Non invasive assessment of renal artery using dual MRA techniques compared with invasive renal angiography in cases of renovascular hypertension


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**KEYWORDS**
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**Abstract**  **Introduction:** Renal artery stenosis (RAS) is one of the leading causes of secondary hypertension, and can result in refractory hypertension or ischemic renal failure. RAS is present in 0.5–5% of all hypertensive patients. It became even more important to diagnose it in the time of intervention. Direct Angiography is the Gold Standard for evaluation of renal artery stenosis and severity. It cannot be used as a screening test because of its invasiveness, high cost and use of nephrotoxic gents. Different non invasive techniques have evolved for the evaluation of renal artery including; captopril renography, computed tomography (CT) angiography, magnetic resonance (MR) angiography and ultrasound (US) Doppler. Recently, the advent of CE 3D MRA appears to be a new promising approach.

**Purpose:** To evaluate the diagnostic value of both contrast enhanced magnetic resonance angiography (CE MRA) and phase contrast MRA (PC MRA) techniques in cases of renal artery stenosis as compared to conventional angiography.

**Methods and materials:** Thirty patients (22 males and 8 females), with mean age 37 years (range 23–72 years). All with suspected renal artery stenosis were evaluated using both CE MRA and PC MRA techniques. All were subsequently subjected to conventional renal angiography.
Results: CE MRA alone compared to direct Angiography (Gold standard) had a 91% sensitivity and 87% specificity. PC MRA had overall 50% sensitivity and 25% specificity. PC MRA alone was unable to differentiate mild stenosis from normal and could not distinguish severe stenosis from total occlusion. Combining both MRA techniques yielded 100% specificity 94% positive and 100% negative predictive values.

Conclusion: The combined approach of non-invasive CE MRA and PC MRA techniques achieves a very high specificity, PPV and NPV for the detection of renal arterial pathomorphologic features as compared to standard renal angiography. Adding PC MRA to CE MRA helps to differentiate between mild and moderate stenoses as well as moderate and severe arterial stenotic lesions. So, CE MRA is a morphological test while PC MRA helps in grading the arterial stenoses.

1. Introduction

The incidence of RAS is about 0.1% in the general population, 4.0% in a hypertensive population, and 10–20% in individuals with hypertension and CAD.1–4 For patients with peripheral vascular disease, the prevalence of atherosclerotic RAS has been estimated to be 30–50% in most studies.5 Overall, ischemic nephropathy may be responsible for 5–22% of advanced renal disease in patients older than 50 years.

There has been considerable debate regarding the value of routine renal arteriography at the time of coronary arteriography. In the largest series of patients undergoing such screening, 1235 unselected, consecutive patients had both coronary arteriography and abdominal aortography.3 Thirty percent of patients had some evidence of atherosclerotic RAS and 15% had lesions with ≥50% diameter stenosis.

2. Material and methods

Patients with either abrupt onset of severe hypertension or any degree of hypertension under the age of 25 or above 50 years were usually scanned for the possible presence of renal artery stenosis as a cause of secondary hypertension. Only cases subjected to direct renal angiography were subjected to complementary MRA studies. Those with suspected lesion with initial MRA were subsequently subjected to direct angiography. A total of 30 patients were included who had the two modalities done.

All patients were subjected to the following:

* Full history taking, including onset and duration of hypertension and drug intake. History suggestive of complication (cerebrovascular, cardiac, peripheral, vascular, and renal) and family history of hypertension.
* Complete clinical examination, including measurement of blood pressure at three different occasions, measurement of blood pressure in the lower limb, signs of endocrinial diseases, fundus examination, cardiac size, auscultation over the aortic area and auscultation of renal angles.
* ECG: for left axis deviation, left atrial or ventricular enlargement, strain pattern and ischemic changes.
* Laboratory investigations including:
  * Blood urea nitrogen and creatinine.
  * Na and K blood levels.
  * 24-h urinary catecholamines.
  * 24-h urinary cortisol.
  * Complete urine analysis.

Any patient with any of the following exclusion criteria was excluded from the study:

* Detection of any endocrinial cause of secondary hypertension such as: pheochromocytoma, Conn’s disease, Cushing syndrome or acromegaly.
* Pregnancy.
* Creatinine level > 1.5 mg/dl.

Thirty patients; 22 males and 8 females, their ages ranging from 23 to 72 years, with suspected renal artery stenosis were evaluated by both contrast enhanced magnetic resonant angiography (CE MRA) with 3D MIP reconstruction. Phase contrast magnetic resonant angiography (PC MRA) techniques. Nineteen patients had subsequent conventional angiography (CA), while one patient with known history of severe allergy to iodinated contrast media, was examined by duplex ultrasonography of the renal arteries. Patients were examined by a superconducting 1.5 Tesla magnet (Magneton expert).

An anteroposterior phased array surface coil was used for signal reception in conjunction with standard receivers. The coil was placed to cover the expected volume containing the renal arteries and the abdominal aorta.

To prevent aliasing, patients were imaged with their arms placed on cushions that elevated them above the abdomen. Following sagittal localizer ORE sequence, a bolus of contrast medium, gadolinium DTPA is injected via a 20-gauge needle placed in the antecubital fossa. A dose of 0.2 mmol/kg body weight was injected by an automatic injector. In our study, the time delay is empirically determined on basis of the patient’s age and the cardiovascular status. Typically, a delay of 10 s between the start of injection and the start of imaging works in the majority of patients when the scan time is 16 s.

We used SPGR T1 weighted sequence for scanning the region of interest twice.

The parameters used are:
This will be followed by axial 3D phase contrast MRA of the renal arteries.

The parameters used are:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR</td>
<td>94 ms.</td>
</tr>
<tr>
<td>TE</td>
<td>11 ms.</td>
</tr>
<tr>
<td>Flip angle</td>
<td>12°</td>
</tr>
<tr>
<td>Slab thickness</td>
<td>48</td>
</tr>
<tr>
<td>Velocity encoding</td>
<td>50 cm/s (30 cm/s in cases with heart or renal failure)</td>
</tr>
<tr>
<td>Partitions</td>
<td>24</td>
</tr>
<tr>
<td>Matrix</td>
<td>160 × 256</td>
</tr>
<tr>
<td>FOV</td>
<td>300</td>
</tr>
<tr>
<td>No. of acquisitions</td>
<td>1</td>
</tr>
<tr>
<td>Scan time</td>
<td>3.34 min</td>
</tr>
</tbody>
</table>

Post processing was done after the techniques using maximal intensity projection (MIP).

3. Results

Thirty patients, 22 males and 8 females, were included in the study. Four patients were below the age of 25 years (mean 21.5 years), 12 patients were above the age of 50 years (mean 62.8 years), and 14 patients were between 30 and 50 years (mean 43.1 years). Their clinical and laboratory data are illustrated in the Table 1.

Notes:

- One case with moderate stenosis was overestimated as severe one by CE MRA due to improper window setting.
- One case with mild renal arterial stenosis was overlooked by CEMRA due to overlapping renal vein.

Thirty patients (60 renal arteries) were evaluated by both MRA techniques (contrast enhanced MRA and 3D phase contrast).

Twenty-nine patients had undergone conventional angiography as Gold standard technique. One patient was examined by Doppler ultrasonography due to known history of severe allergy to iodinated contrast medium.

Table 2 demonstrates the CE MRA findings in cases suspected clinically to have renal arterial stenosis, with reference to conventional renal angiography.

There were five patients with severe arterial stenosis (>75% narrowing) detected. One case was evaluated as severe stenosis traced on CE MRA, yet the corresponding CA showed it as a moderate one. This error was attributed to imaging at narrow window setting.

So, four cases graded as moderate stenosis based on CE MRA, out of five moderate stenosis with reference to Gold standard technique (CA).

Eight cases out of nine were graded as mild stenosis when CE MRA results were compared with CA. One case with mild ostial stenosis was overlooked due to overlapping by the ipsilateral renal vein (mild delay in acquisition after contrast administration).

One normal case was detected in both CE MRA and CA (kidney donor with incidentally detected hypertension).

Table 3 correlates the phase contrast (PC) findings with reference to CA. The 5 patients with moderate stenosis on basis of CA showed mild narrowing on PC. While the nine patients with mild stenosis appeared normal on PC MRA images.

The seven patients with severe stenosis on basis of CA, showed total occlusion in PC MRA images denoting marked spine dephasing.

3.1. Comparing the CE MRA with the PC MRA findings

The 14 patients with normal or mildly stenosed renal arteries based on CE MRA showed normal appearances on PC MRA.

Eight patients were evaluated as having moderate stenosis by PC MRA, while six patients showed evidence of moderate...
stenosis by CE MRA (one patient was overestimated due to improper window setting).

Out of nine patients with severe stenosis on basis of CE MRA, only seven patients showed total occlusion by PC MRA (the severe stenosis caused marked spine, dephasing on PC MRA).

The last case with history of severe allergy to contrast medium was evaluated by Doppler ultrasound and well compared with CE MRA and PC MRA diagnoses as moderate stenosis.

The results of CE MRA alone when compared with CA (Gold Standard) were 95% sensitivity and 90% specificity, while the results of PC MRA were 50% sensitivity and 25% specificity. However, it was 100% sensitivity and specificity in cases of moderate stenosis. (The PC MRA can not differentiate between mild stenosis and normal arteries, nor distinguish between severe stenosis from total occlusion). If results of both CE MRA and PC MRA are combined together, for each patient, the sensitivity and specificity will be almost 100%.

Figs. 1 and 2 show two examples of our cases showing how the two MRA techniques are complementary to each other.

3.2. Case 1

In Case 1 (Fig. 1A and B) contrast enhanced MRA showed severe proximal focal left renal arterial stenosis which was confirmed by phase contrast technique.

3.3. Case 2

While in case 2 the lesion which was seen as severe narrowing by Contrast Enhanced technique was found to be of moderate severity on using the Phase Contrast technique as seen in Fig. 2A and B.

4. Discussion

A specific cause of hypertension can be established in only 10–15% of cases. However, the patients should not be ignored, since correction of these causes may cure their hypertension. Hypertension is both a cause and a consequence of renal disease, and irrespective of etiology, hypertension is a major determinant of renal disease progression. Primary renal parenchymal disease has been observed to be responsible for

<table>
<thead>
<tr>
<th>Grade</th>
<th>Gr by direct angio</th>
<th>By CE MRA</th>
<th>By PC MRA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2 normal and 2 from the mild group (venous contamination hindering proper assessment)</td>
</tr>
<tr>
<td>Mild</td>
<td>12</td>
<td>10</td>
<td>All from mild and 2 categorized in normal</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>8</td>
<td>6</td>
<td>2 were dropped as they were estimated as severe due to motion artifact</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>7</td>
<td>9</td>
<td>7 already severe with another 2 moderate estimated as severe due to motion artifact</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 CE MRA findings of our patients compared to direct CA.

<table>
<thead>
<tr>
<th>Grade</th>
<th>By direct angio</th>
<th>By PC MRA</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>2</td>
<td>14</td>
<td>2 normal + 12 mild seen normal</td>
</tr>
<tr>
<td>Mild</td>
<td>12</td>
<td>0</td>
<td>All cases of mild lesion appeared normal</td>
</tr>
<tr>
<td>Moderate</td>
<td>8</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>7</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 3D PC MRA Findings of our patients compared to direct CA.

Figure 1A  Contrast enhanced MRA showing severe proximal focal left renal arterial stenosis.
3–4% of hypertension, and renovascular disease in around 1%.\textsuperscript{8}

Screening for renal artery stenosis (RAS) should be restricted to patients with a high RAS risk. Captopril renography, computed tomography (CT)-angiography, magnetic resonance (MR)-angiography, and ultrasound (US) Doppler can be used. Most patients should receive medical treatment. If predictive tests suggest a good outcome, revascularisation with percutaneous transluminal renal angioplasty (PTRA) should be considered in patients with refractory hypertension, fibromuscular dysplasia, recurrent pulmonary oedema, bilateral renal artery stenosis or progressive azotemia, and in patients with a narrow stenosis to a single kidney.\textsuperscript{9}

A variety of different imaging techniques have been used for the diagnosis of renal vascular diseases. The wide range of renal vascular diseases include congenital renal artery and vein variations, aneurysms, arteriovenous malformations (AVMs), renal artery stenosis, renal vein thrombosis, vasculitis, and traumatic injuries, such as dissection and vascular pedicle injury. In this article, we discuss the role of invasive and noninvasive imaging in each of these abnormalities and their typical features. Because renal artery stenosis is an important vascular abnormality encountered in clinical practice, imaging of this entity will be emphasized.\textsuperscript{10}

The renal angiogram is the standard test to establish both the presence of a renal artery lesion and aids in the determination of whether the lesion is due to atherosclerosis or to one of the fibrosis or fibromuscular dysplasias.\textsuperscript{11}

Contrast enhanced 3D MR angiography is a useful alternative in the assessment of pathomorphological feature of the renal arteries. Reliable detection of significant stenosis is

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{image.png}
\caption{Phase contrast MRA. SIGNAL loss of the left renal artery denoting tight stenosis.}
\end{figure}

achieved with both high sensitivity and specificity, provided that careful attention is given to the technique.

This fact stands in contrast to that associated with PC MRA technique which depends on the inherent motion sensitivity of the MR experiment to selectively depict flow.\textsuperscript{12}

Furthermore, arterial blood is depicted solely on basis of the presence of paramagnetic contrast medium within it. So, proper timing of data acquisition assures a high quality angiogram free of venous enhancement.

In our study, one case was missed and overlooked. This was most likely due to overlapping by the Tenatvein, i.e. imperfect acquisition of central lines of K-space data. According to Jeffrey Weinreb, there are four different approaches for timing breath-hold CE MRA’s.\textsuperscript{13}

1. Timing dose:
\[ \text{Delay} = \text{circulation time + infusion time - 1/2 imaging time}. \]
1–2 cc Gd is injected, and scanning is repeated at the level of interest.
- This can be simplified by making the infusion time = imaging time.
- This technique can be implemented in any scanner.

2. Automated contrast detection (Smart prep on GE).
3. Fluoroscopy triggering.
4. Time resolved scan.

In our study, the time delay is empirically determined on the basis of the patient’s age and the cardiovascular status. Typically a delay of 10 s between the start of injection and
the start of imaging works in the majority of patients, when 16 s data acquisition is used. This technique was previously described by Dong et al. in 1999.14

Another pitfall met with in our study using CE MRA was over estimation of moderate stenosis due to imaging at a narrow window setting. This pitfall was described by Dong et al. in 1999.14

Other pitfalls described with the use of CE MRA are failure to suspend breathing, inadequate dose of gadolinium contrast material, and artifacts of surgical clip or arterial stents.14 They stated also that eccentric disease may be identified on only one view, thus, it is important to look at renal arteries on multiple views.

The high sensitivity and specificity of CE MRA have been documented in the studies of Steffens (1997), who reported 96% and 95%, in the study of De Cobelli (1996) 100% and 97% and in Bakker (1999) 97% and 92% sensitivity and specificity, respectively.15–17

The 3D PC imaging commonly demonstrates artificial spine dephasing at the renal artery origins. This has been particularly described with severe and occasionally moderate stenosis.14

Also, choosing the phase encoding velocity is occasionally problematic particularly in patients with poor cardiac output, renal insufficiency or aortic aneurysm.18

Although 3D CE MRA provides a high sensitivity and specificity in morphologic assessment of the arterial lumen, yet it is not sufficient for complete evaluation in patients suspected to have renal artery stenosis. It is necessary to evaluate the hemodynamic significance of such stenosis.

Figure 2A  Contrast enhanced MRA showing an (apparently) tight proximal Rt. Renal artery stenosis.

Figure 2B  Phase contrast MRA and angiogram proved the same stenosis to be of moderate degree.
Adding data obtained from 3D PC MRA to those identified by CEMRA, functional assessment of renal arterial stenosis becomes feasible. Mild stenosis detected by CE MRA can be differentiated from moderate ones on basis of the PC MRA which reflects normal flow status in the former group (mild stenosis). 3D PC MRA can differentiate between moderate and severe stenosis identified by CE MRA. Severe spine dephasing simulating total arterial occlusion will be detected in the latter group (severe stenosis), while in moderate stenosis in CEMRA will also show similar degree of narrowing in the PC MRA.

This is the suggested protocol for screening of patients suspected to have renal arterial stenosis.

Recent data on the appropriateness of renal imaging were published by the American college of cardiology.19

5. Conclusion

Duplex ultrasonography is a good screening test in many patients, but it has limitations in larger persons and can overlook small accessory arteries. For patients with normal renal function but a high clinical index of suspicion for renovascular disease, contrast-enhanced magnetic resonance angiography and computed tomographic angiography are the most accurate imaging tests. For patients with diminished renal function, gadolinium-enhanced contrast magnetic resonance angiography is the best imaging test. However, caution is warranted because exposure to gadolinium contrast agents is associated with nephrogenic systemic fibrosis in patients with renal failure. The American College of Radiology has developed appropriateness criteria for imaging tests related to the diagnosis of renal artery stenosis.20

It is concluded that combined CE MRA and 3D PC MRA techniques are useful in the assessment of pathomorphological features of the renal arteries.

Reliable detection of significant stenosis is achieved with both high sensitivity and specificity, provided that careful attention is given to the techniques.

The combined approach of using techniques is a very useful non invasive modality for assessment of renal artery in cases of suspected renovascular pathology as an etiology to the hypertension.

CE MRA has a poorer ability to grade the degree of narrowing which can be overcome by re-looking at the PC pictures to properly estimate the functional significance of the narrowing.

References