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Lower-limb magnetic resonance angiography: performance of extracellular contrast agents versus blood pool contrast agent for both dynamic and high spatial resolution imaging in extended phase

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AIM: To prospectively compare the performance of extracellular space contrast agents (ECSCAs) versus a blood-pool contrast agent (BPCA) for a comprehensive lower-limb magnetic resonance angiography (MRA) protocol in patients with either claudication or critical ischaemia.

MATERIALS AND METHODS: Thirty patients with claudication underwent lower-limb magnetic resonance angiography (MRA) (dynamic crural, three-station bolus chase, and infra-inguinal high resolution) using a triphasic injection method with both a ECSCA and BPCA to allow intra-individual comparison, and 30 patients with critical ischaemia were scanned with either a ECSCA or BPCA. The dynamic, bolus chase, and high-resolution images were scored for quality on a Likert scale (from 1–5). Signal- and contrast-to-noise ratios were analysed and statistical analysis performed.

RESULTS: Overall, there was no statistically significant difference between the ECSCAs and BPCA for arteriographic dynamic imaging, bolus chase MRA, or the high spatial resolution imaging. Venous image quality was rated higher quality for BPCA scans than for ECSCA images for calf veins (not significantly for thigh veins). Venous imaging signal intensity measures were higher for BPCA imaging.

CONCLUSION: Extended-phase imaging using an ECSCA with this protocol provides arteriographic image quality equal to imaging with a BPCA. Venous depiction is good using ECSCAs with this approach, although better with BPCA.

Introduction

Since the introduction of stepping table techniques for contrast-enhanced magnetic resonance angiography (CE-MRA) that allow extended field-of-view coverage from the abdominal aorta to the feet[1] this has become standard

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clinical practice for non-invasive arteriographic assessment of peripheral arterial disease (PAD) in many institutions. There have been improvements in MRI technology both hardware and software over the last decade, such as array coils, parallel imaging, and view sharing techniques, that have further improved the quality of CE-MRA.[2,3] Dynamic imaging has particularly helped overcome difficulties with "venous contamination" that previously hampered the assessment of small calibre tibial arteries in the calves, especially in patients with critical limb ischaemia (CLI) who have shortened arteriovenous transit times. As with all MRI studies there is a trade-off between temporal and spatial resolution for any given acquisition coverage. As imaging in CE-MRA relies upon a short time window during contrast medium passage through the vasculature, spatial resolution has often been compromised and lower than for the competitive non-invasive technique of CT angiography; however, there have also been developments in contrast agent properties for CE-MRA aimed at helping to improve image quality, particularly the introduction of the blood pool contrast agent (BPCA) gadofosveset trisodium.[4] This agent has also spurred the development of higher spatial resolution imaging as the compound has an increased half-life within the circulation, through reversible binding to protein (albumin).[5,6] This allows for an extended phase of imaging known as "steady state" with voxel sizes as small as 125 μm achievable.[7,8] This results in a more comprehensive evaluation for the arteries, as the examination is no longer simply a lumenogram and the vessel wall, plaque, and thrombus, etc., can be evaluated. A further benefit is that the veins are also reliably imaged, providing information such as the presence of concomitant deep venous thrombosis (DVT)[9] as well as saphenous vein calibre, branching pattern, and length, allowing assessment for potential use as venous conduits for bypass surgery.[10] This avoids the need for separate vascular laboratory duplex assessment of the great saphenous veins.

In Glasgow this comprehensive imaging method served us as a "one-stop-shop" for lower-limb vascular imaging. Unfortunately, following a period of commercial availability, the BPCA gadofosveset trisodium (originally marketed as Vasovist, Bayer Schering Pharma, Berlin, Germany, later available in North America as Ablavar, Lantheus, N. Billerica, MA, USA) is currently no longer commercially available in the European Union and this forced us to assess alternative options. Anzidei *et al.*[11,12] published a study reporting the successful use of gadobenate dimeglumine (Gd BOPTA, MultiHance, Bracco, Italy), an extracellular space contrast agent (ECSCA) with weak protein binding properties, to obtain images similar to those obtained with BPCA steady-state imaging by modifying contrast medium injection protocols for carotid and later lower-limb MRA.

Previous work[13,14] has confirmed the feasibility of performing bolus-chase multi-station lower-limb CE-MRA using "single-dose" 0.1 mmol/kg gadobenate with similar image quality to the "double-dose" 0.2 mmol/kg of other ECSCAs usually employed. This is thought to be related to the higher R1 relaxivity in human plasma that gadobenate exhibits (generally quoted 6.3–7.9 l/mmol/s at 1.5 T for human serum albumin concentrations in physiological range) compared to the other commercial agents (3.9–5.2 l/mmol/s at 1.5 T).[15] The concept of "extended-phase" high-resolution imaging with ECS contrast agents, akin to acquisitions in the steady state with BPCA, was applied to CE-MRA of the lower limbs in a pilot study.[16] The purpose of the present subsequent study was to prospectively evaluate image quality of a hybrid triple-phase lower-limb MRA protocol using dedicated BPCA (gadofosveset) versus the conventional ECSCAs gadobenate dimeglumine (MultiHance, Bracco SpA, Milan, Italy) and gadobutrol (Gadovist, Bayer Schering Pharma, Berlin, Germany) employing a comprehensive lower-limb CE-MRA technique that includes dynamic calf, three-station bolus chase, and high-resolution steady-state/extended-phase Imaging.

Materials and methods

Research ethical committee approval was obtained for this prospective randomised study. Sixty patients referred for lower-limb MRA with either claudication (n=30) or CLI (n=30) were prospectively recruited with prior informed written consent. Inclusion criteria were as follows: adult patients age 18 years or over with clinically suspected lower-limb arterial disease (either claudication or CLI) referred for CE-MRA; no contraindications to contrast-enhanced MRI; and Informed written consent to being part of this research study. Exclusion criteria were severe renal impairment (chronic kidney disease stage 4 or 5, eGFR <30 ml/min) or acute kidney injury with rising creatinine; standard safety contraindications to having a MRI examination (e.g., pacemaker dependent with MRI-incompatible device); and inability to provide informed consent to be part of the study.

Recruitment plan

CLI patients received a single scan with one of the contrast agents so that there would be no delay in their definitive management. Fifteen of the 30 critical ischaemia patients were examined with BPCA and the other 15 were randomised to receive one or other of the ECSCAs: seven with gadobenate and eight with gadobutrol.

All the patients with claudication underwent two scans with at least 5 days between appointments, but aiming to be within a 2-week period. Fifteen of these 30 patients with claudication were assigned to receive BPCA plus one or other of the two different ECSCAs on the second occasion (eight gadobenate and seven gadobutrol). The other 15 claudication patients were similarly scanned twice, once with each of the ECSCAs, the order randomised for successive patients: eight patients using gadobutrol then subsequently with gadobenate dimeglumine and seven patients vice versa.

Image acquisition and imaging parameters

The same injection and imaging protocol including scanning parameters was adopted as per a previously published pilot study.[2] All imaging was performed using a 1.5 T Siemens Avanto MRI system (Siemens Medical Solutions, Erlangen, Germany) with Tim 76 × 18 Q-engine

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