PART II: Peripheral arterial disease
Chapter 4: The utility of ce-MR angiography as a first stage diagnostic modality for treatment planning in lower extremity arterial occlusive disease

J. Bosma
A.D. Montauban van Swijndregt
A.C. Vahl
W. Wisselink
Abstract

**Objective:** The aim of this study was to evaluate the applicability of contrast enhanced magnetic resonance angiography (ce-MRA) as a first stage imaging tool for individual treatment planning in patients with lower extremity arterial occlusive disease.

**Methods:** Between August, 2003 and June, 2004, in 128 consecutive patients (182 extremities) with clinical manifestations of lower limb ischemia eligible for invasive therapy, treatment was planned based on clinical assessment, ankle/brachial pressure index measurements combined with ce-MRA. Additional duplex ultrasonography (DUS) or digital subtraction angiography (DSA) was done when necessary. Ce-MRA findings were compared with findings during open surgical, endovascular or combined procedures.

**Results:** In 28 extremities (15%) ce-MRA was found inconclusive and additional imaging was performed. In the remaining patients (85% of the extremities (n=154), treatment was initiated as planned. However, in 19 (11%) of these patients, the treatment plan was altered. In 7 of them, procedural findings did not correspond with those at the time of ce-MRA, including 6 patients (3%) with a falsely diagnosed stenosis or occlusion.

In total, 62 patients received non-operative treatment (34%), 65 an endovascular procedure (36%), 49 open surgical reconstruction (27%) and 6 a combined treatment.

**Conclusion:** We conclude that in the majority of patients treatment can be planned based on ce-MRA images, although sometimes additional DUS or DSA may be required.
Introduction

For treatment planning of invasive therapy in patients with symptomatic peripheral vascular disease the digital subtraction angiography (DSA) is considered the reference standard. However, less invasive alternatives are available, such as duplex ultrasonography (DUS) and contrast enhanced magnetic resonance angiography (ce-MRA).

To date, radiologic research in the field of ce-MRA has mainly focused on three dimensional diagnostic performance and accuracy in the detection of both hemodynamic significance and extent of arterial stenosis and occlusion. [1-7] However, ce-MRA scanning is not yet standardized and a wide range of scanning protocols and equipment have been employed. [8-12]

In recent literature comparisons have been made between ce-MRA, DUS and DSA in relation to endovascular or surgical treatment planning, indicating that ce-MRA may be an effective diagnostic alternative to DSA with better accuracy and reproducibility than DUS [13-16] Because of the three-dimensional images provided, ce-MRA may be more informative than DSA on the presence or absence of patent peripheral run-off arteries which is of importance in predicting the chances of success in bypass surgery [3,9,17] . As it appears, ce-MRA has been established as a reliable, minimally invasive method for stenosis gradation in patients with peripheral arterial occlusive disease (PAOD) [18-22]. Abundant literature exists on the diagnostic accuracy of ce-MRA, but its therapeutic impact is understudied. The purpose of this prospective cohort study was to evaluate ce-MRA, replacing the ia-DSA, as a primary diagnostic instrument for routine individual treatment planning for patients with symptomatic peripheral arterial disease.
Patients and methods

Patient selection

After permission for this study was granted by the hospital ethics board, all patients with lower extremity PAOD presenting over a nine-month period requiring invasive therapy (based on clinical grounds) were subjected to three-dimensional ce-MRA only for treatment planning. Ischemia severity was classified using the Fontaine scale (grade II- claudication, n=121 extremities; grade III- ischemic resting pain, n=32 extremities; grade IV- tissue loss: n=27 extremities, and blue toe syndrome: n=2 extremities). (Table 1) All patients were seen by the vascular surgeon for clinical assessment including a physical exam and ankle/brachial pressure index measurements prior to ce-MRA. Routine duplex ultrasonography was not performed.

<table>
<thead>
<tr>
<th>Patients</th>
<th>128</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>63 (33 – 87) years</td>
</tr>
<tr>
<td>Gender (M / F)</td>
<td>83 / 45 (65% / 35%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>37 (29%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>58 (45%)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>48 (38%)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>22 (17%)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>18 (14%)</td>
</tr>
<tr>
<td>Smoking in history</td>
<td>80 (63%)</td>
</tr>
<tr>
<td>Symptomatic extremities</td>
<td>182</td>
</tr>
<tr>
<td>Claudication (Fontaine II)</td>
<td>121 (66%)</td>
</tr>
<tr>
<td>Pain at rest (Fontaine III)</td>
<td>32 (18%)</td>
</tr>
<tr>
<td>Tissue loss (Fontaine IV)</td>
<td>27 (15%)</td>
</tr>
<tr>
<td>Blue toe (embolus)</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>

Table 1. Patient characteristics
**Image acquisition**

Imaging was conducted on a 1.5 Tesla MR system (Philips Gyroscan Intera T15-N release 8.1.1., Philips Medical Systems, Best, the Netherlands). Patients were placed in supine position and entered into the MR system feet first. The lower legs were immobilized and placed in a surface coil. Axial non-enhanced time-of-flight (TOF) views were made to plan the subsequent image volumes for the ce-MRA scan at the three stations: aortoiliacal, femoral and crural (TR (milliseconds, ms)/TE (ms) 6.9/11.6, flip angle 50 degrees, field of view (FOV) 430 x100 square millimeter (mm²), matrix 256 x 256 mm²). The acquisition of the contrast enhanced images was performed with a fast three-dimensional (3D) spoiled gradient-echo sequence (T1-FFE/M; TR=6.0; TE=1.52; flip angle=35, FOV=430 millimeter (mm), no flow compensation). Subsequently, 3D data sets were obtained at each station.

A paramagnetic contrast agent (0.4 millilitre (ml) gadolinium per kilogram (kg) bodyweight, Gadodiamine 0.5 M (Omniscan®, Nycomed) was injected per patient to enhance the intravascular signal. The body-weight-adjusted dose was diluted with 0.9% saline to a total standard scan volume of 33 ml contrast medium solution. Patients over 82.5 kg for whom the total amount of body-weight-adjusted dose exceeded 33 ml of contrast agent were also maximized to the standard scan volume of 33 ml. A single continuous bolus of contrast medium solution was administered through an 18-gauge intravenous cannula in an upper extremity antecubital vein. The first 10 ml were injected at 1.0 ml/sec, and the remaining contrast at 0.2 ml/sec. Immediately after injection of the contrast solution, 20 ml of saline was administered to flush the tubing and veins. A remote controlled MR compatible injection system (Medrad Spectris, Pittsburgh, PA, U.S.A) was used for all injections.

To minimize venous enhancement, the ce-MRA images were obtained in caudocranial direction. Synchronisation of contrast injection and scanning...
was performed using an automated bolus tracking system (BolusTrak, Philips Medical Systems, Best, the Netherlands).

**Treatment planning**

In a multidisciplinary meeting attended by vascular surgeons and interventional radiologists individual treatments were planned based on hard copy maximum intensity projection (MIP) images. The source images were available on demand. In case of any inconclusiveness, due to technical or patient related factors, additional diagnostic examinations were planned (e.g., duplex ultrasonography or ia-DSA). Follow up data were retrieved from patient charts and the hospital information system. Statistical analysis was conducted by assessing agreement between ce-MRA based treatment planning and actual treatment by calculation of the kappa-value. Values were expressed with 95% confidence intervals.

**Results**

From August, 2003 until June, 2004, 128 consecutive patients (45 female, 83 male; mean age 63 years (29-87)) with 182 symptomatic extremities were included.

In 154 extremities (85%) treatment was planned directly based on ce-MRA. In 28 (15%), additional imaging was ordered because ce-MRA images were found to be inconclusive. (Figure 1)

In 15 (8%) extremities an additional duplex scan was performed because ce-MRA images did not provide enough certainty on the stenosis gradation. Of these, three required duplex scanning because of the known presence of stents and one did not meet minimal quality standards due to movement artefacts.

In 9 extremities (5%) an additional ia-DSA was performed because the extent of the stenosis as observed with ce-MRA was doubted. In 5, DSA
confirmed the suspicions that arose from the ce-MRA studies. In three, imaging of the pedal arteries was required, and one ce-MRA was not sufficient for treatment planning due to artefacts.

In 4 extremities a second ce-MRA was performed because of movement artefacts and technical imperfections.

Figure 1. Ce-MRA and the additional imaging required for symptomatic legs.

Therapy consisted of non-invasive treatment in case of undetectable disease, discrepancy between symptoms and extend of the disease, or when the risk of treatment was assumed to be disproportionate to the expected benefit. Endovascular treatment was offered in most patients with short lesions and surgical treatment or combined surgical and endovascular therapy was considered in those with long lesions. (Figure 2)
Of all extremities included in this study 135 (74%) ultimately received the therapy predicted and/or chosen based on ce-MRA images without the use of additional diagnostic tests. Treatment as planned (including foreseen additional imaging) was performed in 157 extremities (86%; 95% CI 80-90). In 19 extremities the ce-MRA based plan had to be altered. In the majority of these cases this was not related to ce-MRA performance but to other factors (spontaneous clinical improvement, progression of disease, worsened general condition or patient’s preference towards non-operative therapy). (Table 2) In 6 extremities (3%; 95% CI 0.5-5) ce-MRA identified lesions ultimately showed to be false positives that could not be reproduced during the angioplasty procedure. Six patients were lost to follow-up. The agreement between ce-MRA based treatment plans and the subsequently performed procedures or therapies was found to be 89% (157/176), with a kappa value of 0.74. Exclusion of the cases in which the
treatment plan was changed because of the patient’s preference results in an agreement of 95% (157/164).

<table>
<thead>
<tr>
<th>Plan</th>
<th>Treatment</th>
<th>Reason</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-invasive</td>
<td>Femorocrural bypass</td>
<td>Progressive ischemia</td>
<td>2</td>
</tr>
<tr>
<td>Non-invasive</td>
<td>PTA SFA L + stent</td>
<td>Progressive ischemia</td>
<td>1</td>
</tr>
<tr>
<td>Aortobifemoral bypass</td>
<td>Non-invasive</td>
<td>Poor patient’s condition</td>
<td>2</td>
</tr>
<tr>
<td>Single femoro-poplite bypass</td>
<td>Non-invasive</td>
<td>Spontaneous improvement</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral femoro-poplite bypass</td>
<td>Non-invasive</td>
<td>No surgery on patients’ demand</td>
<td>2</td>
</tr>
<tr>
<td>PTA SFA</td>
<td>Non-invasive</td>
<td>Non-significant stenosis at angiography</td>
<td>2</td>
</tr>
<tr>
<td>PTA CIA</td>
<td>Non-invasive</td>
<td>Non-significant stenosis at angiography</td>
<td>3</td>
</tr>
<tr>
<td>PTA ATA</td>
<td>Non-invasive</td>
<td>No intervention on patients’ demand</td>
<td>1</td>
</tr>
<tr>
<td>PTA EIA</td>
<td>Non-invasive</td>
<td>No occlusion found at angiography (spontaneously resolved thrombus?)</td>
<td>1</td>
</tr>
<tr>
<td>PTA CIA</td>
<td>Non-invasive</td>
<td>Stent artefact at ce-MRA: no occlusion at angiography</td>
<td>1</td>
</tr>
<tr>
<td>PTA EIA</td>
<td>Non-invasive</td>
<td>Occlusion; failed attempt at PTA</td>
<td>1</td>
</tr>
<tr>
<td>PTA SFA</td>
<td>Surgery</td>
<td>PTA SFA technical failure, therefore femoropopliteal bypass</td>
<td>2</td>
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</tbody>
</table>

Table 2. Description of the discrepancies in treatment plan and final treatment (n=19). CIA: common iliac artery; EIA: external iliac artery; SFA: superficial femoral artery; ATA: anterior tibial artery.

Discussion

This prospective cohort study indicates that ce-MRA plays an increasingly important role in initial treatment planning in the majority of patients with lower extremity PAOD. In the majority an adequate treatment plan can be planned, solely based on MRA. However, additional studies are sometimes required. In a minority of patients the severity of the disease is underestimated, were as in others false positive findings occur. Nevertheless, treatment as planned was carried out in the majority of our patients, and an agreement between ce-MRA based treatment plans and
the subsequently performed procedures or therapies of up to 95% was found. The use of ce-MRA does not appear to negatively influence the ultimate clinical outcome in patients with lower extremity PAOD. In addition to this study we conducted a randomised diagnostic trial investigating the diagnostic performance of ce-MRA compared to ia-DSA, which was routinely used prior to this current study. Ce-MRA and ia-DSA proved to be equal. [21]

False negative findings in patients in whom surgery is planned may result in more extensive procedures than anticipated. However, this problem is not strictly limited to ce-MRA based treatments and may also occur in patients that had their treatment planned with DSA. Calcifications can be more extensive than imaging suggests. False positive findings resulted in 6 needless attempts at angioplasty.

One of the main problems encountered in ce-MRA based treatment planning is related to stenosis gradation. Anything less than a complete flow void should not be interpreted as a significant stenosis. The reading of ce-MRA MIP-images is occasionally influenced by in-plane saturation and can result in an overestimation of the actual stenosis. In some cases this results in uncertainty regarding the severity of the stenosis. Studying the source images, however, usually reveals the actual stenosis gradation.

A total of 6 (3%) false positive stenoses was observed, resulting in a change of strategy during the PTA procedure. In 3 patients, the severity of the stenosis or occlusion was underestimated. This is partly due to the fact that ce-MRA provides no information on the degree of plaque calcification and morphology, leading to failure of percutaneous revascularisation attempts in these patients. The operating efficiency of ce-MRA is also limited by intra-luminal stents and movement artefacts (e.g., due to resting pain).

Many different protocols and equipment for ce-MRA imaging are available, all delivering a high diagnostic performance. As previous reports have shown, it is more effective to customize scan protocols and equipment for a specific arterial territory of interest, than to use a standardized protocol for all vascular territories. [8,17,23]
In our study, approximately one-third of extremities subjected to ce-MRA did not have any subsequent invasive therapy. This includes patients lacking possibilities for arterial reconstruction and patients refusing invasive treatment. In other cases we expected to find a lesion suitable for minimally invasive treatment that turned out to require more extensive surgery instead. In some of these cases, it was concluded that symptoms were disproportional to the intervention needed to achieve any symptom relief (for example, an infragenual bypass procedure for mild claudication), thus leading to the decision to continue conservative therapy. Poor general health was also a reason to decline more extensive surgery in some. Ce-MRA can be considered a minimally invasive technique with little complications (e.g., false aneurysms, hematomas). Besides the well-documented contraindications for ce-MRA such as claustrophobia, the presence of a cardiac pacemaker and ferromagnetic intracranial clips, relatively new contraindications have gained interest. These include the possible initiation nephrogenic systemic fibrosis resulting from the administration of Gadolineum-containing contrast material in patients suffering from renal failure. [24, 25]

Although the limitations of ce-MRA in treatment planning are clear, it has proven to be a helpful tool in treatment planning in patients with PAOD. In contrast with duplex ultrasonography, the three-dimensional ce-MRA images are easy to interpret, highly reproducible and their quality operator independent. Complications such as hematomas and false aneurysms as seen in DSA do not occur. Routine use of ce-MRA, as new diagnostic standard instead of ia-DSA, does not seem to negatively influence the clinical outcome in patients with PAOD. Customized scanning protocols and equipment fitted for specific regions of interest allow us to omit the more patient-aggravating DSA in a significant and increasing number of patients requiring invasive therapy.
References

12. Bilecen D, Jager KA, Aschwanden M, Heidecker HG, Schulte AC, Bongartz G. Cuff-compression of the proximal calf to reduce venous


