

**American College of Radiology
ACR Appropriateness Criteria®**

Clinical Condition: Sudden Onset of Cold, Painful Leg

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
INV aortography and bilateral lower extremity arteriography	8		Low
CTA lower extremity	7	Distal abdominal aorta should be included.	Med
MRA lower extremity	7	Distal abdominal aorta should be included. See comments regarding contrast in text under “Anticipated Exceptions.”	None
Physiologic noninvasive tests	6	Not required in the acute setting but may provide important physiologic information not obtained on imaging studies to further direct care.	None
US lower extremity with Doppler	5	Limitations include heavily calcified vessels and operator dependency. May be helpful for problem solving.	None
US echocardiography transthoracic	4	Generally not part of the initial workup. May be useful to look for source of emboli.	None
US echocardiography transesophageal	3	Generally not part of the initial work-up. May be useful to look for source of emboli.	None
MRI heart function and morphology with or without contrast	3	Generally not part of the initial work-up. May be useful to look for source of emboli.	None
CT heart function and morphology with contrast	2	Generally not part of the initial work-up. May be useful to look for source of emboli.	High
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

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SUDDEN ONSET OF COLD, PAINFUL LEG

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Summary of Literature Review

Acute onset of a cold painful leg, although not directly a significant cause of mortality, contributes significantly to morbidity. The etiologies of acute onset of a cold, painful leg are limited; the most common cause is arterial occlusion. Total venous outflow occlusion is another much less common cause. It often results in what is known clinically as “phlegmasia cerulea dolens” (precursor to venous gangrene) with lower extremity swelling, pain, and a dusky color. It is differentiated from arterial occlusion by the presence of distal arterial pulses. Other causes, such as prolonged exposure to cold and trauma, are rare and usually clinically obvious.

This condition generally requires urgent treatment, regardless of the etiology. Once the etiology is clinically defined, directing appropriate care of the patient requires assessing the source (ie, embolic vs. thrombotic occlusion) and extent of the underlying arterial obstruction. The available alternatives include noninvasive testing: duplex ultrasound (US), magnetic resonance angiography (MRA), computed tomography angiography (CTA), and catheter angiography.

Catheter Angiography

Digital subtraction angiography (DSA) remains the diagnostic gold standard for detecting peripheral vascular occlusive disease, but new and less invasive modalities are gradually replacing it [1]. Obviously, one of the major benefits is the ability to diagnose and then treat disease with one procedure; a benefit which remains unmatched in vascular disease. There has been extensive debate regarding the cost-benefit ratios when comparing DSA and MRA. At some institutions, DSA is done as an inpatient procedure and therefore may necessitate a 2-day hospital stay [2,3]. If complications from this invasive approach occur, additional intervention and prolongation

of the hospital stay may add cost as well as morbidity or even mortality. To be truly cost-effective, any noninvasive method would have to supplant, not just precede or supplement DSA.

The incidence of complications with DSA varies greatly in published reports. Potential complications include those related to the use of contrast agents. Most worrisome are the rare fatal systemic reactions and contrast-induced nephropathy (CIN). The nephrotoxic effects are important to consider, as many patients who present with the sudden onset of a cold, painful leg are elderly, diabetic, and have impaired renal function [2]. Also, many patients will have repeated angiography over the course of their disease, and minimizing the patient’s radiation exposure should always be taken into consideration. Angiography has also always been criticized for its imperfect evaluation of outflow vessels, specifically for limited visualization of patent distal vessels beyond significant obstructive lesions [1].

Magnetic Resonance Angiography

One of the most heavily investigated alternatives is MRA. With improving speed of examinations as well as improving technology that reduces artifacts and venous contamination, it is proving to be a feasible, noninvasive alternative to catheter DSA. More recent research has demonstrated high sensitivity and specificity for detecting acute occlusive disease when compared to DSA [3-11]. Much of the success comes as a result of 3D contrast-enhanced replacing 2D MRA, allowing for thinner slices and higher signal-to-noise ratios [8,11]. MRA is an attractive alternative for diagnosing arterial disease, as it is noninvasive and has few associated complications. Its current speed and resolution have enabled MRA to become a reliable method of quickly and accurately imaging the entirety of the lower vascular system [4].

Whereas, older techniques and sequences would require the patient to remain still for 30 minutes or more, contrast-enhanced scans can be completed much more quickly. Most of the information that interventionalists or vascular surgeons need can be gathered with MRA, including a general road map of arterial anatomy, including runoff vessels and collaterals, as well as the location and extent of significant stenoses and occlusions. Limitations include less accurate evaluation of smaller arteries and better results requiring more time-consuming technologies, including lower extremity coils [4,6]. Also, limited information can currently be obtained on a routine basis regarding the character of vessel walls and flow dynamics, although time-resolved contrast-enhanced.

MRA techniques are beginning to provide qualitative flow information. Overestimation of stenosis in patients with vascular stents secondary to artifacts has been reported, as has routine overestimation [10]. The latter

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appears to be dependent on the specific technique used and may or may not be a clinical problem in specific cases. This uncertainty highlights another barrier to the institution of MRA: the lack of a consensus on the best method for performing the study. In part, this is a function of the continuing evolution of technology, both software and hardware. Another concern with MRA is that most techniques have required the administration of a gadolinium-based contrast agent. With the realization of the risk of nephrogenic systemic fibrosis (NSF) in patients with underlying renal dysfunction who receive these contrast agents, there has been increased interest in using another imaging modality in such patients, in limiting the use of contrast in MRA, or in developing improved techniques of MRA that do not depend on the administration of contrast agents (see Anticipated Exceptions).

Computed Tomography Angiography

As with MRA, there have been significant recent advances with CTA, with shorter imaging times and significantly better spatial resolution thanks to the advent of multidetector CT (MDCT). Where previously one contrast bolus was limited to imaging 40 cm of a given vascular territory, MDCT is capable of acquiring thin slices from the diaphragm to the ankles in less than 40 seconds using a single contrast bolus [12,13]. Sophisticated postprocessing tools allow for 3D volumetric imaging for superior diagnostic accuracy and improved ease of interpretation. Postprocessing of massive amounts of raw data has proven vital to the success of CTA. Although it may be time-consuming, recent software platforms have made such efforts easier. The average postprocessing time varies, but this is a complicated task that requires the subtraction of bony structures, which are often at the center of the image, and takes an average of over 20 minutes [12].

The two most popular techniques for vessel analysis are volume rendering (VR) and maximum intensity projection (MIP), each with advantages and disadvantages. MIPs are very accurate for larger vessels (as distal as the infrapopliteal region) but less accurate for smaller vessels [12,14]. Where MIP imaging cannot evaluate the vessel lumen, VR is good for evaluating embolic or vascular endothelial injury. It is also valuable in the evaluation of heavily calcified vessels. It is not sufficient, however, for the sole evaluation of stenotic or occluded vessels [14].

CTA has proven accurate for evaluating arteries from the infrarenal to the infrapopliteal levels [12,14]. To date, there have been no direct comparisons of CTA and MRA. CTA, however, has advantages over MRA due to its widespread availability and its usability in patients who have contraindications to MR, such as those who have defibrillators in place [15]. CTA is also felt to be more accurate in depicting mural calcifications although heavy calcifications (over 50%) may also create artifact and

overestimate the degree of stenosis [13,14,16]. Discussions of cumulative radiation dosage have raised concerns, as MDCTA has been increasingly used for both preprocedure planning and postprocedure surveillance. Studies have emerged, however, that show lower radiation dosages for a single CTA examinations compared to DSA [12]. Also, techniques tailored to the evaluation of lower limb vasculature have been published that allow reduced patient radiation by decreasing kVp, with preserved ability to evaluate the smaller lower limb vessels [13,15,17].

Other Imaging Examinations

Duplex US is limited by the need for operator expertise, by poor accessibility of vessels, by heavy calcification, and often by poor overall accuracy if multilevel disease is present [19]. Its advantages are that it can provide useful physiologic as well as anatomic information. Further, it is noninvasive, widely available, and relatively inexpensive.

Transthoracic echocardiography (TTE) or the more specific and more invasive transesophageal echocardiography (TEE) may be useful if it is thought that the onset of symptoms is related to embolization from the heart. The suspicion for this is particularly high in patients with known atrial fibrillation. It is not likely in the acute setting, however, that this knowledge will affect further evaluation or alter therapy for the acutely cold, painful leg. Similarly, cardiac MRI may be useful in defining the presence of cardiac thrombus or areas of cardiac dysfunction that might be the source of emboli, but this knowledge is not likely to have clinical impact in the acute setting.

Noninvasive Physiologic Testing

This includes measurement of ankle-brachial index (ABI), plethysmography, transcutaneous oxygen pressure measurement (TCPO₂) and exercise treadmill testing. ABI measurement is simple and reliable and serves both as confirmation of arterial occlusion as the etiology of sudden onset of cold leg and as a baseline to guide further intervention [20]. Useful physiologic information may also be obtained. In this clinical setting, other noninvasive tests generally are not helpful, as they do not provide specific information that will alter or guide therapy [21].

Summary

Minimally invasive methods of vascular imaging have grown in leaps and bounds over the past decade and will continue to evolve. DSA remains the gold standard for diagnosing peripheral vascular disease and continues to be the only modality that allows diagnosis and simultaneous treatment of pathology. This alone will ensure that DSA continues to be a valuable tool. However, noninvasive imaging to evaluate the vasculature before an angiogram, or surgery, is becoming a more and more reasonable step. CTA and MRA have become accurate and attractive, less invasive modalities

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for initial evaluation. Peripheral vascular disease is a significant and growing problem, and continued research and development of current and emerging technologies will ultimately shape the standard of care.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF), also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF [22-24], a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (eg, >0.2mM/kg) and to agents in which the gadolinium is least strongly chelated. The FDA has recently issued a “black box” warning concerning these contrast agents (http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705HCP.pdf).

This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m²), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s) [23].

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

References

1. Schindler N, Calligaro KD, Lombardi J, Dougherty MJ, Raviola CA, D'Orazio E. Has arteriography gotten a bad name? Current accuracy and morbidity of diagnostic contrast arteriography for aortoiliac and lower extremity arterial disease. *Ann Vasc Surg* 2001; 15(4):417-420.
2. Hentsch A, Aschauer MA, Balzer JO, et al. Gadobutrol-enhanced moving-table magnetic resonance angiography in patients with peripheral vascular disease: a prospective, multi-centre blinded comparison with digital subtraction angiography. *Eur Radiol* 2003; 13(9):2103-2114.
3. Loewe C, Schoder M, Rand T, et al. Peripheral vascular occlusive disease: evaluation with contrast-enhanced moving-bed MR angiography versus digital subtraction angiography in 106 patients. *AJR* 2002; 179(4):1013-1021.
4. Deutschmann HA, Schoellnast H, Portugaller HR, et al. Routine use of three-dimensional contrast-enhanced moving-table MR angiography in patients with peripheral arterial occlusive disease: comparison with selective digital subtraction angiography. *Cardiovasc Intervent Radiol* 2006; 29(5):762-770.
5. Huegli RW, Aschwanden M, Bongartz G, et al. Intraarterial MR angiography and DSA in patients with peripheral arterial occlusive disease: prospective comparison. *Radiology* 2006; 239(3):901-908.
6. Ruehm SG, Nanz D, Baumann A, Schmid M, Debatin JF. 3D contrast-enhanced MR angiography of the run-off vessels: value of image subtraction. *J Magn Reson Imaging* 2001; 13(3):402-411.
7. Sueyoshi E, Sakamoto I, Matsuoka Y, Hayashi H, Hayashi K. Symptomatic peripheral vascular tree stenosis. Comparison of subtracted and nonsubtracted 3D contrast-enhanced MR angiography with fat suppression. *Acta Radiol* 2000; 41(2):133-138.
8. Sueyoshi E, Sakamoto I, Matsuoka Y, et al. Aortoiliac and lower extremity arteries: comparison of three-dimensional dynamic contrast-enhanced subtraction MR angiography and conventional angiography. *Radiology* 1999; 210(3):683-688.
9. Swan JS, Carroll TJ, Kennell TW, et al. Time-resolved three-dimensional contrast-enhanced MR angiography of the peripheral vessels. *Radiology* 2002; 225(1):43-52.
10. Winterer JT, Laubenberger J, Scheffler K, et al. Contrast-enhanced subtraction MR angiography in occlusive disease of the pelvic and lower limb arteries: results of a prospective intraindividual comparative study with digital subtraction angiography in 76 patients. *J Comput Assist Tomogr* 1999; 23(4):583-589.
11. Dellegrataglie S, Sanz J, Macaluso F, et al. Technology Insight: magnetic resonance angiography for the evaluation of patients with peripheral artery disease. *Nat Clin Pract Cardiovasc Med* 2007; 4(12):677-687.
12. Edwards AJ, Wells IP, Roobottom CA. Multidetector row CT angiography of the lower limb arteries: a prospective comparison of volume-rendered techniques and intra-arterial digital subtraction angiography. *Clin Radiol* 2005; 60(1):85-95.
13. Jakobs TF, Wintersperger BJ, Becker CR. MDCT-imaging of peripheral arterial disease. *Semin Ultrasound CT MR* 2004; 25(2):145-155.
14. Portugaller HR, Schoellnast H, Hausegger KA, Tiesenhause K, Amann W, Berghold A. Multislice spiral CT angiography in peripheral arterial occlusive disease: a valuable tool in detecting significant arterial lumen narrowing? *Eur Radiol* 2004; 14(9):1681-1687.

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15. Rubin GD, Schmidt AJ, Logan LJ, Sofilos MC. Multi-detector row CT angiography of lower extremity arterial inflow and runoff: initial experience. *Radiology* 2001; 221(1):146-158.
16. Schertler T, Wildermuth S, Alkadhi H, Kruppa M, Marincek B, Boehm T. Sixteen-detector row CT angiography for lower-leg arterial occlusive disease: analysis of section width. *Radiology* 2005; 237(2):649-656.
17. Willmann JK, Mayer D, Banyai M, et al. Evaluation of peripheral arterial bypass grafts with multi-detector row CT angiography: comparison with duplex US and digital subtraction angiography. *Radiology* 2003; 229(2):465-474.
18. Leiner T, Kessels AG, Nelemans PJ, et al. Peripheral arterial disease: comparison of color duplex US and contrast-enhanced MR angiography for diagnosis. *Radiology* 2005; 235(2):699-708.
19. Krnic A, Vucic N, Susic Z. Duplex scanning compared with intra-arterial angiography in diagnosing peripheral arterial disease: three analytical approaches. *VASA* 2006; 35(2):86-91.
20. Sprynger M, Fassotte C, Verhaeghe R. The ankle-brachial pressure index and a standardized questionnaire are easy and useful tools to detect peripheral arterial disease in non-claudicating patients at high risk. *Int Angiol* 2007; 26(3):239-244.
21. Gale SS, Scissons RP, Salles-Cunha SX, et al. Lower extremity arterial evaluation: are segmental arterial blood pressures worthwhile? *J Vasc Surg* 1998; 27(5):831-838; discussion 838-839.
22. Broome DR, Girguis MS, Baron PW, Cottrell AC, Kjellin I, Kirk GA. Gadodiamide-associated nephrogenic systemic fibrosis: why radiologists should be concerned. *AJR* 2007; 188(2):586-592.
23. Kanal E, Barkovich AJ, Bell C, et al. ACR guidance document for safe MR practices: 2007. *AJR* 2007; 188(6):1447-1474.
24. Sadowski EA, Bennett LK, Chan MR, et al. Nephrogenic systemic fibrosis: risk factors and incidence estimation. *Radiology* 2007; 243(1):148-157.

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