



DIAGNOSTIC IMAGING AND ENDOVASCULAR TREATMENT OF RENOVASCULAR HYPERTENSION

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The article by Martin in this issue¹ outlines the recommendations for medical management of hypertension, and for most hypertensive patients, that is all they need. There are, however, secondary causes of hypertension that may require additional workup and more invasive treatment; the most common of these is renovascular hypertension (RVH).

Atherosclerosis is the underlying pathologic process in the vast majority of patients with RVH. Though relatively rare, fibromuscular dysplasia (FMD) is the second most common cause. Overall, RVH is said to account for 1-5% of patients with hypertension, and this percentage increases with age. It is difficult to precisely determine its actual prevalence, as the presence of a renal artery stenosis (RAS) does not necessarily lead to hypertension, and the hypertension caused by RAS may induce permanent changes in the kidneys that perpetuate high blood pressure even after the stenosis is relieved. Nevertheless, in a subgroup of hypertensive patients, it would appear there is a correctable anatomic lesion responsible for their hypertension.

Three important questions are:

1. Who should be screened for RVH?
2. What is the best screening test?
3. Which patients, if any, should undergo invasive treatment for RAS?

As we shall see, there are no definitive answers to any of these questions, but there is some hope for better data in the future.

WHO SHOULD BE SCREENED FOR RVH?

There are those who believe that there is little or no indication for treatment of RVH with anything other than medical therapy. In this scenario everyone gets the same treatment, so no one needs to be screened. Most practitioners, however, feel that some patients should be evaluated for this condition. The most obvious patients are those who fail medical therapy or cannot tolerate

the side effects of multiple antihypertensive agents. The majority of practitioners feel that failure to control BP on a 3-drug regimen is an indication to look for other etiologies. Additional indications may include onset of hypertension before age 30 or after age 55; the sudden onset of hypertension; or worsening of previously well-controlled blood pressure. Other predictors of RAS include an abdominal bruit, renal insufficiency, and generalized atherosclerosis.²

WHICH IMAGING TEST IS BEST³?

1. *Captopril Renography*: was the major imaging test for a number of years, but it is now used very infrequently in most centers. This exam is performed with a radioisotope that undergoes glomerular filtration. The study relies on the effect of captopril, an angiotensin-converting enzyme inhibitor, to reduce glomerular filtration in an ischemic kidney and increase it in the contralateral normal kidney. This difference can be imaged under a gamma camera. This test has reasonably good sensitivity and specificity, but is limited in bilateral RAS (which is very common) and fails to directly visualize the renal arteries.
2. *Renal Artery Doppler Ultrasound (RADU) (Fig.1)*: In theory, this is the ideal test for RAS, since there is no radiation, no nephrotoxic contrast, and the cost is relatively modest. Although a few centers report high sensitivity and specificity, most of us find this a very frustrating examination, as the proximal renal arteries (where most narrowings occur) can only be directly visualized in about 50% of our patients due to obesity and overlying bowel gas. Even in slender, gasless patients, a successful exam requires a highly skilled technologist and more than 1 hour of scanning. Images of waveforms in the parenchymal renal arteries are somewhat easier to obtain, but the interpretation of the resulting signals is rather subjective, with considerable overlap between normal and abnormal findings. Despite these limitations, we have

Figure 1: (A) Normal intra-renal Doppler waveform with rapid early systolic acceleration (arrow). (B) Abnormal waveform in the opposite kidney with a severe stenosis. Note the blunted upstroke (arrow) compared with (A). Unfortunately many patients have Doppler signals which lie between these two extremes.

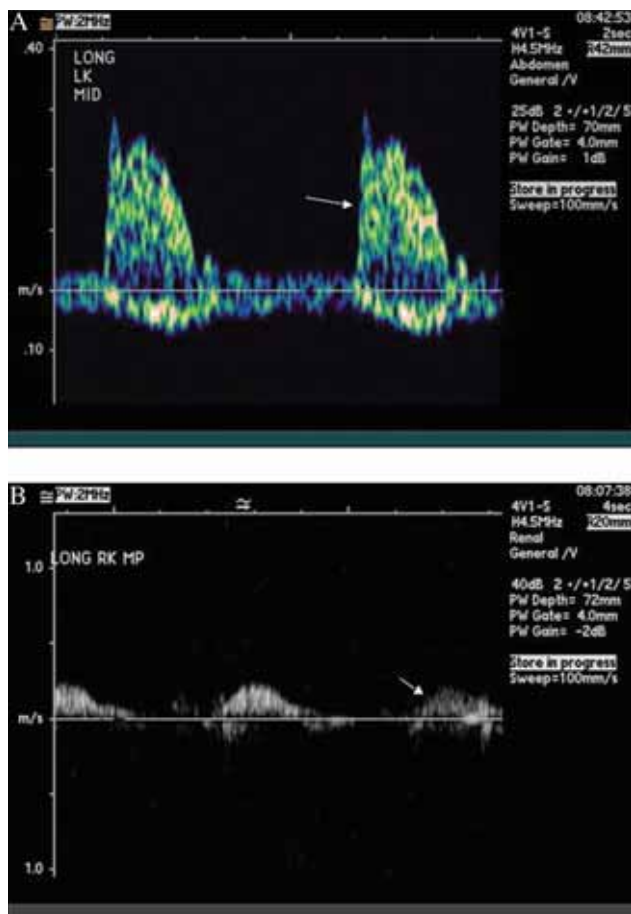
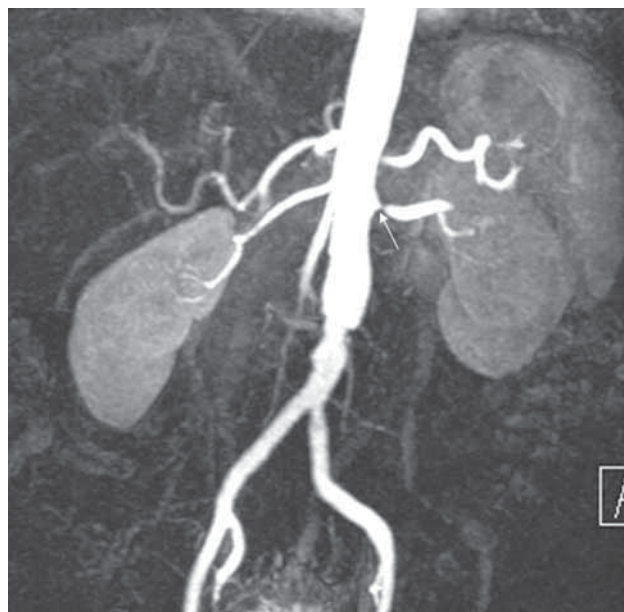


Figure 2: Gadolinium-enhanced MRA shows high grade left renal artery stenosis (arrow).



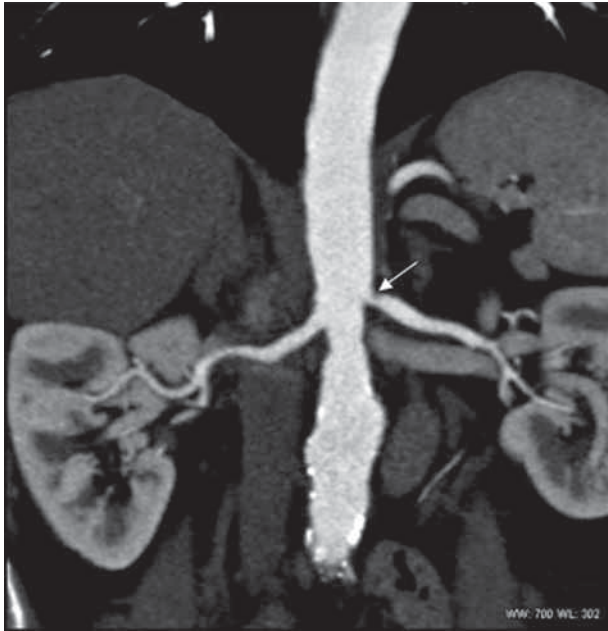
Finally, it was initially thought that Gadolinium, the usual contrast agent for MRA, was a safe agent in patients with renal insufficiency, and that the only significant contraindication to MRA was a pacemaker or similar device. Alas, the recent description of nephrogenic systemic fibrosis (NSF) in patients who received gadolinium agents, especially those with renal insufficiency, has dampened enthusiasm for this procedure in patients with less than normal renal function.^{4,5} This latter problem is, of course, common in elderly hypertensive individuals. Though there are some promising non-contrast MR techniques for visualizing the renal arteries, they require very recent scanners and have not yet reached widespread clinical use. Work is ongoing to determine if some gadolinium agents are safer than others, which would allow the more widespread use of MRA.

seen a significant increase in requests for this test, especially since the number of patients who can undergo MRA has decreased, as discussed below.

3. **MR Angiography (MRA) (Fig.2):** This was the test of choice in most practices until recently, despite its significantly higher cost than Doppler ultrasound. It is a nearly perfect screening test for atherosclerotic RAS because it provides excellent visualization of the renal arteries in almost all patients, and there are virtually no false negative exams. If the main renal arteries are found to be normal on MRA, no further workup is needed. Unfortunately, there is a significant false positive rate, as MR tends to exaggerate the degree of narrowing. MRA is of very limited value in patients with fibromuscular dysplasia, as it lacks adequate spatial resolution. There are also MR artifacts that can mimic FMD.

4. **CT Angiography (CTA) (Fig.3):** If the patient has normal renal function, this probably represents the best screening test. It is much faster to perform than MRA, is less prone to false positive results, and has superior spatial resolution. CTA may even detect the thin webs present in FMD, which can rarely be diagnosed with confidence on MRA. Pacemakers are no problem. Its accuracy is limited by dense calcification, which may obscure the contrast-filled lumen and make accurate measurement of the degree of stenosis difficult or impossible. Unlike

Figure 3: CTA reveals soft plaque at the orifice of the left renal artery (arrow).



MRA or RADU, ionizing radiation is of concern as well.

5. *Renal angiography (DSA) (Fig.4):* Direct catheter angiography, although more invasive than any of the other tests, has significant advantages for evaluation of patients with RVH. With current technology, the study can be done with very small catheters and minimal (<20 ml) contrast. The risks of arterial puncture are very small, spatial resolution is superb,

and, should treatment be required, the catheter is already in place. FMD and branch stenoses, often missed with less invasive tests, can be clearly seen. In patients with a high clinical suspicion for RAS, this can often be the best single test to do.

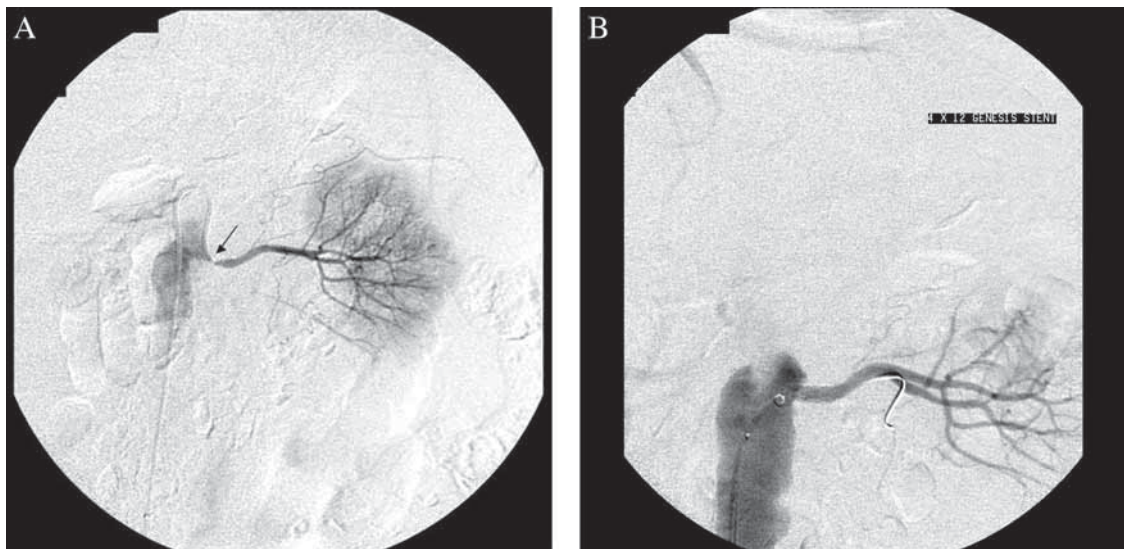
Which patients, if any, should undergo invasive treatment for RAS?

Although there is a long history of surgical therapy for RAS, it has been relegated to a very small number of patients as catheter-based techniques have matured. Surgery is obviously highly invasive, and there are no clear predictors for who will benefit and who will not. Balloon angioplasty and stent placement are now the techniques of choice.

In patients with FMD, the treatment is clear. Angioplasty alone works very well, and has a high rate of cure or substantial improvement in hypertension. Stents should be avoided in these patients, as most are young, and angioplasty alone has been shown to work well.

For the much larger group of patients with atherosclerotic RAS, the picture is much cloudier.^{6,7,8} Despite the many clinical successes seen in appropriately selected patients by those of us who perform renal angioplasty and stenting, the largest studies that compared renal intervention with medical therapy have had major methodological problems and have all failed to show a benefit for invasive treatment over medication alone. Although

Figure 4: (A) Digital angiogram indicates tight proximal renal artery stenosis (arrow). (B) Following stent placement, there is no residual stenosis.



everyone agrees that “cure” of hypertension is rare after intervention, the value and frequency of improved BP control using fewer medicines is difficult to quantify. In patients with progressive renal insufficiency secondary to RAS, is stenting that achieves stabilization (but not a decline) of the creatinine level a success or a failure? The natural history in most RAS patients is progressive worsening of renal function. Intervention is not without significant risk, as about 10% of patients will worsen after catheter-based therapy.

All of us who work in this field hope that answers to many of these questions will come from the CORAL trial (Cardiovascular Outcomes in Renal Atherosclerotic Lesions). This multi-center NIH-sponsored study is enrolling over 1000 patients to compare best medical therapy to renal angioplasty with stenting plus best medical therapy in patients with RAS.⁹ We at LGH are a major contributor of patients to this study, and look forward to the final analysis of the data in this important study.

REFERENCES

1. Martin J. Hypertension Guidelines: Revisiting the JNC 7 Recommendations. *J Lanc Gen Hosp* 2008;3:91-97.
2. National Kidney Foundation; Kidney Disease Outcomes Quality Initiative. Guideline 4: Evaluation for Renal Artery Disease. 2002.
3. Calhoun DA, Jones D, Textor S, et al. Resistant Hypertension: Diagnosis, Evaluation and Treatment: A Scientific Statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Circulation* 2008;117:e510-e526.
4. O'Connor JP, Ariyanagam-Baksh SM, Carroll LE. Nephrogenic Systemic Fibrosis – A Clinical and Pathologic Perspective. *J Lanc Gen Hosp* 2007;2:122-125.
5. Leslie, PA. Nephrogenic Systemic Fibrosis; A Radiologic Perspective. *J Lanc Gen Hosp* 2007;2:126-128.
6. Balk E, Raman G, Chung M, et al. Effectiveness of Management Strategies for Renal Artery Stenosis: A Systematic Review. *Ann Intern Med* 2006;145:901-912.
7. Cooper CJ, Murphy TP. Case for Angioplasty and Stenting of Atherosclerotic Renal Artery Stenosis. *Circulation* 2007;115:263-270.
8. Dworkin LD, Jamerson KA. Case Against Angioplasty and Stenting of Atherosclerotic Renal Artery Stenosis. *Circulation* 2007;115:271-276.
9. Murphy TP, Cooper CJ, Dworkin LD, et al. The Cardiovascular Outcomes with Renal Atherosclerotic Lesions (CORAL) Study: Rationale and Methods. *JVIR* 2005;16:1295-1300.

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