Gadolinium-enhanced Magnetic Resonance Angiography, Colour Duplex and Digital Subtraction Angiography of the Lower Limb Arteries from the Aorta to the Tibio-peroneal Trunk in Patients with Intermittent Claudication

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Objectives. To evaluate the sensitivity, specificity, positive and negative predictive value of contrast-enhanced (gadolinium) magnetic resonance imaging (CE-MRA) and colour duplex ultrasound (CDU) of lower limb arteries.

Design. Prospective, single centre study.

Material and methods. A consecutive series of 58 patients with intermittent claudication (IC) were examined with CE-MRA and CDU from the infrarenal aorta to the tibio-peroneal trunk with digital subtraction angiography (DSA) as reference. The arterial tree was divided into 15 segments, pooled into three regions; suprainguinal, thigh and knee. Sensitivity, specificity, positive and negative predictive values for significant obstructions were calculated. Cohen Kappa statistics was used to establish agreement between the three methods.

Results. The sensitivity (specificity in parentheses) for significant obstructions in the suprainguinal region were 96% (94%) for CE-MRA and 91% (96%) for CDU, in the thigh region 92% (95%) for CE-MRA and 76% (99%) for CDU, and in the knee region 93% (96%) for CE-MRA and 33% (98%) for CDU. CDU failed to visualize 10% of suprainguinal, 2% of thigh and 13% of knee-region arterial segments.

Conclusions. Both CE-MRA and CDU are good alternatives to DSA in the suprainguinal- and thigh-region. In the knee region only CE-MRA can be relied upon as an alternative to DSA. Imaging by CDU is not suited to situations were evaluation of runoff vessels is important.

Keywords: DSA; MRA; Colour duplex ultrasound; Lower limb arteries.

Introduction

Digital subtraction angiography (DSA) has routinely been used for imaging of the aorta and the arteries of the lower limb. Alternative methods are colour duplex ultrasound (CDU), magnetic resonance angiography (MRA) and CT angiography (CTA). Generally, DSA is still regarded as the gold standard. MRA and CDU do not require exposure to ionizing radiation and arterial catheterization and are often preferred initially. Different MRA techniques have been developed, contrast enhanced MRA being the most promising for evaluation of lower limb arteries.1,2

CDU has a high accuracy in the detection of arterial stenoses and occlusions.3–5 However, direct visualization of the iliac or distal femoral arteries may not be possible due to reflections by bowel gas and tissue absorption, respectively, although significant proximal obstruction or occlusion in most cases are discovered by the downstream Doppler spectrum. Furthermore, CDU is operator dependent. A variety of MRA techniques are available based on inflow (time of flight),6,7 phase shifts caused by flowing blood (phase-contrast MRA)8,9 and gadolinium contrast enhanced MRA (CE-MRA).10–13 Few studies have directly compared CDU, MRA and DSA in the evaluation of native pelvic and lower limb arteries of patients with intermittent claudication (IC).14–17 In the two studies using CE-MRA,16,17 a total of 69 (3916 + 3017) patients were included, 54 (3416 + 2017) of whom had IC. However, in both studies only aortoiliac segments were examined.
The aim of the present study was to compare the accuracy of CDU and CE-MRA, using DSA as the reference standard in the evaluation of arterial disease in patients with IC. In the comparison, aortoiliac-, femoropopliteal- and the tibio-peroneal trunk arteries were studied.

Materials and Methods

Patients

During a 12-month period, a consecutive series of patients with IC (Fontaine stage IIa/IIb) referred from the Department of Vascular Surgery for angiography of the lower extremities were included. Fifty-eight patients, 36 men and 22 women, with a median age of 66.5 years (47–80), with no previous vascular or endovascular treatment were included. None of these patients had any contraindication to MRA. Concurrent illnesses are given in Table 1. Written informed consent was obtained and the study was approved by the regional ethical committee.

Gadolinium-enhanced MRA

All patients were examined using a 1.5-T scanner (Siemens Magnetom Symphony) with automatic table translation. Three coil systems were used: bodyarray coil and spinearray coil which covered the lower abdomen and the pelvis, and the dedicated peripheral angio array coil (Siemens). Patients were examined in a supine position. The knees and ankles were raised on foam cushions. A fatsaturated T1-Flash sequence was used (pelvis: 3.8 ms/1.4 ms/25°, thigh: 3.8 ms/1.4 ms/25°, lower leg: 4.4 ms/1.5 ms/25°). The main sequence used a coronal slab from 9 to 12 cm. The examination was performed in three steps: lower abdomen/pelvis, thighs and lower legs, including a plain and a contrast-enhanced data set. The contrast agent (Magnevist 469 mg/ml, Schering, Berlin) was injected in the following way: first 14 ml, at 2.5 ml/s, was given immediately followed by 23 ml, at 0.3 ml/s. Finally, 20 ml saline was infused to ensure deployment of all contrast agent. The main sequence was started manually when the contrast medium reached the upper abdominal aorta. From this point on the examination was pre-programmed.

After image reconstruction, the unenhanced data were subtracted from the corresponding enhanced data algorithm. An experienced vascular radiologist reviewed both maximum intensity projection (MIP) and source images with multiplanar reformating (MPR) for interpretation.

Digital subtraction angiography (DSA)

DSA was performed by three angiographers with more than 15 years of experience using a Siemens Multistar TOP single-planar X-ray unit. Puncture was made in the common femoral artery. Contrast was injected in the distal aorta with a 4-French side-hole catheter. At the discretion of the angiographer, supplementary injections were made in the ipsilateral or contralateral external iliac artery using a 5-French end-hole catheter. Images of the pelvic arteries including the lower abdominal aorta were obtained in the frontal and two 25° oblique projections. Images of the thighs and lower legs in both extremities were obtained in the frontal projection. Supplementary projections were made at the discretion of the angiographer to cover all arterial segments. For visualization of the complete arterial tree, an average of 105 ml contrast agent (Visipaque 270 mg/ml, Amersham Health, Oslo, Norway) was necessary.

Colour duplex ultrasound (CDU)

All patients were scanned by the same experienced sonographer, using a GE Vingmed System V ultrasound colour duplex scanner with a 5 MHz linear transducer. The diagnosis was based on colour duplex, power mode (intensity) Doppler, and ultrasound Doppler velocity findings. A stenosis was defined as significant (≥50% diameter reduction) when there was a 100% rise in the Doppler peak velocity of the jet as compared to velocities in a normal adjacent proximal or distal segment. An arterial segment was defined as occluded when colour flow, power mode Doppler and Doppler velocity signals were absent. Both extremities were examined. In patients where aortoiliac segments could not be visualized, the diagnosis of major arterial obstruction, either
significant stenosis or occlusion, was based on the finding of a monophasic Doppler signal in the respective common femoral artery.18,19

Evaluation

The CE-MRA, CDU and DSA examinations were interpreted by one observer for each modality, blinded to the findings by the other modalities. The arterial tree was divided into 15 segments; the infrarenal abdominal aorta, right and left common iliac (CIA), external iliac (EIA), common femoral (CFA), deep femoral (DFA), superficial femoral (SFA), popliteal (PA) and tibio-peroneal trunk arteries (TPT) (Fig. 1). Thus, a total of 870 segments were examined. Each segment was graded into three groups according to the most pronounced lesion: (1) normal or mildly stenosed (0–49% diameter reduction), (2) severely stenosed (50–99% diameter reduction) or (3) occluded. The grade was compared segment by segment for each patient for all three modalities. Segments were pooled into three regions: (1) The suprarenal region, containing infrarenal aorta, CIA and EIA. (2) The thigh region, containing CFA, DFA and SFA. (3) The knee region, containing PA and TPT arteries.

Vascular segments that CDU failed to visualize and, therefore, could not give any score were discarded from the calculation of sensitivity, specificity, positive and negative predictive values. For CE-MRA and DSA the closest normal vessel was used as a reference for calculating the diameter reduction at the site of the stenosis. In two cases (one for DSA and one for CE-MRA) where no normal nearby vessel could be identified, the contralateral vessel was used as a reference.

Total examination times for all three modalities were approximately 45 min.

Statistical analysis

The aim of this study was to evaluate the concordance between the two diagnostic methods CE-MRA and CDU in the evaluation of arterial disease, as compared to what is still considered the golden standard, DSA. For this purpose a dichotomous classification was used. Negative findings consisted of vessels that were normal or mildly stenosed. Vessels with severe stenoses (50–99% diameter reduction) or occlusions were considered positive findings.

The sensitivity, specificity, positive and negative predictive values of the method were estimated.20 The Cohen Kappa statistics was used to establish agreement between the three methods. There was no interobserver variation in each technique as there was one observer for each modality.

Kappa coefficient between 0.81 and 1.0 indicate a perfect concordance, 0.61–0.80 very high concordance, 0.41–0.60 moderate concordance, and a coefficient between 0.21 and 0.40 only fair agreement. The Kappa was presented with its 95% confidence limits. Also, a power analysis was performed to estimate the sample size required to determine whether Kappa of a given magnitude is significantly higher than 0.4 (fair or good agreement) or 0.6 (good agreement). This was done according to the method of Donner and Eliasziw.21

Fig. 1. Schematic outline of the lower extremity arteries studied. AA, distal abdominal aorta; CIA, common iliac artery; EIA, external iliac artery; CFA, common femoral artery; DFA, deep femoral artery; SFA, superficial femoral artery; PA, popliteal artery and TPT, tibio-peroneal trunk arteries.
Results

Significant obstructions in the population

A total of 870 vascular segments were examined. The findings at DSA are summarized in Table 2.

CE-MRA and CDU compared to DSA

The grading of all segments with CE-MRA and CDU compared to DSA are summarized in Table 3. CE-MRA has a higher sensitivity and a somewhat lower positive predictive value in detecting significant obstructions than CDU when all segments are pooled. Table 4 summarizes the gradings of CE-MRA and CDU compared to DSA for the pooled regions.

The superficial femoral artery was the segment with most occlusions (Table 2). The accuracy of CE-MRA and CDU in detecting occlusions in this segment is summarized in Table 5. Length estimates of these occlusions are given in Table 6. Both CE-MRA and CDU have a tendency for overestimating the length of an occlusion.

All 870 vascular segments were successfully visualized with CE-MRA. In some patients CDU failed to visualize one or more vascular segments. This was the case in 10% of the segments in the suprainguinal region, in 2% in the thigh region and in 13% in the knee region.

Taking into consideration the power methods underlined in the statistics section, an acceptable power was found for all three pooled regions of CE-MRA (suprainguinal, thigh and knee region) and for CDU in the thigh region. CE-MRA had a higher sensitivity in detecting significant lesions than CDU in all arterial segments.

When dividing the arterial tree into the three regions, suprainguinal, thigh and knee region we observed large differences in the ability of CDU in detecting significant obstructions. This was reflected by sensitivities varying from 91% (suprainguinal) to 33% (knee). The sensitivity at knee level is considerably lower than previously reported. This finding may relate to poor site localisation for CDU. In contrast to the studies of Wikström et al. and Lundin et al. which evaluated CDU and MRA in the pelvic region, we found a higher sensitivity for CDU, 91%, as compared to 72% in both the other studies.

CE-MRA has a high sensitivity and specificity in detecting significant obstructions in all regions of the examined arterial tree. Based on the finding of a low positive predictive value, a tendency for overestimation of stenoses by CE-MRA when using DSA as reference was noted. This tendency is also suggested by other studies. This was most pronounced in the suprainguinal region with a positive predictive value as low as 64%. CDU overestimated stenoses in the suprainguinal region to the same extent with a positive predictive value of 67%. The depth and angles at which iliac vessels run make this segment difficult to insonate. The angles also affect CE-MRA because the voxels used are non-isotropic. Gas-filled overlying

Table 2. Significant stenoses (≥ 50% diameter reduction) and occlusions at DSA, based on 870 evaluated segments

<table>
<thead>
<tr>
<th>Segments</th>
<th>Stenosis (≥50%)</th>
<th>Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Common iliac artery</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>External iliac artery</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Common femoral artery</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Deep femoral artery</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Superficial femoral artery</td>
<td>18</td>
<td>34</td>
</tr>
<tr>
<td>Popliteal artery</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Tibio-peroneal trunk artery</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 3. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and kappa value (κ), with 95% confidence intervals for CE-MRA and CDU in detecting significant stenoses and occlusions, all segments pooled, with DSA as reference

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV</th>
<th>NPV</th>
<th>κ</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE-MRA</td>
<td>94 (89–98)</td>
<td>95 (93–97)</td>
<td>76 (69–83)</td>
<td>99 (98–100)</td>
<td>0.81 (0.74–0.87)</td>
<td></td>
</tr>
<tr>
<td>CDU</td>
<td>70 (61–78)</td>
<td>98 (96–99)</td>
<td>82 (74–90)</td>
<td>95 (94–97)</td>
<td>0.72 (0.65–0.79)</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Patients with intermittent claudication constitute a large and demanding group with a chronic disease. Many of these patients may later need visualization of their arteries to determine the appropriate treatment, which requires correct identification of the site and extent of stenoses or occlusions. DSA, CDU and MRA can all provide this kind of information.

Both MRA and CDU have a major advantage of being non-invasive. DSA is still regarded as the gold standard but many vascular departments now use non-invasive methods to plan treatment, and use DSA only when in doubt after CDU or MRA. CE-MRA had a higher sensitivity in detecting significant lesions than CDU in all arterial segments. When dividing the arterial tree into the three regions, suprainguinal, thigh and knee region we observed large differences in the ability of CDU in detecting significant obstructions. This was reflected by sensitivities varying from 91% (suprainguinal) to 33% (knee). The sensitivity at knee level is considerably lower than previously reported. This finding may relate to poor site localisation for CDU. In contrast to the studies of Wikström et al. and Lundin et al., which evaluated CDU and MRA in the pelvic region, we found a higher sensitivity for CDU, 91%, as compared to 72% in both the other studies.

CE-MRA has a high sensitivity and specificity in detecting significant obstructions in all regions of the examined arterial tree. Based on the finding of a low positive predictive value, a tendency for overestimation of stenoses by CE-MRA when using DSA as reference was noted. This tendency is also suggested by other studies. This was most pronounced in the suprainguinal region with a positive predictive value as low as 64%. CDU overestimated stenoses in the suprainguinal region to the same extent with a positive predictive value of 67%. The depth and angles at which iliac vessels run make this segment difficult to insonate. The angles also affect CE-MRA because the voxels used are non-isotropic. Gas-filled overlying
bowel loops sometimes reduce the visualization of the complete arterial segment, when using CDU. Poor visualization in the suprainguinal arteries is, however, often compensated by studying the downstream Doppler signal (signal damping, change in velocity contour, spectral broadening and pulsatility index).\(^{18,19}\)

A tendency of overestimation by CDU and MRA in detecting significant obstructions could potentially be explained by an underestimation of degree of stenoses by DSA. As discussed by Wikström et al.\(^{17}\) intrarterial pressure measurements provide a more correct assessment of arterial stenoses, and hence might have been a better reference. However, the technique is impractical and time-consuming when large anatomic areas are to be evaluated. On the other hand both CDU and CE-MRA have excellent negative predictive values, 99 and 100%, respectively, in the suprainguinal region. This has great clinical impact when using these imaging modalities for screening.

In the thigh region CDU had an excellent positive predictive value of 94% as compared to 80% for CE-MRA. The cause of overestimation with CE-MRA is not fully understood. Suboptimal image subtraction due to patient movement, limited spatial resolution and dephasing from complex- or high-velocity flow can to some extent explain this phenomenon.

Occlusions in the thigh region are very well evaluated by both CE-MRA and CDU with positive- and negative-predictive values of more than 97%. In this case no invasive diagnostic procedure is needed.

The recent developments in multidetector CT (MDCT) has revolutionized CT angiography (CTA). A few studies have been published comparing CTA with DSA of the lower limb arteries in patients with symptomatic peripheral arterial disease showing promising results.\(^{24}\) A disadvantage of CTA of lower limb arteries is the use of high radiation doses although substantial efforts are made to reduce exposure. As with DSA, CTA also requires potentially nephrotoxic contrast agents. In the present study, CTA was not included because such a CT scanner was not available at our institution when the study was planned.

Calcified plaques may reduce ultrasound penetration and hence obscure underlying anatomic details and flow information (acoustic shadowing). This is especially important in deeply located vessels, where ultrasound attenuation may present a challenge. Ultrasound contrast may be applied to reduce or overcome this problem.\(^{25,26}\) Based on our own experience we believe that ultrasound contrast enhancement would improve CDU accuracy, especially in the distal examinations. However, this option was not included in the study protocol.

In conclusion, we have shown that both CE-MRA and CDU are good alternatives to DSA in the suprainguinal and thigh region, but the tendency of overestimation should be noted. In the knee region CE-MRA is a reliable method, whereas CDU is not. In situations were evaluation of runoff vessels are important for the choice of treatment, CDU is not an appropriate imaging modality.

### Table 4. Sensitivity (Sens.), specificity (Spec.), positive predictive value (PPV), negative predictive value (NPV), and kappa value ($\kappa$), with 95% confidence intervals for CE-MRA and CDU in the different segments regarding significant stenoses and occlusions, with DSA as reference

<table>
<thead>
<tr>
<th>Regions</th>
<th>Sens. (%)</th>
<th>Spec. (%)</th>
<th>PPV</th>
<th>NPV</th>
<th>$\kappa$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suprainguinal: Aorta + CIA + EIA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CE-MRA</td>
<td>96 (90–100)</td>
<td>94 (91–97)</td>
<td>64 (50–79)</td>
<td>100 (99–100)</td>
<td>0.74 (0.63–0.85)</td>
</tr>
<tr>
<td>CDU</td>
<td>91 (79–100)</td>
<td>96 (93–98)</td>
<td>67 (50–83)</td>
<td>99 (98–100)</td>
<td>0.74 (0.62–0.86)</td>
</tr>
<tr>
<td>Thigh: CFA + DFA + SFA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CE-MRA</td>
<td>92 (86–99)</td>
<td>95 (92–97)</td>
<td>80 (71–89)</td>
<td>98 (97–100)</td>
<td>0.82 (0.72–0.93)</td>
</tr>
<tr>
<td>CDU</td>
<td>76 (66–87)</td>
<td>99 (98–100)</td>
<td>94 (88–100)</td>
<td>95 (92–97)</td>
<td>0.81 (0.71–0.92)</td>
</tr>
<tr>
<td>Knee: PA + TPT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CE-MRA</td>
<td>93 (84–100)</td>
<td>96 (94–99)</td>
<td>80 (67–93)</td>
<td>99 (97–100)</td>
<td>0.84 (0.71–0.97)</td>
</tr>
<tr>
<td>CDU</td>
<td>33 (14–52)</td>
<td>98 (96–100)</td>
<td>67 (40–93)</td>
<td>91 (87–95)</td>
<td>0.40 (0.27–0.52)</td>
</tr>
</tbody>
</table>

Common iliac artery (CIA), external iliac artery (EIA), common femoral artery (CFA), deep femoral artery (DFA), superficial femoral artery (SFA), popliteal artery (PA) and tibio-peroneal trunk arteries (TPT).

### Table 5. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and kappa value ($\kappa$), with 95% confidence intervals for CE-MRA and CDU, in detecting occlusions in the superficial femoral artery, with DSA as reference

<table>
<thead>
<tr>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV</th>
<th>NPV</th>
<th>$\kappa$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE-MRA</td>
<td>97 (91–100)</td>
<td>99 (96–100)</td>
<td>97 (91–100)</td>
<td>99 (96–100)</td>
</tr>
<tr>
<td>CDU</td>
<td>94 (86–100)</td>
<td>100 (100–100)</td>
<td>100 (100–100)</td>
<td>98 (94–100)</td>
</tr>
</tbody>
</table>
Table 6. Length of occlusions in the superficial femoral artery for CE-MRA and CDU with DSA as a reference. Within 2 cm from the length measured at DSA is considered correct.

<table>
<thead>
<tr>
<th></th>
<th>Too short (%)</th>
<th>Correct (%)</th>
<th>Too long (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CE-MRA</td>
<td>9</td>
<td>70</td>
<td>21</td>
</tr>
<tr>
<td>CDU</td>
<td>7</td>
<td>65</td>
<td>28</td>
</tr>
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</table>

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References


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