The limitations of magnetic resonance angiography in the diagnosis of renal artery stenosis: Comparative analysis with conventional arteriography

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Purpose: Gadolinium-enhanced magnetic resonance angiography (MRA) is commonly used as a screening modality for the detection of renal artery stenosis. However, evidence supporting its utility in clinical practice is lacking; few rigorous studies have compared MRA with contrast arteriography (CA). After making anecdotal clinical observations that MRA sometimes overestimated the degree of renal artery stenosis, we decided to determine the interobserver variability, sensitivity, specificity, and diagnostic accuracy of MRA compared with CA.

Methods: From September 1999 to April 2003, we evaluated 68 renal arteries in 34 patients with clinically suspected renal artery stenosis using both MRA and CA. All studies were independently reviewed by four blinded observers. Renal arteries were categorized by MRA as normal, <50%, and >50% stenosis/occlusion. The sensitivity, specificity, and accuracy of MRA detection of renal artery stenosis were compared to CA as the gold standard. Interobserver variability (κ) was also calculated.

Results: MRA demonstrated 87% sensitivity, 69% specificity, 85% accuracy, 95% negative predictive value, and 51% positive predictive value for the diagnosis of renal artery stenosis. Interobserver agreement was moderate for MRA (κ = 0.53) and good for CA (κ = 0.76). In 21 arteries (31%), MRA was falsely positive.

Conclusions: In patients with a high clinical suspicion of renal artery stenosis, MRA is 87% sensitive in the detection of >50% stenosis. However, MRA is relatively nonspecific compared with CA and results in significant overestimation of renal artery stenosis in nearly one third of patients. To reduce unnecessary CA, clinicians should consider supplemental studies. (J Vasc Surg 2005;41:462-8.)

Renal artery stenosis is a clinically significant problem with an estimated prevalence of 1% to 3% among all patients with arterial hypertension.1,2 However, as many as 40% of hypertensive patients who are refractory to medical therapy may harbor significant renal artery stenosis.3 Contrast arteriography (CA) is the diagnostic gold standard, but its invasiveness, expense, and attendant risks make it unsuitable as a screening test.

As therapy for renal artery stenosis has improved with the availability of lower-profile introducer, catheter, guidewire, angioplasty, and stent technology, the need for an accurate, less-invasive screening test for renal artery stenosis has assumed greater importance. The goals of such a screening test are to reliably detect those patients with hemodynamically significant renal artery stenosis who could potentially benefit from CA and either percutaneous transluminal angioplasty (with or without stent) or bypass while excluding those individuals with normal renal arteries for whom contrast CA would be unnecessary.

A wide array of noninvasive tests such as duplex ultrasonography scanning, renal scintigraphy before and after captopril administration, computed tomographic angiography, and magnetic resonance angiography (MRA) have been proposed as screening tests for renal artery stenosis, but their relative merits have not been established, and their use seems to be determined primarily by local practice patterns.

Duplex ultrasonography scanning has high sensitivity and specificity in experienced hands; however, it can be tedious and time-consuming, is highly operator-dependent, does not reliably visualize accessory or multiple renal arteries, and 8% to 15% of exams are nondiagnostic.4-7 Renal scintigraphy has never been widely accepted. The test protocols are complex and diagnostic criteria are not well standardized.8,9 Scintigraphy was also recently shown to be of limited use in populations with a low prevalence of renovascular disease.10 Because of the inadequacy of these screening tests, a relatively high proportion of patients may therefore be subjected to CA that turns out to be normal.

The introduction of three-dimensional (3D) contrast-enhanced MRA (CE-MRA) has resulted in the increasing use of this technology as a screening test for renal artery stenosis. Potential advantages of gadolinium-enhanced MRA over CA include intravenous rather than intra-arterial contrast administration, lack of ionizing radiation, low risk of nephrotoxicity, no need for supervised recovery after the
procedure, and lack of catheter-related complications such as hematoma, pseudoaneurysm, and athereobolism.

All these advantages make CE-MRA a potentially attractive screening method for patients with suspected renal artery stenosis. CE-MRA was first described by Prince et al in 1993. It provides anatomic images that are similar to CA and also offers the advantage of multiplanar reformatting. High-performance MR gradient systems now allow acquisition of 3D volumes in a single-breath hold <30 seconds rendering renal artery images with excellent spatial resolution. CE-MRA may be more accurate than CA owing to multiplanar reconstruction capabilities. At CA, eccentric stenoses may be underestimated because of the limited number of planes of projection. Also in the case of a tortuous aorta, the origins of the renal arteries may be difficult to visualize.

CE-MRA, however, is not without its own potential limitations. Complex regional blood-flow disturbances may result in signal loss and subsequent overestimation of both the length and degree of stenosis. In addition, several clinical reports have suggested that CE-MRA for renal artery stenosis has a rather high interobserver variability.

In our tertiary care vascular practice, patients suspected of having renal artery stenosis often undergo CE-MRA before referral to our service for further management. Our anecdotal experience suggested that CE-MRA not infrequently overestimated the degree of renal artery stenosis compared with CA. A preliminary review of the literature revealed a relative lack of rigorous clinical studies comparing the accuracy of CE-MRA to CA in the evaluation of patients suspected of having renovascular hypertension. We conceived the present study to evaluate the sensitivity, specificity, accuracy, and interobserver and intermodality variability of CE-MRA compared with CA in the determination of the presence and degree of renal artery stenosis in patients undergoing evaluation for renovascular hypertension using four blinded observers.

METHODS

The findings in 34 patients who underwent both CA and gadolinium-enhanced 3D MRA (CE-MRA) at the University Medical Center, Tucson, Arizona, between September 1999 and April 2003 were retrospectively reviewed. The decision to obtain renal artery imaging was made on clinical grounds by either the referring physician or the vascular surgery attending. Suspicion of renal artery stenosis was based primarily on the presence of new onset or medically refractory hypertension or unexplained renal insufficiency.

Study techniques. CE-MRA was performed on a 1.5 Tesla machine (Siemens, Erlangen, Germany) using a phased-array body coil. 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 256 × 160 matrix. Partition thickness and field of view were adjusted to patient body habitus and ranged from 1.6 to 2 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 of 0.3 mmol/kg body weight of gadolinium diethylene triamine penta-acetic acid infused at 0.3 mL/s. The timing protocol determined from the contrast travel time from the antecubital venous injection site to the abdominal aorta using a 2-mL test bolus.

GE Medical Systems postprocessing software was utilized and included maximum intensity projections and 3D multiplanar reformations. The former is an algorithm that allows display of a 3D volume of image data as a 2D projection and renders images similar to those of CA. The 3D multiplanar reformations, the more important technique, allow the user to view the 3D imaging volume in cross section in any desired plane. Maximum intensity projections of the source phase-contrast images were generated by scanner software.

CA was performed with the Seldinger technique via a percutaneous femoral approach using a 5F pigtail catheter introduced into the abdominal aorta just above the level of the renal arteries. Intra-arterial, nonionic contrast material was injected (volume 30 to 40 mL; injection rate, 15 to 20 mL/s; frame rate 2/sec). Imaging was initially performed in the posteroanterior projection. Multiple injections with different projections, magnification views, and selective runs were performed as required.

CA was performed from 1 day to 5 months after MRA (mean, 45 days). The techniques for CE-MRA and CA were consistent over the study period.

Methodology of renal artery stenosis determination. Four readers (STP, JLM, GTC, KRG) independently assessed the CA and MRA images to calculate the degree of renal artery stenosis. Only the main renal arteries were assessed. Each reader was blinded to the clinical data and to each other’s interpretations. Observers were also not aware of CA findings when they analyzed MRA findings and vice versa.

Image analysis was based on original CE-MRA data sets, maximum intensity projections reconstructions, and CA. The degree of renal artery stenosis was graded as a percentage of the luminal diameter. Maximal stenosis was determined by comparing the narrowest diameter within the stenosis (SD) and the diameter of the nearest downstream normal diameter (ND) segment of the main renal artery [% stenosis = (ND − SD)/ND × 100].

When vessel branching or poststenotic dilatation precluded precise measurement of a normal distal renal artery segment, the nearest normal upstream renal artery segment was used to make an estimate. When two or more stenoses were identified in a single renal artery, the most severe stenosis was used for grading and analysis.

The degree of renal artery stenosis was graded by each reader by using the projection that demonstrated the maximal stenosis: normal, <50% stenosis, and >50% stenosis/occlusion. We used an approach similar to that of Hany...
et al.\textsuperscript{23} and regarded stenoses $>50\%$ as hemodynamically significant.

The quality of each study was rated as adequate or inadequate by each observer on the basis of technical adequacy and the presence of significant motion artifacts. The mean value of all four observers derived from CA was the standard of reference. The Cohen $\kappa$ statistic, including 95\% confidence intervals (CI), was then determined for each pair-wise comparison between the four readers.\textsuperscript{24} The $\kappa$ values for interobserver agreement were assessed for both CE-MRA and CA. Typically, $\kappa$ values <0.4 indicate poor agreement; 0.4 to 0.7 indicate good agreement; and >0.75 indicate excellent agreement. The sensitivity and specificity for renal artery stenosis detection were calculated for CE-MRA on the basis of findings at CA using a $>50\%$ threshold for hemodynamically significant renal artery stenosis. All statistical analyses were performed with Statistical Package for the Social Sciences (SPSS) software for Windows version 9.0 (SPSS, Chicago, IL).

Three months after initial assessment, two observers (STP and GTC) used the same protocol to review the studies a second time to determine intraobserver variability. No information from the first assessment was available to the observers at this time.

RESULTS

The study group consisted of 22 men and 12 women with a mean age of 54 years (range, 37 to 85). Suspicion of renal artery stenosis was based on refractory hypertension (63\%) or unexplained renal insufficiency (37\%). The patient group had a high rate of vascular comorbidities and risk factors such as diabetes mellitus (53\%), symptomatic peripheral arterial disease (63\%), hyperlipidemia (55\%), and cigarette smoking (59\%). The prevalence of $>50\%$ renal artery stenosis or occlusion in our patient cohort was 73\%.

Images were considered of high quality in 98\% of CA and 83\% of MRA studies. Poor-quality MRAs were noted in 17\% of patients; in the latter subgroup, best possible estimates of the degree of renal artery stenosis were made based on the available reconstructed images.

Overall, MRA demonstrated an 87\% sensitivity, 69\% specificity, 51\% positive predictive value, and 95\% negative predictive value for the diagnosis of $>50\%$ renal artery stenosis (Table I). If poor-quality MRAs were excluded, MRA demonstrated an 84\% sensitivity, 74\% specificity, 57\% positive predictive value, and 92\% negative predictive value for the diagnosis of $>50\%$ renal artery stenosis. Interobserver agreement (Table II) was good for MRA ($\kappa = 0.53$ [95\% CI, 0.42 to 0.62]) and excellent for CA ($\kappa = 0.76$ [95\% CI, 0.62 to 0.79]).

For the clinically important determination of $>50\%$ renal artery stenosis, MRA was falsely positive in 21 arteries (31\%). For 42 (62\%) of 68 individual main renal arteries, all four readers of MRA’s were in perfect agreement. In comparison, for CA, there was perfect interobserver concordance for 74\% of the vessels. Four patients had renal artery occlusion. All four readers were in agreement with the diagnosis of renal artery occlusion, both when interpreting MRA images as well as for CA studies.

Three months after the initial assessment, the studies were reviewed a second time by two observers (STP and GTC) using the same protocol. The intraobserver $\kappa$ for MRA for observer 1 and 2 were 0.75 (95\% CI, 0.44 to 0.89) and 0.80 (95\% CI, 0.62 to 0.95). The intraobserver $\kappa$ for CA for observer 1 and 2 were 0.83 (95\% CI, 0.54 to 0.93) and 0.92 (95\% CI, 0.74 to 0.98).

DISCUSSION

The widespread availability of MRA has led to its increasing use in the evaluation of patients with peripheral arterial disease, not only for those who present with suspected cerebrovascular and lower extremity occlusive disease but also for patients with possible visceral or renal artery stenosis. Images are generated that are familiar to the clinician and are quite similar to those obtained by CA.\textsuperscript{15,16} Despite its ongoing evolution, our impression was that one of the limitations of CE-MRA as currently performed was its tendency to overestimate the degree of stenosis in patients with lesions of moderate severity.

We therefore evaluated 68 renal arteries in 34 patients and determined that CE-MRA had an 87\% sensitivity and a 95\% negative predictive value in the detection of a $>50\%$ renal artery stenosis. However, CE-MRA was relatively nonspecific compared with CA and resulted in significant overestimation of the degree of renal artery stenosis in 31\% of patients (Figs 1 and 2).

Available studies have reported variable results in the evaluation of CE-MRA to determine the presence of renal
artery stenosis. Sensitivity and specificity for the detection of >50% renal artery stenosis have ranged from 67% to 100% and 76% to 95%.25-33 A recent meta-analysis of 499 patients who underwent CE-MRA and CA reported that the sensitivity and specificity of MRA were 97% and 93% respectively.34 Other investigators have also identified the problem of overestimation of renal artery stenosis by CE-MRA compared with CA; this problem has been noted in 26% to 32% of patients in multiple clinical series, primarily in the radiology literature.18-20

Several alternatives to CE-MRA are available for the noninvasive evaluation of suspected renal artery stenosis. Renal duplex is an established noninvasive method for the detection of renal artery stenosis in many institutions.8,35-39 Duplex criteria for significant renal artery stenosis include renal artery peak systolic velocity (PSV) >180 cm/sec, renal PSV >200 cm/sec, and a renal artery-to-aortic velocity ratio >3.5; two recent reports demonstrated that a PSV >180 to 200 cm/s reliably indicated a >60% stenosis with >90% sensitivity.38,39

The resistive index has proved to be a highly valuable parameter for the prediction of patient improvement after percutaneous transluminal angioplasty.40 Renal duplex scanning is limited, however, by an inherent operator-dependence, a technical failure rate of 10% to 20%, and the inability to visualize accessory renal arteries. The specificity and sensitivity of ultrasonography scanning is reportedly lower than either CA or CE-MRA.4-7 De Cobelli et al31 and Leung et al30 compared CE-MRA and duplex scanning and reported greater sensitivity for CE-MRA than for duplex imaging.

Nuclear imaging (renal scintigraphy) in conjunction with angiotensin-converting enzyme inhibition provides valuable information regarding differential function. How-

**Fig 1.** A, Magnetic resonance angiography (MRA) demonstrates bilateral high-grade renal artery stenoses. B, Contrast arteriography in the same patient indicates <50% stenosis of the right renal artery and high-grade stenosis of the left renal artery. MRA overestimated the significance of the right renal artery lesion.

**Fig 2.** A, Magnetic resonance angiography indicates high-grade stenosis of the left renal artery. B, Selective contrast arteriography indicates a normal left renal artery.
ever, the sensitivity and specificity vary between series and limitations occur in the assessment of patients with renal impairment, bilateral renal artery stenosis, and intrarenal disease. Computed tomographic angiography is minimally invasive and has a high negative predictive value but requires a high contrast load. These and other limitations will likely limit the widespread use of such techniques for renal artery screening.

One advantage of CE-MRA is that it can produce multiplanar images quite comparable to standard CA. Gadolinium is also not nephrotoxic and accessory and multiple renal arteries are more adequately visualized with CE-MRA than duplex ultrasound scanning. However, MR studies cannot be performed on patients with implanted pacemakers, certain metallic stents, or other metallic devices such as hip prostheses; patient cooperation and claustrophobia can also present problems. As demonstrated in the present study, renal MRA as currently performed still suffers from the disadvantage of overestimation of moderate stenoses. The accuracy of CE-MRA interpretation depends on the sophistication of the image reconstruction software and the facility with which a radiologist can manipulate images using that software. As software improves, it is likely that the problem of stenosis overestimation will be overcome (Fig 3).

Another advantage of CE-MRA is that not only morphologic data can be acquired but also functional information of blood flow and perfusion. Newer MRA applications identify changes in blood flow, flow pattern, and renal tissue perfusion. A multicenter trial has shown that flow profile evaluation with CE-MRA significantly reduced interobserver variability and improved overall accuracy compared to CA, with sensitivities and specificities exceeding 95%. Several papers have reported poor interobserver agreement for both CA and CE-MRA. Such variability can be explained in part because precise measurement of the degree of stenosis is influenced by both interobserver subjectivity as well as variable interpretations of the measurement criteria (Table III).

The present report suggests that CE-MRA may have an increasingly important role in the detection of hemodynamically significant renal artery stenosis. It is sensitive in the detection of >50% renal artery stenosis. Its major limitation is overestimation of the significance of moderate lesions, a problem that occurred in 31% of cases in the present report. Until this limitation is overcome, physicians

Fig 3. A, Magnetic resonance angiography (MRA) indicates irregularities of the distal third of the right renal artery suggestive of fibromuscular dysplasia. B, Contrast arteriography of the same artery indicates an essentially normal right renal artery. C, A multiplanar reconstruction of the MRA indicates the lack of significant stenoses of the right renal artery.
Table III. Comparison with other studies

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CA, Contrast arteriography; MRA, magnetic resonance angiography.

should perform CA before intervention for renal artery stenosis.

REFERENCES


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