Magnetic Resonance Angiography Versus Duplex Sonography for Diagnosing Renovascular Disease

Daniel A. Leung, Ulrich Hoffmann, Thomas Pfammatter, Thomas F. Hany, Lisa Rainoni, Paul Hilfiker, Ernst Schneider, Gesine G. Zimmermann-Paul, Jörg F. Debatin

Abstract—Noninvasive testing for renovascular disease is required to identify patients who may benefit from revascularization procedures without exposing an unnecessary amount of patients to the risks of catheter angiography. All available methods of diagnosing renal artery stenosis have significant limitations. We compared a new technique, contrast-enhanced magnetic resonance angiography, with an established technique, duplex ultrasonography, for the detection of renal artery stenosis using catheter angiography as the standard of reference. Eighty-nine patients with clinically suspected renovascular disease underwent duplex renal scanning and contrast-enhanced magnetic resonance angiography. Sixty of these also underwent catheter angiography. All studies were interpreted for the presence of renal artery stenosis blinded to the results of the other imaging modalities. For detection of hemodynamically significant ($\geq 60\%$ diameter reduction) main renal artery stenosis, sensitivity and specificity were 90% and 86%, respectively, for magnetic resonance angiography and 81% and 87% for duplex sonography. Most false readings involved differential grading of stenoses detected with all 3 techniques. When patients with fibromuscular dysplasia were excluded from the analysis, the sensitivity of magnetic resonance angiography increased to 97%, with a negative predictive value of 98%. Magnetic resonance angiography detected 96% and duplex 5% of accessory renal arteries seen at catheter angiography. Contrast-enhanced magnetic resonance angiography is a useful technique for diagnosing atherosclerotic renovascular disease. It overcomes the major limitations of duplex renal scanning. However, duplex has the advantage of providing hemodynamic information and appears better suited for the assessment of patients with suspected fibromuscular dysplasia. (Hypertension. 1999;33:726-731.)

Key Words: arteries ■ hypertension, renovascular ■ magnetic resonance imaging ■ renal artery obstruction ■ ultrasound

The diagnosis and management of renovascular disease remain difficult. Initial clinical manifestations vary from incidental finding of renal artery stenosis\(^1\)–\(^3\) to refractory hypertension\(^4\)–\(^5\) and progressive renal failure.\(^6\)–\(^7\) Advances in pharmacological therapy allow correction of hypertension in most patients. Blood pressure control is not always optimal, however, and medication is expensive and associated with side effects as well as compliance problems. In addition, the progressive nature of renal artery occlusive disease\(^8\)–\(^9\) may lead to loss of renal function despite blood pressure control.\(^10\)

It is therefore important to identify patients with renovascular hypertension and/or ischemic nephropathy who may benefit from anatomic correction of renal artery stenosis.\(^11\)–\(^13\)

Conventional catheter angiography remains the gold standard for the diagnosis of renovascular disease. However, the relatively high complication rate and cost associated with catheter arteriography preclude its use as a primary diagnostic measure. A less invasive screening test is therefore desirable.\(^14\)–\(^15\) Color-flow duplex sonography of the renal arteries has been shown to be a useful noninvasive method for the detection of renal artery stenosis\(^16\)–\(^18\) and is a well-established technique in many institutions, including our own. On the basis of differential flow velocity in the aorta and renal artery, the hemodynamic significance of a renal artery lesion is functionally assessed. Duplex renal scanning is limited, however, by an inherent operator-dependence, a technical failure rate ranging from 10% to 20%, and the inability to visualize accessory renal arteries.\(^16\)–\(^18\)

Because of its flow sensitivity, magnetic resonance imaging (MRI) has also been used for noninvasive depiction of the renal arteries.\(^19\)–\(^21\) However, lengthy imaging times, inconsistent visualization of distal renal artery segments, and difficulty in grading stenoses have remained barriers to the clinical acceptance of conventional magnetic resonance angiography (MRA). Recent advances in magnetic resonance hardware have allowed the development of a new approach to MRA whereby rapid breath-hold data acquisition is combined with dynamic contrast medium infusion.\(^22\)–\(^24\) The aim of the
current study was to prospectively assess the diagnostic value of breath-hold three-dimensional (3D) contrast-enhanced MRA of the renal arteries compared with color-flow renal duplex scanning in patients with clinical suspicion of renovascular disease using conventional catheter angiography as the standard of reference.

Methods

Patients

Clinical inclusion criteria for enrollment in the study are listed in Table 1. These represent the generally accepted clinical indicators of renovascular disease.\(^ {14,15}\) During a 1-year period, 89 (62 men, 27 women; mean age, 58; range, 24 to 83 years) of 105 patients who fulfilled 1 or more of the inclusion criteria (Table 1) were willing to participate in the study. Pertinent clinical information included hypertension (n=89), hypertension refractory to standard medication (n=33), unexplained or progressive renal failure (n=24), symptomatic occlusive peripheral vascular disease (n=56), diabetes mellitus (n=19), history of cigarette smoking (n=61), and positive family history for hypertension or vascular disease (n=24). Eighteen patients presented with a suggestive abdominal bruit and 7 patients with incidentally detected asymmetry of renal size. Mean systolic and diastolic blood pressures were 169±29 and 96±17 mm Hg, respectively. Mean serum creatinine was 118±68 μmol/L (range, 60 to 800 μmol/L). All patients underwent MRA and duplex sonography. Sixty patients underwent catheter arteriography of the renal arteries. These included all patients with pathological findings at either duplex or MRA, as well as patients with concomitant peripheral vascular disease who underwent conventional angiographic evaluation of the abdominal aorta and lower extremities. All studies were performed in accordance with the guidelines set forth by the institutional review board. Written informed consent was obtained from all patients.

MR Imaging

MR examinations were conducted on a 1.5-T scanner (Signa Horizon Echospeed, GE Medical Systems) using a phased-array surface coil (Torso coil) for signal reception. The pulse sequence used for MRA was a coronal spoiled gradient-echo acquisition with a repetition time of 4.7 milliseconds, an echo time of 2.1 milliseconds, a flip angle of 50°, and a matrix of 256×160. Partition thickness and field of view were adjusted to patient size and ranged from 1.6 to 2.0 mm and 30 to 38 cm, respectively. The data were acquired in a breath-hold interval lasting 27 seconds timed to coincide with the arterial phase of a dynamic bolus infusion of 0.3 mmol/kg body wt gadolinium DTPA at a rate of 3.0 mL/s. The timing protocol was based on determination of the contrast travel time from the antecubital venous injection site to the aorta using a 2-mL test bolus.\(^ {28}\)

Duplex Sonography

All renal duplex studies were performed by the same vascular technologist using a duplex scanner with a 3.5-MHz transducer (Acuson 128 XP-10, Acuson Corp). Doppler velocity waveforms were obtained along the entire course of the renal arteries as well as the abdominal aorta at the level of the renal arteries. Duplex studies were considered diagnostic if the entire renal artery could be interrogated by velocity waveform analysis. A focal increase in the angle-adjusted peak systolic velocity in a renal artery indicated stenosis. If this was followed by turbulence and the ratio of maximum peak systolic velocity in the renal artery to the peak systolic velocity in the adjacent aorta was ≥3.5, the stenosis was considered hemodynamically significant (≥50% diameter reduction). Renal artery occlusion was diagnosed by the lack of flow signal in a visualized renal artery associated with low amplitude velocity signal from the renal parenchyma and a small kidney (<9 cm).

Duplex scans with diagnosis of hemodynamically significant renal artery stenosis where the contralateral renal artery was not adequately visualized (n=3) were considered diagnostic examinations because the patient would proceed to conventional angiography on the basis of that finding alone.

Conventional Angiography

Catheter arteriography was performed in digital subtraction or cut film technique (Siemens Digitoron 3). Initially, an anteroposterior abdominal aortogram was obtained with a transfemorally inserted 5F pigtail catheter positioned at the level of the renal arteries. Multiple injections at different projections, magnification views, and selective runs were performed as required.

Image Interpretation and Statistical Analysis

All examinations were interpreted blinded to the results of the other diagnostic tests. With all 3 modalities, main and accessory renal arteries were graded on a 4-point scale as (1) normal, (2) not significantly stenosed (≤50%), (3) significantly stenosed (≥60%), or (4) occluded. Renal arteries with evidence of fibromuscular dysplasia were graded as significantly stenosed (grade 3) because it was assumed that such lesions are hemodynamically significant in patients with clinical findings suggestive of renovascular disease.

Duplex scans were interpreted by the same vascular technologist performing the examination. Magnetic resonance images and conventional angiograms were interpreted independently by 2 magnetic resonance radiologists and 2 vascular radiologists, respectively. With both techniques, discordant cases were reviewed by the 2 interpreters so a consensus could be reached.

With conventional angiography and MRA, the examining radiologist simply recorded the observable decrease in luminal diameter. Magnetic resonance images were interpreted at a console with the postprocessing software provided by GE Medical Systems. Postprocessing techniques used for MRA included maximum intensity projections and 3D multplanar reformations. The former is an algorithm that allows display of a 3D volume of image data as a two-dimensional projection and renders images similar to those of conventional angiography. 3D multplanar reformations, the more important technique, allows the user to view the 3D imaging volume in cross section in any desired plane.

Sensitivity, specificity, positive and negative predictive values, and two-sided 95% confidence intervals of MRA and duplex sonography regarding the detection of significant main renal artery stenosis were calculated. For these calculations, renal arteries graded as normal or not significantly stenosed were considered negative findings, and those graded as significantly stenosed or occluded were considered positive findings. The statistical significance of the differences in sensitivities between MRA and duplex were assessed by means of the McNemar test.\(^ {28}\) Interobserver variability in the interpretation of conventional angiography and MRA were computed using the κ statistic including 95% confidence intervals.

---

**Table 1. Clinical Inclusion Criteria**

- Onset of hypertension before age 30 or after age 50
- Moderate to severe hypertension in a female patient between ages 10 and 50
- Hypertension refractory to standard medication
- Hypertension with a suggestive abdominal or flank bruit
- Hypertension associated with incidentally detected asymmetry of renal size
- Hypertension associated with occlusive vascular disease of another region
- Unexplained and/or progressive renal insufficiency
- Hypertension with elevation of serum creatinine induced by an angiotensin converting enzyme

Patients with 1 or more of these manifestations were eligible for inclusion in the study.
Results
The average examination time, including positioning the patient and, in the case of MRA, obtaining an intravenous access, was 50.3±8.5 minutes for duplex ultrasound and 16.2±3.7 minutes for MRA. This difference was statistically significant (P<0.001). Eighteen of 89 duplex scans (20%) were considered nondiagnostic because of obesity and/or excess bowel gas. The average body mass index of patients with nondiagnostic duplex scans was 30.0±2.1 compared with 24.1±1.9 for those with diagnostic duplex scans (P<0.05). Six patients suffered from claustrophobia. Since the study design prohibited the use of sedatives, these patients were not examined with MRA. A further 2 MRA studies (2%) were considered technically unsatisfactory: in one case due to poor contrast timing and in the other as a result of respiratory motion artifacts.

Thirty-four patients had positive findings for significant renal artery stenosis confirmed by conventional angiography, (Figures 1 and 2) including 5 renal arteries in 4 patients with fibromuscular dysplasia (bilateral disease in 1 patient) and 40 renal arteries in 30 patients with atherosclerosis (bilateral disease in 10 patients). A total of 60 patients containing 119 kidneys underwent catheter arteriography. The varying number of nondiagnostic studies with duplex and MRA resulted in a total of 85 main renal arteries that had a reading with all 3 tests. A correlation between MRA and conventional angiography was available in 109 main renal arteries, and a correlation between duplex and conventional angiography was available in 90 main renal arteries. With MRA, 10 false-positive and 4 false-negative readings were recorded. Three of the 4 false-negative findings involved renal arteries with fibromuscular dysplasia, and 1 was a borderline atherosclerotic lesion that was graded as significant at conventional angiography and not significant at MRA. Both of these readings were determined by consensus opinion following divergent readings by the individual reviewers. The 10 false-positive MRA readings were overestimations of stenoses graded at conventional angiography to be not significantly stenosed. Three of the 10 lesions were also graded as significant stenoses at duplex.

With duplex ultrasound, 7 false-positive and 7 false-negative readings for significant renal artery stenosis were recorded. Five of the 7 false-positive readings involved atherosclerotic lesions that were interpreted as significant.
with duplex and not significant at conventional angiography. Four of these were graded as significant stenoses following consensus reading at conventional angiography, and 3 of these were graded as significant stenoses at MRA. Of the 7 false-negative readings with duplex, 1 was a renal artery with discrete distal fibromuscular dysplasia that was also missed by MRA, and 3 were stenoses graded as not significant at duplex and significant at conventional angiography and MRA.

Sensitivity, specificity, positive and negative predictive values for duplex sonography, and MRA are shown in Table 2 along with probability value of the McNemar statistic for comparison of differences in sensitivities between MRA and duplex. The interobserver variability in the grading of stenotic renal artery lesions (grades 1 to 4) with conventional angiography and MRA were identical, with a $\kappa$ value of 0.77 and 95% confidence intervals ranging from 0.67 to 0.86. For the detection of hemodynamically significant lesions, interobserver variability was 0.87 (0.78 to 0.95) for MRA and 0.88 (0.79 to 0.97) for conventional angiography.

Multiple renal arteries were present in 16 patients (27%). Twenty-four of 25 (96%) accessory renal arteries detected with conventional angiography were also seen with MRA, including 2 significant stenoses and 20 normal arteries that were correctly graded. One accessory renal artery with a nonsignificant stenosis and another with a significant stenosis at conventional angiography were falsely graded by MRA as significant and not significant, respectively. Both were extremely small arteries. With duplex scanning, 1 of 20 (5%) accessory renal arteries was detected and correctly graded as normal.

**Discussion**

The presented results support earlier reports that duplex sonography has good sensitivity and specificity for the detection of renal artery stenosis compared with conventional angiography.\textsuperscript{16–18} However, as with the other studies, the statistical analysis here fails to incorporate the 20% of patients who remain undiagnosed following ultrasound examination. We recorded a statistically significant difference in the body mass index of patients with diagnostic compared with nondiagnostic duplex examinations, which indicates that obese patients are unsuitable for renal duplex scanning. Although the constellation of normal main renal arteries and a stenosed accessory renal artery was not encountered in this study, the inability to detect supernumerary arteries remains a drawback to duplex sonography. Patients with a normal renal duplex scan and persistent high clinical suspicion of renal artery stenosis thus may require further angiographic evaluation.

Breath-hold contrast-enhanced MRA appears to overcome the limitations of duplex renal scanning. The examination is fast, is operator-independent, is reliable in the detection of accessory renal arteries, and has a low technical failure rate. In clinical practice, the problem posed by claustrophobia can, at least in part, be mitigated by the use of sedatives. Since arterial contrast is derived from the presence of a contrast agent rather than being flow-dependent, contrast-enhanced MRA does not suffer from the saturation- and turbulence-induced signal loss inherent to conventional noncontrast MRA.\textsuperscript{19–21} Indeed, the results of this study show good correlation between contrast-enhanced MRA and conventional arteriography for grading stenotic renal artery lesions. When patients with fibromuscular dysplasia were excluded from the analysis, the sensitivity was 97% and the negative predictive value 98%. This low rate of false-negative findings demonstrates the potential usefulness of MRA as a screening test for renal artery stenosis in a patient population with clinical suspicion of renovascular disease. The McNemar test, which assesses the statistical significance of the observed differences in the sensitivities between MRA and duplex, yielded a $P$ value of 0.125 when patients with fibromuscular dysplasia were excluded. This represents a statistical trend suggesting that the two techniques are not equally sensitive, thus favoring MRA over duplex in this patient subset.

Contrast-enhanced MRA is similar to conventional angiography in that both techniques provide a luminogram of arterial morphology. Grading of stenoses with both techniques is based on measuring the amount of luminal narrowing. The similarity between the 2 techniques is mirrored in the comparable $\kappa$ values for interobserver variability. However, in its present form, contrast-enhanced MRA has a spatial resolution inferior to that of catheter angiography. This is reflected in the poor performance of MRA in the present study regarding diagnosis of fibromuscular dysplasia. MRA is a rapidly evolving technique, however, and improvements

| TABLE 2. Sensitivities, Specificities, Positive and Negative Predictive Values, and Probabilities for Comparison of Differences in Sensitivities |
|----------------|----------------|----------------|
|                | Sensitivity     | Specificity    | PPV  | NPV  | $P^*$  |
| All patients   |                 |                |      |      |       |
| MRA            | 90% (76–97)     | 86% (75–93)    | 79%  | 93%  | 0.344 |
| Duplex         | 81% (64–92)     | 87% (75–95)    | 79%  | 88%  |       |
| Patients with atherosclerosis (excluding patients with fibromuscular dysplasia) | | | |
| MRA            | 97% (85–99)     | 85% (76–93)    | 80%  | 98%  | 0.125 |
| Duplex         | 81% (62–93)     | 86% (74–94)    | 78%  | 88%  |       |

Values in parentheses are 95% confidence intervals. PPV indicates positive predictive value; NPV, negative predictive value.

*For detection of hemodynamically significant stenosis (≥60% diameter reduction).
in both spatial and temporal resolutions can be expected in the future. Moreover, since 3D multiplanar reformations allow visualization of the MR data in operator-defined cross-sectional planes, MRA does not share the projection-related limitations of conventional arteriography. This facilitates depiction of eccentric lesions and permits reliable localization of renal artery origins in patients with vascular tortuosity. Although the acquisition of MRA examinations is operator-independent, considerable expertise is required for effective postprocessing and interpretation of the images. The morphological depiction and display offered by MRI represents an advantage of MRA over duplex ultrasound, not only for therapeutic planning purposes but also for the assessment of additional soft tissue lesions. One patient from this study was diagnosed to have renal cell carcinoma at MRA, which had been missed at duplex scanning.

Several methodological limitations of this study need to be considered. Patients with nondiagnostic duplex examinations as well as claustrophobic patients unable to undergo MRA were excluded from the modality-related statistical analysis, thereby possibly introducing a selection bias. Furthermore, only 60 of the 89 enrolled patients underwent conventional angiography. Although use of conventional angiography as the standard of reference for the entire study population would have been preferable, ethical concerns regarding potential risks of catheter angiography led to the exclusion of those patients with concordant negative MRA and duplex sonography studies. This may have contributed to a possible underestimation of false-negative findings. Finally, accessory renal arteries were not included in the sensitivity and specificity analysis because most were missed with duplex sonography. With MRA, on the other hand, 24 of 25 accessory vessels were visualized.

Similar to conventional angiography, the major drawback of contrast-enhanced MRA is the reliance on purely morphological criteria for the diagnosis of renovascular disease. The advantage of duplex sonography is that it assesses the hemodynamic effects of renal artery lesions. Although with inferior temporal resolution compared with duplex, accurate renal flow velocity measurements are possible with motion-sensitive MR pulse sequences. A recent study reported high sensitivity and specificity for detection of renal artery stenosis using MR flow velocity profiles. Lack of functional data may also be implicated as the cause for the suboptimal performance of conventional angiography in a recent study comparing selective catheter angiography with intraarterial pressure measurements for the assessment of hemodynamically significant renal artery stenosis. So despite its exquisite spatial resolution, catheter angiography is by no means an absolute measure of hemodynamic significance. Hence, the results of the present study must be interpreted with caution because most of the false readings with MRA as well as duplex involved differential grading of stenoses detected with all 3 techniques. Indeed, the hemodynamic significance of a borderline stenosis seen at MRA and conventional angiography may best be evaluated by measuring the flow alteration with duplex sonography.

For a diagnostic test to be useful in routine clinical practice, particularly as a screening method, it needs to be available, cost-effective, and safe as well as diagnostically accurate. Contrast-enhanced MRA requires the intravenous administration of a contrast agent. In contrast to iodinated contrast agents, gadolinium is not nephrotoxic and can thus be used in patients with renal insufficiency without the risk of further impairment of renal function. Both the availability and cost of MRA are less suitable than those of duplex sonography; however, considering the substantial rate of nondiagnostic examinations as well as the lengthy examination times of duplex compared with MRA, the ultimate cost-effectiveness of the 2 techniques regarding the detection of renovascular disease will need to be addressed in future studies.

In conclusion, our results demonstrate that breath-hold contrast-enhanced MRA is a useful technique for the detection of atherosclerotic renal artery stenosis. Although the spatial resolution appears inadequate for consistent detection of fibromuscular dysplasia, improvements can be expected in the future. Contrast-enhanced MRA is fast, operator-indepedent, and reliable in the detection of accessory renal arteries and thus overcomes most of the limitations inherent in duplex sonography. Duplex, on the other hand, has the advantage of providing functional flow information and is therefore useful for assessing hemodynamic significance. At present, we can recommend MRA for the morphological assessment of suspected atherosclerotic renal artery stenosis, particularly in obese patients who are not amenable to ultrasound examination. However, duplex appears to be better suited for the assessment of patients with suspected fibromuscular dysplasia.

Acknowledgment

This work was supported by Swiss National Science Foundation grant 32-45688-95.

References


Magnetic Resonance Angiography Versus Duplex Sonography for Diagnosing Renovascular Disease

Daniel A. Leung, Ulrich Hoffmann, Thomas Pfammatter, Thomas F. Hany, Lisa Rainoni, Paul Hilfiker, Ernst Schneider, Gesine G. Zimmermann-Paul and Jörg F. Debatin

Hypertension. 1999;33:726-731
doi: 10.1161/01.HYP.33.2.726

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/33/2/726

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org/subscriptions/