Imaging in the diagnosis and evaluation of peripheral artery disease

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Abstract
Peripheral artery disease (PAD) is a disease of the systemic arterial tree and is a growing concern globally. It commonly affects the lower extremities and leads to increased mortality and morbidity due to its known association with coronary artery disease and strokes. Over the past several decades, advanced imaging has become a major part in the diagnosis and management of PAD, but there is still no consensus agreement as to the preferred initial imaging test of choice. Over the years, several different trials, reviews, and analyses have compared the three primary imaging modalities in PAD: ultrasound, magnetic resonance angiography (MRA), and computed tomographic angiography (CTA). In large comparison reviews, MRA showed sensitivity ranging from 92% to 99.5% while CTA showed sensitivity ranging from 89% to 99% and ultrasound showed sensitivity ranging from 80% to 98%. Total costs, however, were significantly lower for CTA than for MRA or ultrasound. Overall, the literature suggests that while MRA may have a slight advantage in accuracy, CTA may be the better initial test of choice due to patient comfort and cost-effectiveness. However, each imaging modality has its own risks and contraindications that should be carefully reviewed prior to utilization. This is a review of the current available literature comparing the use of ultrasound, MRA, and CTA in the diagnosis and management of lower extremity PAD.
1. Introduction
Peripheral artery disease (PAD) refers to atherosclerosis and luminal narrowing of non-coronary vasculature caused by deposition of lipid and fibrous material within vessel walls. Symptomatically, it most commonly affects the lower extremities, but it can also play a significant role in mesenteric ischemia, renal disease, and strokes.\(^1\) The prevalence of PAD has increased over the preceding decade and its incidence is growing by 0.3% per year in men ages 40-55 and 1% per year in men over age 75.\(^2\), \(^3\) Although the diagnosis of PAD can often be made clinically based on history and examination findings, imaging has now become an integral part of diagnosis and preoperative planning prior to intervention. However, there is no clear consensus guideline recommendation for which imaging modality to use initially in diagnosing and evaluating PAD. This review of the current literature compares the three primary noninvasive imaging modalities used to diagnose PAD: ultrasound, magnetic resonance angiography (MRA), and computed tomography angiography (CTA). For the purposes of this review, we will focus on lower extremity PAD.

2. Ultrasound
Ultrasound was the first imaging technique to be widely used to assess lesion morphology and severity. Studies from as early as the 1990s showed that duplex ultrasound was more effective than simple ankle-brachial index measurements to assess lesion morphology and changes in flow velocity in stenotic areas, and that it even compared to direct angiography.\(^4\) Color-assisted duplex sonography resulted in a sensitivity of 88%, specificity of 95%, and accuracy of 93% when compared to angiography in detecting femoropopliteal arterial lesions with >50% stenosis.\(^5\) However, the accuracy of ultrasound appeared to be worse for more distal lesions. In 1996, a separate meta-analysis of 16 studies showed that the sensitivity and specificity of detecting >50% stenosis in the aortoiliac arteries was 86% and 97%, respectively, while only 80% and 98%, respectively, in the femoropopliteal arteries. The sensitivity and specificity of detecting infragenicular disease was even lower at 83% and 84%, respectively.\(^6\) In addition to the location of the stenosis, the accuracy of ultrasound is also limited by the skill of the operator and overall quality of the image.

3. MRA
Although early studies of MRA were not very impressive,\(^7\) the diagnostic accuracy of MRA appeared to improve with advancements in technology and technique. A meta-analysis of 32 studies using contrast enhanced MRA demonstrated a pooled sensitivity of 94.7% and specificity of 95.6% in detecting segmental stenotic occlusions.\(^8\) In a prospective comparison including 295 patients, contrast-enhanced MRA outperformed duplex ultrasound in sensitivity (84% vs 76%, \(p=0.002\)) and specificity (97% vs 93%, \(p=0.03\)) for detecting stenotic lesions,\(^9\) and it appeared to be more effective than ultrasound in treatment planning as well.\(^10\) However, the diagnostic accuracy of MRA varied with technique,\(^11\) and its use is still limited by relative cost, availability, presence of stents.
or other metallic devices, and patient comfort.

4. CTA

CTA is another imaging modality that has become more widely used over the past decade, especially in the detection of coronary disease. However, its use in detecting peripheral artery disease has also been shown to be effective. Three separate meta-analyses published between 2007 and 2013 demonstrated that the sensitivity and specificity of CTA for detecting >50% stenosis ranged from 92% to 96% and from 93% to 96%, respectively.\textsuperscript{12-14} Multiple studies reported excellent correlation with digital subtraction angiography while reducing effective radiation dose by 75%\textsuperscript{15}.\textsuperscript{16} Because advancements in technology, such as the use of multislic, dual energy, and dual source scanners, often outpace validation studies, it’s possible that these values were underestimates of true sensitivities and specificities. The use of CTA involves radiation exposure and requires contrast administration, sometimes precluding its use in patients with very severe renal disease or contrast allergies, although newer techniques and types of contrast media have reduced the amount of contrast required.

5. Comparison

In 2007, Collins et al. published a large systematic review of 113 studies comparing ultrasound, MRA, and CTA in diagnostic accuracy, patient comfort, and cost-effectiveness. The review showed that contrast-enhanced MRA had the highest diagnostic accuracy for detecting arterial stenosis >50% with sensitivity ranging from 92% to 99.5% and specificity ranging from 64% to 99%, followed by CTA with sensitivity ranging from 89% to 99% and specificity from 83% to 97%. Ultrasound was the least sensitive out of the three modalities, with sensitivity ranging from 80% to 98%. In terms of patient comfort, CTA was the least uncomfortable followed by MRA. Based on this same retrospective data, ultrasound was shown to be the most cost-effective imaging modality for examinations of the entire leg, but two-dimensional time-of-flight MRA was more cost-effective in segmental analysis.\textsuperscript{17} However, a multicenter randomized controlled trial known as the DIPAD trial was later published comparing the costs and effects of noninvasive diagnostic imaging in PAD. The DIPAD trial was a prospective, randomized trial that directed patients with PAD to either MRA, CTA, or duplex ultrasound as the initial imaging modality for evaluation. It showed that total costs were significantly lower for CTA than for MRA or ultrasound at 6 month follow-up, and CTA resulted in significantly fewer additional imaging tests required than duplex ultrasound (0.06 vs 0.23, p =0.01).\textsuperscript{18} The authors concluded that that both CTA and MRA are clinically more useful than duplex sonography and that CTA leads to cost savings compared with both MRA and duplex sonography in the initial imaging evaluation of peripheral arterial disease.

6. Conclusion

All three imaging modalities can be effectively used in the diagnosis and management of lower extremity PAD. Based
on currently available data, it appears that MRA is the most sensitive imaging modality in detecting significant arterial stenosis, while CTA is the most cost-effective and comfortable. This may be subject to change with further advancements in technology and technique; It is highly likely that CTA will become increasingly sensitive and specific given new advances including more detectors, iterative reconstruction, gemstone detectors and faster rotation speeds. Nevertheless, each imaging modality has its own limitations and contraindications and the choice of the best initial imaging test should be made on a patient-centered case-by-case basis.
7. References


