging is challenging in these patients because the disease is often multisegmental with a predilection for the distal tibial and peroneal arteries. Occlusive lesions and the arterial wall itself are often calcified and patients presenting with ischemic complications frequently have underlying renal insufficiency. Intra-arterial digital subtraction angiography (DSA), contrast enhanced magnetic resonance angiography (MRA), and more recently, computerized tomographic angiography (CTA) have been used as imaging modalities in lower extremity ischemia. Each has specific advantages and shortcomings in this patient population, which will be summarized and contrasted in this review. DSA is an invasive technique most often performed from a femoral arterial puncture and requires the injection of arterial contrast, which can occasionally cause allergic reactions. In patients with pre-existing renal insufficiency, contrast infusion can result in worsening renal failure; although usually self-limited, it may occasionally require hemodialysis, especially in patients with diabetes. However, DSA provides the highest degree of spatial resolution and image quality. It is also the only modality in which the diagnosis and treatment of arterial disease can be performed simultaneously. MRA is noninvasive, and when enhanced with gadolinium contrast injection provides arterial images of comparable quality to DSA and in some circumstances may uncover distal arterial targets not visualized on DSA. However, spatial resolution is inferior to DSA and erroneous interpretations due to acquisition artifacts are common. Specialized equipment and imaging techniques are necessary to minimize their occurrence in the distal lower extremity. In addition, due to the risk of inducing nephrogenic systemic fibrosis, gadolinium-enhanced MRA cannot be used in patients with renal insufficiency. CTA is noninvasive and rapidly performed, with better spatial resolution than MRA, but requires the largest volume of contrast infusion, exposes patients to high-doses of radiation, and is subject to interpretive error due to reconstruction artifacts especially in heavily calcified arteries, limiting its usefulness in many patients with diabetes. For patients in whom the planned intervention is a surgical bypass, DSA and MRA will provide high quality images of the lower extremity arterial anatomy. For patients in whom a catheter-based intervention is the likely treatment, a diagnostic DSA immediately followed by a catheter-based treatment in the same procedure is the preferred approach. In patients with pre-existing renal dysfunction, in which gadolinium-enhanced MRA is contraindicated, DSA or CTA can be performed. However, patients should have an infusion of intravenous normal saline solution or sodium bicarbonate before the procedure to reduce the incidence of contrast-induced nephropathy. (J Vasc Surg 2010;52:81S-91S.)

Precise, comprehensive anatomic imaging is the cornerstone of successful revascularization of the ischemic lower extremity in patients with diabetes mellitus. Contrast arteriography has been the mainstay for many years and remains the gold standard due to its superior image resolution and being the only modality used for both diagnosis and treatment. However, magnetic resonance angiography (MRA),[1-3] and more recently, computerized tomographic angiography (CTA),[4,5] have become viable alternatives due to being inherently less invasive with image quality rivaling digital subtraction angiography (DSA). Imaging of arterial anatomy in the lower extremity of patients with diabetes presents unique challenges due to the distal location of the occlusive lesions, most commonly involving the crural and pedal arteries. Detailed imaging of these vessels is critical in planning endovascular procedures or surgical bypass. The presence of multisegment disease, the frequency of calcification of both the atherosclerotic lesions and the wall of the arteries involved, and the presence of renal insufficiency are additional challenges often encountered. Consequently, all three modalities have advantages and disadvantages in specific patients based on their clinical presentation and comorbidities.

Contrast arteriography. The use of cut-film radiographs and rapid film changers has long given way to intra-arterial DSA, the current standard for contrast arteriography of the lower extremity. DSA has especially improved the imaging of diabetic arterial occlusive disease due to its superior ability to visualize distal small caliber vessels with less contrast. Currently available machines have completely automated sequences that set exposure values and frame speed for the various arterial segments studied in the abdomen, pelvis, and lower extremity. Improved computer processing power and equipment design has made the commonly used techniques such as subtraction, re-masking,

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Fig 1. A hybrid, endovascular operating suite. Note the anesthesia equipment and ceiling mounted C-arm that can be moved away from the table during surgery. The fluoroscopy table can be tilted like a typical operating room table and has attachments for the connection of self-retaining retractors.

pixel shifting and stacking, or view tracing fast and simple. Road-mapping and unsubtracted image referencing (fluoro-save mode) used during catheter-directed interventions are easily performed by the operator at the table. Gantry angle, table position, collimation, magnification, and edge filters are easily changed by the operator to optimize imaging for any arterial segment.

Perhaps the most important improvement has been the development of high-resolution flat panel image intensifiers that have outstanding image quality and minimize parallax distortion. The newest flat panels on fixed imaging systems have a larger field of view (FOV) of 48 cm (19 inches) which can cover larger areas of interest, translating into fewer injections and radiation exposure. DSA imaging is available on portable units, primarily used in the operating room, or in a dedicated fixed-mount angiography suite.

More recently, hybrid operating rooms with fixed-mount angiographic equipment have become available making it possible to perform sophisticated, high quality DSA in a surgical environment for hybrid procedures involving the simultaneous performance of surgery and angiography such as endovascular aneurysm repair (Fig 1). Gantries are usually ceiling-mounted in hybrid rooms and can be moved away from the table during conventional surgical procedures. Fixed-mount units have more powerful generators that provide detailed imaging with far superior image resolution 10 times that of portable systems. The primary advantages of portable units are portability and availability. They can be used in any operating suite and can theoretically be moved to the location of the patient in clinical circumstances when transportation to an angiography suite is not possible. Portable systems are also far less expensive. A mobile C-arm is usually less than $200,000, while a high quality fixed-mount system in an angiography suite can cost between 1.5 and 3 million dollars. Many vascular surgeons have had limited access to fixed systems because they have traditionally been located in interventional radiology or cardiology departments, making mobile units in the operating room the only alternative available. Although it is possible to perform virtually any diagnostic or interventional procedure on portable units, the superior capabilities of fixed-mount systems in a dedicated angiography suite or hybrid operating room make them the ideal and preferred location when available.

The principal disadvantages of DSA are complications resulting from arterial access and the infusion of contrast agents. Complications related to femoral access have decreased with the use of lower profile catheters and sheaths. In most cases, diagnostic angiography can easily be performed with a 4F sheath and compatible catheters, whereas most lower extremity interventions can be performed with a 5F or a 6F system. DSA is most commonly performed from an ipsilateral or contralateral femoral puncture. The author prefers the use of contralateral femoral puncture with placement of a multi-side-hole flush catheter in the infrarenal abdominal aorta to perform an aortoiliac injection followed by access of the contralateral distal external iliac or proximal common femoral artery over the aortic bifurcation to obtain images of the extremity in question. In our practice, we routinely perform femoral puncture guided by ultrasound scan imaging (Fig 2), which has improved our ability to easily gain access in any patient including those who are obese and without a palpable femoral pulse. Ultrasound scan-guided punctures are especially useful for antegrade femoral approaches and for the preclose technique in endovascular aneurysm repair. An additional advantage is the ability to both clearly identify the common femoral artery and direct the entry needle into the "best" spot on the anterior wall of the artery. Since its routine use in our procedures, ultrasound scan-guided puncture has reduced our rate of access-related complications (unpublished data).

Contrast agents enhance the details of the arterial circulation due to a radiodensity that is higher or lower than surrounding tissues. Typical agents with a density higher than soft tissues are iodine-containing compounds, which are either ionic or nonionic. Nonionic agents have an osmolality of 320 to 880 mosm compared to 1500 to 1700 mosm for ionic agents. Plasma has an osmolality of 285 mosm. Contrast agents can be delivered by power injection or manually through a syringe or manifold depending on the circumstances. Toxic side effects of contrast agents result from their hyperosmolality. Common side effects include nausea, vomiting, and pain in the area of the arterial bed being studied. Pain is especially common in the more distal arterial beds of the lower extremity and may cause unintentional movement or twitching, resulting in image degradation. Nonionic agents with lower osmolality cause less pain,[6] hemodynamic instability,[7] can be diluted with little loss of image quality on fixed imaging systems, and have largely replaced ionic contrast in our practice. Allergic reactions due to the release of histamine are another important side effect and most common with

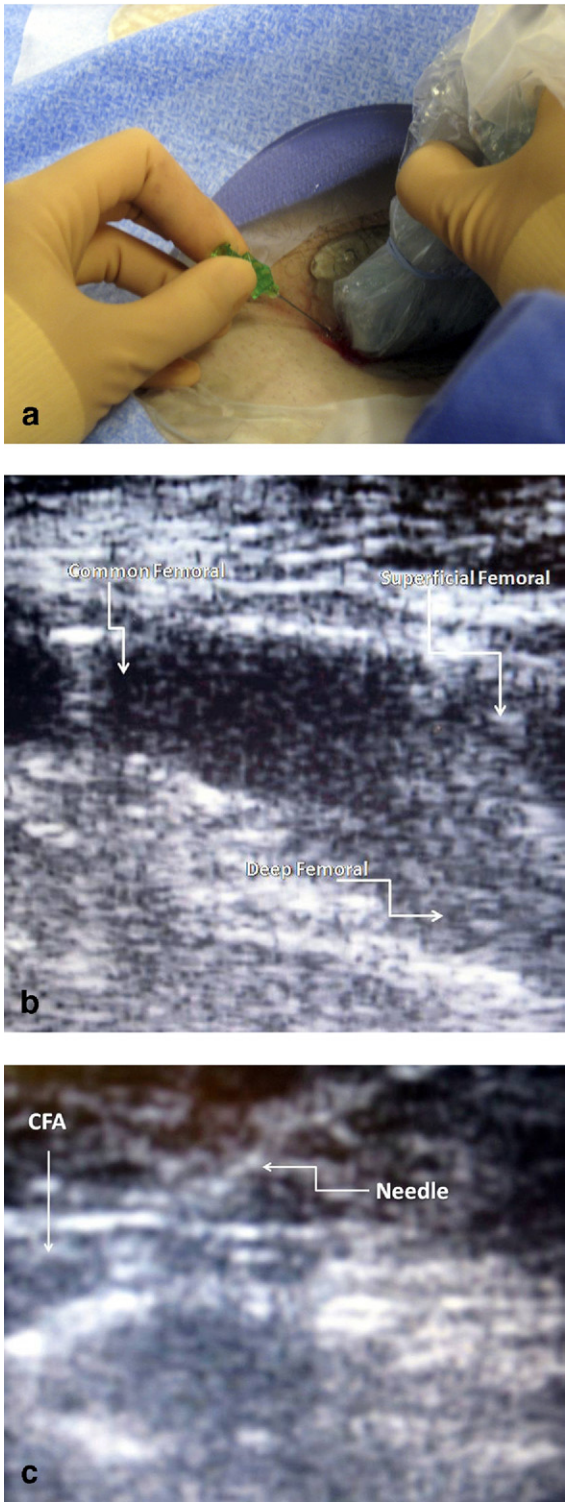

Fig 2. Ultrasound scan-guided femoral arterial access is performed by one operator. In this example, the right hand controls the ultrasound probe **(a)** to image the common femoral artery just proximal to the femoral bifurcation **(b)**. The left hand punctures the artery with the access needle, which can be seen as it enters the common femoral artery **(c)**.

ionic, high osmolality agents.[8,9] Most reactions are minor, manifested by urticaria, although more severe reactions including bronchospasm, laryngeal edema, and anaphylactic shock leading to cardiopulmonary arrest can occur.[10] In patients with a history of contrast-induced allergic reactions, premedication with oral methylprednisolone before angiography alone can significantly reduce allergic reactions[11,12] along with the avoidance of ionic, high osmolality agents.[13]

Nephrotoxicity is a particularly important concern in patients with diabetes mellitus and underlying renal insufficiency. It is a common cause of acute renal failure in hospitalized patients.[14] Clinical manifestations can range from a mild, reversible rise in serum creatinine levels to renal failure requiring hemodialysis. Pre-existing renal dysfunction remains the most important risk factor for the precipitation of contrast-induced nephropathy (CIN) in patients[15] and is independent of the type of contrast agent used, either ionic or nonionic, and the volume infused, although it occurs less frequently with low-osmolality agents.[16] The physiologic basis of contrast-induced nephropathy seems to be transient local ischemia in the renal tubule. It is postulated that as contrast material is filtered without re-absorption, an osmotic pressure gradient is created that results in increased intra-tubular pressure, afferent arteriolar vasoconstriction, and a decrease in the glomerular filtration rate. The decrease in glomerular filtration rate results in regional tubular ischemia.[17] There is a relationship between the degree of renal insufficiency and the likelihood of developing contrast-induced nephropathy. Although it occurs in only 1% to 2% in patients with normal renal function, it increases to 10% in patients with serum creatinine levels between 1.3 and 1.9 mg/dL and to 62% in patients with levels greater than 2 mg/dL.[15,18]

Although diabetes itself is not considered an independent risk factor for the occurrence of CIN, the incidence is higher in patients with diabetes presumably due to the higher incidence of subclinical renal insufficiency. Patients with type 1 diabetes are more susceptible than those with type 2 diabetes. Patients with diabetes are also more likely to require hemodialysis from CIN.[19-22] Special care should be taken in patients undergoing arteriography while taking dimethylbiguanide (Metformin), an oral hypoglycemic agent. Metformin use in the presence of renal dysfunction can result in lactic acidosis in patients developing contrast-induced nephropathy. It has been recommended that the patients terminate the use of Metformin for 48 hours before and after contrast angiography.[23]

The prevention of CIN has been studied extensively. Increasing the transit time of contrast through the renal tubule by inducing a brisk diuresis is the goal of therapy. Currently, intravenous hydration is the most effective preventive measure using 0.9% normal saline solution or alternatively intravenous sodium bicarbonate administered for 4 hours before contrast exposure.[24-26] The use of diuretics such as furosemide and mannitol has not been effective and may be deleterious.[25] The antioxidant N-acetylcysteine

(Mucomyst) given at the dose of 600 mg prescribed orally before and after the procedure may also be protective.[27]

Carbon dioxide (Co_2)[28] and gadolinium have been used in place of conventional contrast in patients with renal insufficiency or a history of severe allergic reactions. CO_2 is non-toxic when injected into the arterial circulation and is visible due to a radiodensity that is substantially lower than the surrounding soft tissues. It requires some additional equipment for automated infusion and images must be acquired at a higher frame rate due to the rapidity with which it dissipates. In the past, images obtained were of poor quality and it was rarely used for diagnostic imaging in the extremities. With the superior imaging and postprocessing capabilities of modern equipment, it has proven to be very useful especially in patients with compromised renal function.[29] Image quality of the aortoiliac segment is quite good with CO_2 angiography but degrades significantly in the smaller caliber arteries of the distal lower extremities, especially with diffuse disease. The inability to completely fill the lumen of distal small arteries leads to overestimation of the degree of stenosis.[30] Consequently, a commonly used imaging strategy in our practice is to use CO_2 for imaging the aortoiliac segment and switch to conventional contrast for the extremities in diabetic patients with compromised renal function.

Another alternative to conventional contrast with better opacification of vessels than CO_2 for patients with renal insufficiency is the intra-arterial injection of gadolinium agents usually used in MRA as an off-label use. However, this technique has largely been abandoned due to nephrogenic systemic fibrosis.

In patients with renal insufficiency, contrast exposure can be decreased by studying only the extremity when the femoral pulse is normal or by using CO_2 for the aorta and pelvis. Additionally, it has been our practice to dilute full strength contrast to a 50% concentration with normal saline solution so as to further reduce the amount infused. For patients with extensive tibial and peroneal disease and a patent superficial femoral artery, catheter advancement into the distal superficial femoral or popliteal artery improves imaging of the distal tibial and pedal vessels with less contrast than is required from a more proximal injection in the external iliac artery.

The imaging technique used can have a significant effect on the resolution and opacification of the distal tibial and pedal arteries. Having a patient who is immobile, comfortable, cooperative, and proper positioning of the extremity and imaging equipment is critical to maximize information, especially in the distal lower extremity. Many surgeons study the lower extremity by a single injection from the aorta using bolus chase or stepping technique. Fixed-mount systems come with imaging software that automates the sequence making it simple and fast to perform and it can be used to study both limbs simultaneously. However, in patients with diabetes with extensive multisegment disease or slow transit times, image acquisition can take more than 2 minutes to complete.[31] Limiting movement is critical to maximize image quality, which may be impossible for even the most cooperative patient during long acquisition times resulting in poor resolution, especially of tibial and pedal vessels. For many years, our preference in the diabetic extremity has been selective single field static imaging as described by Gates and Hartnell.[31] For each station, the patient and C-arm can be positioned to optimize imaging while choosing appropriate collimation, magnification, and time delays.

Complete imaging of the infrageniculate arteries requires two planes of view, the most important being oriented perpendicular to the interosseous membrane to separate the anterior tibial and peroneal arteries in the lower leg and tarsal and plantar vessels in the foot. In some circumstances, catheter advancement to the distal superficial or popliteal arteries may be necessary (Fig 3). Use of this technique produces high quality images in most patients, even those with diffuse tibial-peroneal disease. Additionally, single field imaging uses less contrast. A typical bolus-chase study can require 80 to 100 mL of full-strength contrast, while selective single field imaging of the extremity can be performed in sequential fashion using hand injection or power injection with dilute contrast at significantly smaller volumes (40-45 cc with an aortic run, 25-30 cc without an aortic run).

Computed tomographic angiography. The development of the slip-ring gantry led to the development of spiral CT scanning, which for the first time permitted the continuous linear motion of the patient through a gantry containing the radiograph emitter and detector rows continuously sweeping over a 360° arc. Data are acquired rapidly over a continuous volume (the Z axis) rather than as a number of discontinuous single slices. Because the data are collected over a continuous volume, axial slices can be reconstructed from the digital data set at very small intervals without requiring additional radiation exposure. More recently, the development of multi-detector CT scanners has made it possible for CT scanners to capture multiple separate slices per 360° rotations. Slices can be acquired at 1 mm or even submillimeter thickness with rotation time in the range of 0.3 seconds. Complete imaging of the abdominal vasculature can be accomplished in a fraction of the time of previous generation scanners while improving image resolution and decreasing artifacts. Advances in both hardware and computer software technology have improved the graphic image display despite the reduction in scan time.

Current scanners typically generate a 512×512 matrix or, if needed, 1024×1024 matrix. Each data point in the matrix is mapped to a gray scale for display. Both the size of the matrix and FOV has a direct impact on the resolution of the display. Data points depicted as a two-dimensional image are known as a pixel (picture element). However, because the data are actually acquired in three-dimensions in spiral CT, each data point actually represents a three-dimensional image known as a voxel (volume element). The size of each voxel is determined by the FOV and the thickness of the radiograph beam. Current generation CT scanners displaying images in a 512×512 or greater matrix

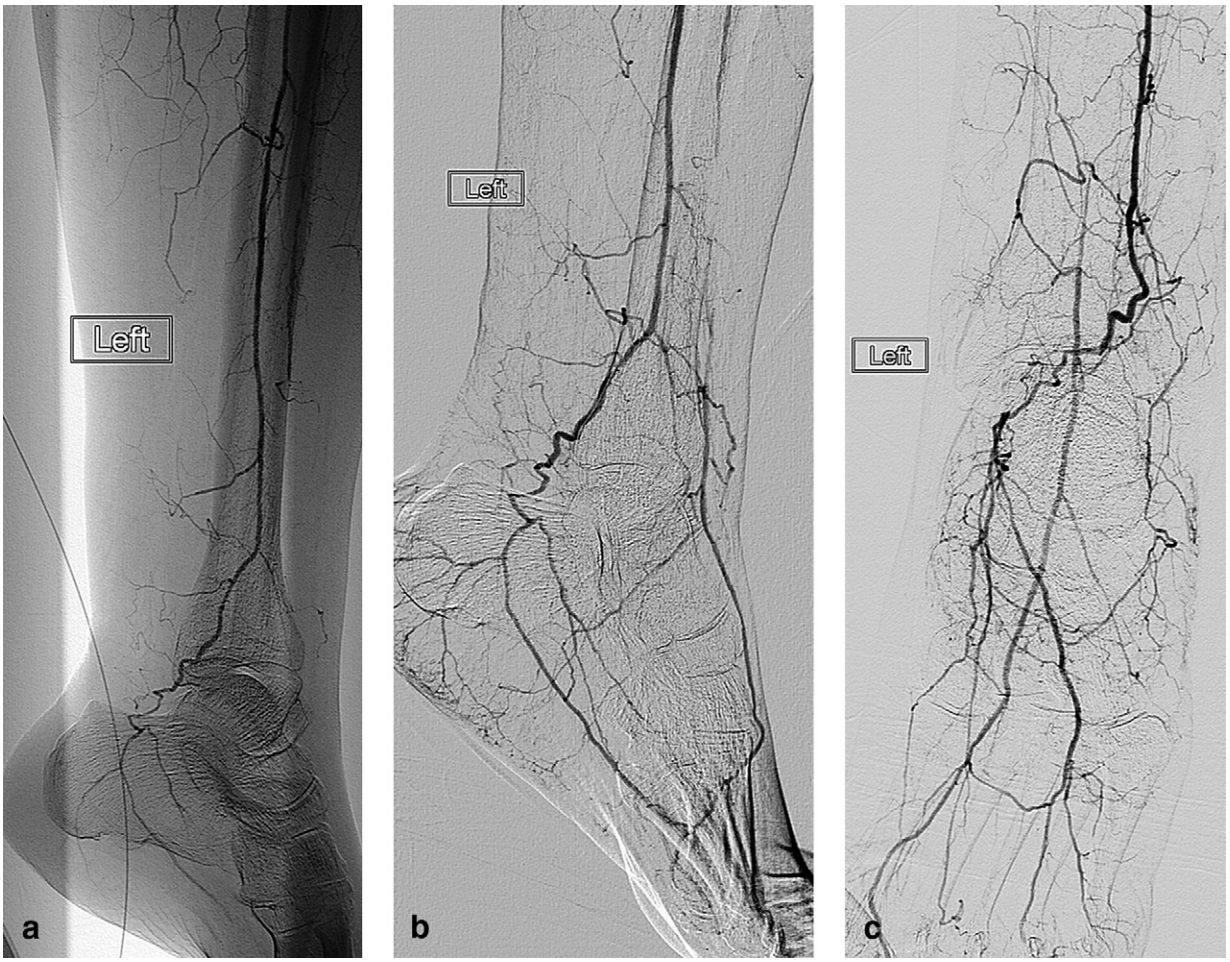

Fig 3. Foot arteriogram of a woman with toe gangrene: **(a)** In a contrast injection performed from the external iliac artery with a superficial femoral artery occlusion, the foot arteries are not visualized suggesting a poor situation for either bypass surgery or an intervention. After angioplasty and stenting of the superficial femoral artery, the catheter was repositioned in the proximal popliteal artery. The dorsalis pedis artery and arch vessels are now clearly seen in lateral **(b)** and anterior/posterior views **(c)**.

have a resolution of 0.2 to 1 mm^2 for each pixel, which is approximately twice the resolution of a typical magnetic resonance imaging (MRI).

Improvements in resolution and acquisition time with multi-detector spiral scanners made CTA possible.[32] As with conventional arteriography, the administration of contrast allows a differentiation of the similar densities of blood and soft tissues. Because contrast generally flows rapidly through the blood stream, CT acquisition must occur rapidly, "chasing" the bolus of contrast over a relatively long distance, only made possible by the fast scanning capabilities of current scanners. Timing of the initiation of image acquisition is crucial in that the contrast volume must reach its maximum intensity in the area of interest as acquisitions are being obtained. Dedicated computer algorithms have been developed by CT scanner manufacturers to make this possible. All are based on a stationary continuous scan of a single slice in which contrast density is measured in the area of interest, usually a large vessel like the proximal abdominal aorta, and CT acquisition is triggered automatically once the machine senses that the contrast volume has reached an appropriate concentration at that slice. Multiple factors beyond the scope of this discussion, such as KVP (tube voltage) and MA (radiation dose/second), collimation, table feed and pitch, patient positioning, and contrast injection parameters can be manipulated during the pre-scan process along with post-scan parameters such as increment slice within the FOV, windowing, and a variety of reconstruction algorithms to provide high quality images of the arterial anatomy in both the abdomen and lower extremity rivaling those of conventional angiography.[33]

Protocols based on a series of settings of these parameters, along with specific technician and patient instructions, have been developed to generate a set of images that is optimal for any specific anatomic area of interest. The

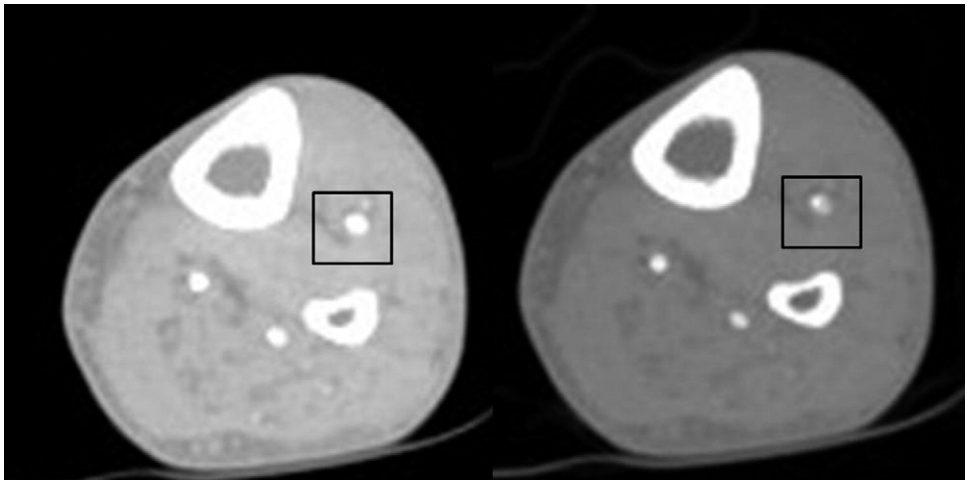

Fig 4. Axial images of a computed tomography (CT) angiogram of the distal lower extremity through the proximal portion of the anterior tibial artery (within the *boxes*). In the image on the *left*, setting the window level with too much brightness makes it impossible to differentiate calcium from contrast giving the appearance that the anterior tibial artery is occluded. In the image on the *right*, after decreasing the brightness, the anterior tibial artery can be seen to be patent with contrast visible within the lumen adjacent to a calcified plaque.

data set can be reconstructed in a variety of ways including axial images, maximum intensity projections (MIPs) that resemble conventional angiograms, and detailed two-dimensional sagittal and coronal views. Striking three-dimensional surface shaded displays of the vasculature often portrayed in color, can be rotated to interpret the area in question from any point of view. When viewed in its entirety, the portfolio of reformatted images from a CTA provides the vascular surgeon with an unrivaled ability to understand completely the anatomic features of any blood vessel being studied.

Although CTA has in many cases become a preferred imaging modality for many vascular surgeons, it does have shortcomings which must be recognized. All of the images depicted in standard CTA protocol are "artificial" reconstructions and are, therefore, subject to potential reconstruction-based artifacts. These include partial volume effects, beam hardening artifacts, motion artifacts, and volume averaging artifacts, which are particularly troublesome when imaging calcified plaques within arterial structures. Stair-step artifacts occur when the reconstruction interval on a spiral CT is too large giving the vessels step-like appearance, which can give the erroneous impression of an area of stenosis. Window level setting errors affect the ability to differentiate calcium in the plaque or arterial wall from contrast (Fig 4). Setting a window level too narrowly results in a significant increase in visible noise that will degrade the visualization of fine structural details, whereas a window that is too wide will abolish small differences in contrast.[33] Adjusting the window setting to differentiate calcification from contrast is perhaps the most important concept to understand when evaluating occlusive lesions in a CTA, although in some cases, especially in small heavily calcified arteries so commonly encountered in the ischemic diabetic extremity, it may be impossible to determine the difference between a calcified stenosis and total occlusion. This phenomenon is especially evident when viewing MIPs, which display calcified plaque and metallic stents prominently.[34] Reconstructions using multipath curved planar reformatting have been developed to overcome this problem (Fig 5). For patients with advanced multi-segment disease or slow transit times, image acquisition may out run the contrast bolus requiring a second acquisition sequence in reverse.

Two additional problems with CTA are the high-radiation dose, particularly when multiple CT scans are being performed over a relatively short period of time,[35] and the large volumes of contrast that are necessary, upward of 150 to 180 cc, with full-strength nonionic contrast for a single CTA run.[36] The latter issue may be especially problematic if the patient is facing a catheter-based intervention requiring further contrast infusion.

Magnetic resonance angiography. MRI uses three types of applied external magnetic fields singly or in combination to produce signals inside the patient that are converted into images. The external magnetic field magnetizes the subject causing protons within the subject to line up in parallel with the external field. The physical characteristics of the protons and the size of the external magnetic field determine the resonance frequency of the proton. Field gradients alter the uniform magnetic field in any of three different directions causing the protons to alter their resonance frequency according to the magnetic field gradient's position. Resonant coils placed adjacent to the area being studied, such as the leg or foot, produce the radiofrequency (RF), which is tuned to the resonance frequency of the protons. The applied RF along with the gradients manipulates the protons to generate a signal detected by

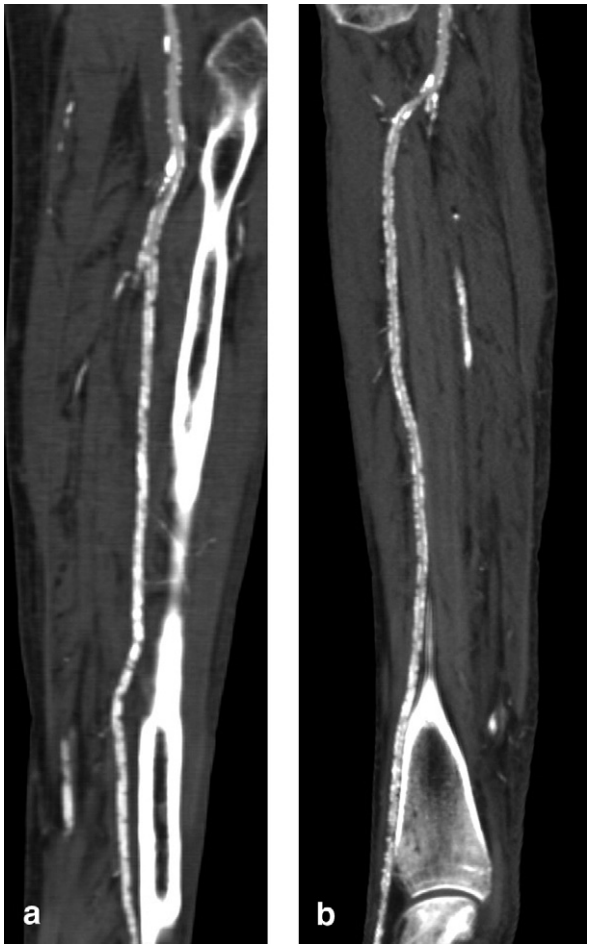

Fig 5. Maximum intensity projections (MIPs) of an anterior tibial artery displays calcium and stents brightly and can obscure luminal detail making it impossible to determine if the artery is patent **(a)**. With the use of curved planar reformatting, the image of the anterior tibial artery can be reconstructed repeatedly as it is rotated along the center line of the artery allowing visualization of many different points of view **(b)**. The same arterial segment reconstructed from a different perspective demonstrates that the artery is patent.

the adjacent receiver coil, analogous to a radio receiver tuned to a specific frequency on the dial. This signal is amplified, digitized, and processed to produce the image. The strength of the magnetic field determines the speed of image acquisition and its resolution. For an MRA a field strength of 1.5 or 3 tesla is used.

The contrast in MR images depends on the characteristics of the object being imaged and on the specifics of the sequence chosen. Images are typically referred to as either T1-weighted or T2-weighted images. T2-weighted images display simple fluids as bright and other tissues as black. An MRA is performed with T1-weighted image sequences. Objects that are bright on T1-weighted images include fat, methemoglobin, flow effects, and MRI contrast agents. A combination of RF and gradients can be used to create an image in MRI, known as MR pulse sequencing, characterized as spin echo or gradient echo sequences. Gradient echo sequences are used to create T1-weighted images seen in an MRA. All pulse sequences have fundamental parameters known as echo time (TE) and repetition time (TR) that determine image contrast. T2-weighted images have a longer TE and TR. Because of this, these sequences are slower and not appropriate for contrast-enhanced MRA. T1-weighted images have very short TR and TE, which is most appropriate for most angiographic examinations. As with CTAs, MR image sequences include the FOV and image matrix. For two-dimensional images, the FOV may be 40 $\times$ 30 cm with a slice thickness of 5 mm with resolution determined by the number of pixels within the FOV, which is determined by image matrix. Most MRAs, however, are performed with three-dimensional imaging. In this case, the FOV is measured in three dimensions (voxel) such as 40 $\times$ 30 $\times$ 30 with the corresponding voxel size determined by the matrix.[37]

An MRA can be performed either without contrast or with contrast-enhanced techniques. Because of superior image resolution, contrast-enhanced MR has generally replaced non-contrast techniques for imaging of the distal lower extremity arterial circulation, most relevant to the current discussion.[38-40] However, the recent description of the nephrogenic systemic fibrosis (NSF)[41] in patients receiving gadolinium contrast agents has limited its utility in patients with diabetes with compromised renal function (see below).The most common non-contrast-enhanced MR technique used is time of flight (TOF angiography). TOF uses a rapid T1-weighted pulse sequence in either sequentially acquired two-dimensional slices or a three-dimensional imaging slab. In a single slice image, when the data are gathered rapidly, the protons within the slice lose much of their magnetization resulting in less signals from these protons and the tissues within the slice are not well seen. When fully magnetized protons in a vessel flow into the slice of interest, they produce much greater signals than the surrounding tissue resulting in a white image, which is very bright with the surrounding tissues being relatively dark. Special RF pulses can be applied to the tissue either above or below the slice to eliminate magnetization from that tissue. If an inferior saturation pulse was used in an axial image, only the protons flowing into the slab from the arterial vessels above the slice would be bright and the veins would be eliminated. The series of such images obtained would produce two-dimensional TOF abdominal angiogram. Newer non-contrast techniques include steady state free precession,[42] arterial spin labeling,[43] and half-Fourier fast spin echo imaging[44] with flow spoiled gradients. All of these techniques are combinations of several different methods designed to accentuate the signal from flowing blood and attenuate that from non-moving structures and tissues with signal characteristics different from blood.

Contrast-enhanced MR angiography (CMRA) uses an agent comprised of the rare element gadolinium chelated with another substance to avoid the release of free gadolinium, which is toxic, into the body. Two common agents

are gadolinium DTPA, and gadobenate dimeglumine (Gd-BOPTA). CMRA is usually performed as a three-dimensional imaging sequence. Three-dimensional sequences are typically faster and of higher resolution than non-contrast enhanced angiograms and provide a similar level of coverage. In a sense, describing gadolinium as contrast is incorrect because it is not actually "seen" on the image but shortens the T1 of the protons in the vicinity making them more conspicuous on T1-weighted imaging. Like CTA angiography, CMRA involves imaging a large volume over a long distance. Obtaining images with adequate spatial resolution requires a long acquisition time and is adversely effected by the patient's motion or breathing. Moreover, as with CTA contrast, intravenously administered gadolinium flows into the studied volume in a time-dependent fashion based on cardiac output and the severity and extent of proximal occlusive lesions. If image acquisition occurs before the contrast reaches the area of interest, not all vessels in the region will be optimally enhanced, and if obtained too late it will be "contaminated" by contrast enhancement of the adjacent veins.

The quality of images as a function of contrast timing to image acquisition is referred to as temporal resolution. Optimizing spatial and temporal resolution in CMRA of the extremity requires a step table technique that divides the volume of interest into four stations, abdomen/pelvis, thighs, calves, and feet. Maximizing image quality in the lower leg and the foot requires a set of specialized coils to improve the signal-to-noise ratios and specialized software to control the table movement. Venous contamination is a common problem in the more distal stations when using the step table technique, although methods have been developed to minimize it. Similar to CTA, the data set of a contrast-enhanced three-dimensional MRA can be reconstructed in a variety of ways to create images from multiple perspectives to optimize visualization of the anatomy. The most commonly used algorithm is the MIP, which resembles a conventional arteriogram.

Recently, a rare condition known as NSF, previously described as nephrogenic fibrosing dermopathy, has been reported in patients receiving gadolinium contrast agents in the presence of chronic renal failure.[41] NSF is characterized by skin thickening and hyperpigmentation of the extremities and the trunk, somewhat analogous to scleroderma. In patients with more severe involvement, contractures, organ fibrosis, and death have been reported. All reported cases have occurred in patients with renal insufficiency, primarily those with very poor kidney function in the setting of chronic renal failure, although it has been occasionally reported in acute renal failure as well. There is no specific treatment other than attempting to improve renal function. Steroids and other anti-inflammatory treatments have been used along with hemodialysis and photopheresis.[45] The association between NSF and gadolinium-containing contrast agents was reported in 2006 in a cohort of patients on dialysis undergoing MRA.[41] Since that time, there have been hundreds of reported cases in patients both receiving dialysis and not.[46] There seems to be a dose-dependent response with the disease more commonly occurring in patients receiving larger doses of gadolinium contrast agents or undergoing repeated studies. Gadolinium agents are generally cleared rapidly by the kidneys with normal renal function but the clearance time may be increased 100-fold in those with severe renal insufficiency. To date, no cases of NSF have been reported in patients receiving gadolinium agents with normal renal function. The majority of cases have occurred with the use of Gadodiamide (Omniscan, GE Healthcare, Piscataway, NJ) with smaller numbers associated with Gadobenate Dimeglumine (Magnevist, Bayer HealthCare Pharmaceuticals, Berlin, Germany), and Gadoversetamide (OptiMARK, Covidien Imaging Solutions, Hazelwood, Mo). Omniscan has the weakest binding of gadolinium ions to the chelating agent, which may explain its higher incidence of NSF, thought to occur as a reaction to free gadolinium ions. Based on the reported observations of NSF with these agents, the use of gadolinium contrast agents is now contraindicated in patients with a glomerular filtration rate of less than 30 mL/minute or acute renal insufficiency.

The technique for CMRA of the distal arterial circulation in patients with diabetes requires a system with the fastest and strongest gradients available. This results in faster acquisition times with higher degrees of spatial resolution and improved signal-to-noise ratios. As described previously, the use of dedicated coils for specific vascular beds are useful especially for imaging the distal pedal and foot circulation. When administering contrast, a dual-chamber power injector is best for rapid administration of contrast followed by a "saline chaser" which decreases the amount of contrast used. One disadvantage is the powerful magnetic field, which requires specialized patient monitoring equipment, which can be troublesome in critically ill patients. Specialized software is needed to enable step table and parallel imaging. Venous contamination can be diminished in CMRA by the use of special blood pressure cuffs placed around the extremity. Postprocessing can be complex and requires specialized workstations. Although MIP images are favored by vascular surgeons because they resemble angiograms, like CTA images, they are artificial constructs and subject to reconstruction artifacts. Correct interpretation of MRA imaging requires review of both source images and maximum intensity projections and for most surgeons is best done with a radiologist.

Imaging strategies. Diagnostic imaging is a misnomer. For the experienced vascular specialist, the diagnosis of lower extremity ischemia should be straightforward in most cases, based on a careful history and physical examination augmented by noninvasive studies. For the most part, anatomic imaging should be considered strategic – only performed once a clinical decision has been made to intervene due to the presenting symptoms and physical findings. In the past, choosing the optimal anatomic imaging study was a trade-off balancing the superior image quality provided by DSA at the expense of being invasive with the attendant complications previously outlined.

Contrast-induced nephrotoxicity was especially worrisome in many patients with diabetes.

The development of MRA and especially contrast-enhanced three-dimensional MRA[38,39] provided an alternative that was noninvasive, cost-effective,[47] with imaging capabilities equal to or superior to DSA.[48] Comparing the diagnostic utility and accuracy of MRA and DSA has been the subject of numerous studies over many years. In early studies, MRA and DSA were in agreement in 80% to 85% of the time, although DSA was clearly superior for imaging very distal arteries, especially pedal vessels. With the development of contrast-enhanced MRA, three-dimensional imaging techniques, and specific coils for the distal leg and foot, more recent studies have demonstrated the superiority of MRA in imaging very distal crural and pedal arteries in comparison to DSA,[49,50] in addition to being less invasive and more cost-effective. One disadvantage was the relatively long acquisition times resulting in timing sequence errors in contrast acquisition, venous contamination, and the inability to image multiple vessels simultaneously with different rates of blood flow without additional contrast injections. Many of these shortcomings have been overcome with time-resolved imaging of contrast kinetics (TRICKS)[51] MRA and the use of newer three tesla magnets which permit more rapid sequencing with a higher degree of spatial and temporal resolution.[1]

It is important to recognize that many studies fail to adequately describe the specifics of their angiographic technique, which can greatly affect the results of DSA. Specifically, the use of bolus-chase arteriography, injection of inadequate volume of contrast, or improper catheter positioning may result in inadequate filling of distal vessels and an erroneous interpretation (Fig 3). The recognition of nephrogenic systemic fibrosis as a potentially fatal complication of gadolinium contrast agents in patients with renal insufficiency has resulted in the virtual abandonment of contrast MRA in these patients. Moreover, the widespread use of catheter-based interventions for treating lower extremity ischemia has led to a resurgence of interest in DSA imaging. In many practices, including our own, an additional advantage is the efficiency and convenience of being able to perform the intervention during the same procedure as the diagnostic angiogram.

Although CTA can provide imaging which rivals the quality of DSA or MRA, difficulties interpreting images in areas of heavy calcification in distal target arteries and the added contrast exposure are significant disadvantages which limit its usefulness in the diabetic ischemic extremity.

In current practice, in which catheter-based interventions have become a mainstay for treating lower extremity ischemia, a clinical evaluation followed straight away by a diagnostic arteriogram is probably the most efficient and cost-effective approach in most patients requiring treatment. If a treatable lesion is found, a catheter-based intervention can be accomplished at the same time. For patients in whom surgery is the only planned treatment, MRA imaging or CTA provide excellent noninvasive alternatives to DSA. The decision of which modality to use is mostly driven by physician preference and local availability/expertise with either CTA or MRA. The Table includes a summary of the advantages and disadvantages of the three imaging modalities.

Table. Advantages and disadvantages of DSA, CTA, and MRA for lower extremity arterial imaging

Modality	*Advantages*	*Disadvantages*
DSA	Best resolution Combines diagnosis and treatment "gold standard"	Invasive, radiation exposure Access complications Adverse reactions to contrast Allergic reactions Contrast nephropathy
MRA	Noninvasive, no radiation Images not obscured by calcium Can image arteries not seen on DSA	Inferior spatial resolution Long acquisition times Acquisition artifacts NSF
CTA	Noninvasive Excellent spatial resolution Rapid image acquisition time Multiple reconstruction techniques	Obscured by calcium Highest contrast volume Adverse reactions to contrast Radiation exposure Imaging artifacts

CTA, Computed tomography angiography; *DSA,* digital subtraction angiography; *MRA,* magnetic resonance angiography; *NSF,* nephrogenic systemic fibrosis.

Patients with renal dysfunction present a difficult challenge because MRA is contraindicated due to concerns about NSF and CTA exposes them to a significantly larger volume of contrast than DSA. Some centers have reported excellent results with preoperative duplex ultrasonography either as a stand-alone imaging modality[52,53] or as an adjunct to contrast arteriography, in which duplex imaging can identify areas of significant stenosis limiting the contrast arteriogram to a specific area requiring treatment. In our practice, we prefer DSA in these patients using strategies to limit contrast exposure including the use of nonionic iso-osmolar contrast diluted to 50% strength, using CO_2 for proximal arteries or avoiding aortoiliac imaging altogether. All patients are hydrated with normal saline solution or sodium bicarbonate and receive acetylcysteine premedication as previously described.

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