

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:**                      **Renovascular Hypertension**

**Variant 1:**                                      **High index of suspicion of renovascular hypertension and normal renal function.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRA abdomen with contrast	8	Requires intravenous gadolinium contrast agents and is accurate in diagnosing renal artery stenosis. See statement regarding contrast in text under “Anticipated Exceptions.”	None
CTA abdomen	8	Similar to MRA in accuracy; requires intravenous iodinated contrast media.	Med
US kidney retroperitoneal with Doppler	6	Useful if there is a dedicated team of physicians and technologists who are skilled in the examination.	None
ACE-inhibitor renography	6	Although the technique has not been standardized, it appears to have a relatively high sensitivity and specificity in patients with normal renal function.	Med
Arteriography kidney (IADSA)	4	Considered the gold standard for diagnosing renal artery stenosis, but it is invasive. Probably not indicated as the primary diagnostic method but must be performed prior to transluminal angioplasty. Reserved for confirmation and for angioplasty or stent placement.	Med
Renal vein renin assays	3	Should not be used as a screening test but rather to confirm the clinical significance of a renal artery stenosis.	NS
X-ray intravenous urography	1	Significantly less sensitive than other examinations.	Med
Venography kidney (IVDSA)	1	Difficult to perform on a reliable basis due to high number of inadequate studies.	NS
<b><u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate</b>			<b>*Relative Radiation Level</b>

**Clinical Condition:****Renovascular Hypertension****Variant 2:****High index of suspicion of renovascular hypertension and diminished renal function.**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
MRA abdomen with contrast	8	Useful in older patients with arteriosclerotic vascular disease (ASVD) with diminished renal function who most likely have proximal renal artery stenosis. See statement regarding contrast in text under "Anticipated Exceptions."	None
US kidney retroperitoneal with Doppler	8	Reliable if there is a dedicated team of physicians and technologists who are skilled in the examination.	None
ACE-inhibitor renography	4	Although diminished renal function can affect the sensitivity and specificity of the examination, it is still reliable as a screening tool.	Med
Arteriography kidney (IADSA)	4	Better than conventional angiography because it requires less contrast media. It is often used to guide angioplasty or stent placement.	Med
Renal vein renin assays	3	Should not be used as a screening examination.	NS
X-ray intravenous urography	2	Significantly less sensitive than other examinations and uses contrast media.	Med
Venography kidney (IVDSA)	1	Not indicated because of large contrast load to the kidneys.	NS
CTA abdomen	1	Not indicated because of contrast load to kidneys.	Med
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

**Variant 3:****Low index of suspicion of renovascular hypertension ("essential" hypertension).**

<b>Radiologic Procedure</b>	<b>Rating</b>	<b>Comments</b>	<b><u>RRL*</u></b>
X-ray intravenous urography	1		Med
Arteriography kidney (IADSA)	1		Med
US kidney retroperitoneal with Doppler	1		None
Venography kidney (IVDSA)	1		NS
Renal vein renin assays	1		NS
ACE-inhibitor renography	1		Med
CTA abdomen	1		Med
MRA abdomen with contrast	1		None
<b>Rating Scale:</b> 1=Least appropriate, 9=Most appropriate			<b>*Relative Radiation Level</b>

# RENOVASCULAR HYPERTENSION

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## **Summary of Literature Review**

Renovascular hypertension caused by a reduced perfusion pressure to one or both kidneys is usually due to renal artery stenosis and is, therefore, correctable on reversal of the stenosis. A critical problem in diagnosing renovascular hypertension is the selection of an appropriate end point against which to judge the accuracy of new tests. Calculations of the sensitivity, specificity, and accuracy of these examinations are normally based on a comparison with a standard such as conventional angiography. However, the definition of a significant renal artery stenosis has varied. Most investigators consider a 50% stenosis to be significant, yet perfusion pressure in a large artery is generally not reduced until stenosis exceeds 70%. Ultimately, the defining criterion for renovascular hypertension is a fall in blood pressure after intervention (angioplasty, intravascular stent placement, or surgery). Bilateral renal artery disease remains a problem in that it is difficult in such cases to quantify the effect on blood pressure of one side versus the other.

To improve the predictive value of diagnostic imaging examinations, a variety of clinical findings are associated with an increased likelihood of renovascular hypertension. These include, an abdominal bruit, malignant or accelerated hypertension, significant (diastolic >110) hypertension in a young adult (<35 years of age), new onset after age 50, sudden development or worsening of hypertension, refractory hypertension, deterioration of renal function in response to angiotensin-

converting enzyme (ACE) inhibitors, and generalized arteriosclerotic occlusive disease with hypertension.

The following is a discussion of each of the noninvasive diagnostic imaging examinations for renovascular hypertension.

## **Hypertensive Intravenous Urography**

Bookstein et al reviewed the data from a cooperative study on renovascular hypertension and concluded that a hypertensive intravenous urography (IVU) had 84% sensitivity in detecting renal artery stenosis in all patients who presented with hypertension [1,2]. Thornbury et al performed a retrospective analysis at their institution and reanalyzed the data from the cooperative study of renovascular hypertension [3]. They found the IVU not to be useful, with a sensitivity of 60% for detecting surgically correctable disease. In a retrospective review of rapid-sequence IVU of 241 patients with features suggestive of renovascular disease, Cameron et al demonstrated that a normal-sequence IVU excluded renovascular disease with a 93% probability but failed to diagnose 20% of cases [4]. Currently, most clinicians and diagnostic radiologists believe that the hypertensive IVU is not useful as a screening test and has *no role* in the evaluation of patients with suspected renovascular hypertension.

## **Intravenous Digital Subtraction Angiography**

Intravenous digital subtraction angiography (IVDSA) was developed in the late 1970s, and many reports came out in the early 1980s describing the potential utility of this examination for evaluating patients with renovascular hypertension [5-7]. In spite of early optimism about the procedure, many investigators have been unable to reproduce the impressive initial results. Apparently, a relatively high percentage of patients have technically inadequate studies, and the contrast load is often substantially higher than for arteriography, making the procedure hazardous in patients with diabetes or renal insufficiency. The resolution of the procedure does not compare with that of arterial studies, and fibromuscular lesions of branch arteries may be missed [8-10]. IVDSA does not appear to be indicated as a screening examination for renovascular hypertension [11].

## **Selective Renal Vein Renin Assays**

Although selective renal vein renin assays are not used as the sole screening test in patients with suspected renovascular disease, this examination is often used in some medical centers to confirm the clinical significance of a renal artery stenosis. Various parameters have been described, including renal vein/inferior vena cava (IVC) ratios, right renal vein/left renal vein ratios, etc. The examination has several major limitations, including variable sampling techniques, a 2-3-day delay in reporting results, and limited sensitivities (65%-74%) [12]. Specificity of this examination, however, can be quite high (up to 100%) [12,13]. Most clinicians use this

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technique to confirm the clinical significance of a renal artery stenosis. Peripheral renin concentration in the normal range may be used as an indicator of no benefit from intervention [14]. Therefore, this examination should probably be used not as a screening test but rather as a confirmatory examination when there is a clinical question of whether the renal artery stenosis is in fact causing hypertension.

### **Duplex Doppler Sonography**

Duplex Doppler sonography is an attractive technique as a noninvasive screening test in that it is relatively inexpensive, does not require contrast medium, and can be used in patients with any level of renal function. As with many of the noninvasive imaging examinations, there are numerous parameters and abnormal criteria indicating possible renovascular disease. The most frequently quoted parameters are a peak systolic velocity in the renal artery exceeding 180 or 200 cm/s and a renal artery/aortic velocity ratio exceeding 3.5 [15]. Using these parameters, early investigators have quoted sensitivities from 85%-90%. Specificities were also quite high at 95%. However, many investigators have had trouble duplicating these results and have reported extremely poor sensitivities, as low as 0% [16,17].

Variations in results are largely due to technically inadequate studies and using 100 cm/s as a threshold for normal velocity, thereby producing a high number of false-positive studies. A major problem in many of these studies is that approximately 10%-20% of patients may have technically inadequate studies secondary to obesity or overlying bowel gas [18]. In addition, examination times have varied from 10 to 15 minutes to up to 1.5 hours. The variability in examination time has no doubt contributed to the variability in sensitivity rates reported in the literature. Doppler ultrasound (US) is less useful than invasive angiography for diagnosing fibromuscular dysplasia and detecting accessory renal arteries [19].

Some reports have advocated segmental renal artery waveform analysis using measurements such as acceleration time and acceleration index, as well as "parva and tarda" waveform appearances. Using upper, middle, and lower pole segmental artery waveform analysis in the kidneys, these investigators have found the technique to be approximately 85%-90% sensitive. An increase in acceleration time (normal <70 milliseconds) and loss of the early systolic peak (ESP) appear to be the most useful parameters. Administration of US contrast agent improves the quality of renal artery images, reduces mean examination time, and improves visualization of the entire length of the main renal arteries [20]. Although this technique has not been duplicated yet in the literature, many academic centers believe it may hold significant promise in the evaluation of patients with renovascular hypertension.

Because of the difficulty and time involved in the examination, duplex Doppler sonography should be used in medical centers where it has proven to be reliable and where dedicated technologists and physicians are skilled

in the examinations. Several recent comparative studies have demonstrated that Doppler sonography with or without administration of captopril or US contrast is more sensitive and specific than ACE-inhibitor scintigraphy. Doppler sonography may be of use in predicting the outcomes for renal artery interventions. When resistive index values exceed 0.8, the results in terms of reducing hypertension or improving renal function are usually poor [21-24].

### **ACE-Inhibitor Renography and Scintigraphy**

Renal scanning with radionuclide agents is noninvasive and safe, even in patients with renal insufficiency. In addition, many reports have been very positive, showing a high degree of sensitivity and ability to accurately identify patients who will benefit from surgical or angioplasty intervention. However, the literature is nonuniform concerning techniques, radionuclide agents, and interpretation parameters. For example, iodine-131 hippuran, DTPA, and Tc-99m MAG3 have all been advocated for use in captopril or other ACE-inhibitor renograms [25]. MAG3 and hippuran are primarily excreted via tubular secretion, whereas DTPA is totally eliminated by glomerular filtration [26]. When using Tc-99m MAG3 is used, a renogram curve showing a prolonged time to peak activity and delayed washout suggests renovascular hypertension. The extraction fraction of DTPA is approximately 20%, and for MAG3 it is 40%-50%. MAG3 is preferred over DTPA in patients with suspected obstruction and impaired renal function [27-29].

Because the glomerular filtration rate (GFR) in kidneys with a partial vascular obstruction is significantly reduced by an ACE-inhibitor, the utility of ACE-inhibitor GFR renography (using DTPA) is quite dramatic. Apparently, renal tubular secretion is also dramatically affected by the addition of an ACE-inhibitor, and thus iodine-131 hippuran and Tc-99m MAG3 are also sensitive in detecting renal artery stenosis. Tc-99m MAG3 provides superior images and counting accuracy compared to iodine-131 hippuran. Currently iodine-131 orthoiodohippurate is not recommended for routine use [29].

A review of the current literature regarding all methods of captopril renography revealed sensitivities generally in the range of 80%-100%. Several studies have pointed out that captopril renography is highly specific in identifying patients who will benefit from surgical or angioplasty intervention. This seems to be more evident with the tubular secretion agents (iodine-131 hippuran and Tc-99m MAG3). Normal findings on ACE inhibition renography indicate a low probability of renovascular hypertension. Abnormal baseline findings that improve after ACE inhibition also indicate a low probability of renovascular hypertension. ACE inhibition renography is less accurate in azotemic patients. The ability to identify the patient who will benefit from surgery or angioplasty is considered highly valuable. The relatively high sensitivity and specificity of this examination have enabled it to be a primary screening modality for renovascular hypertension, especially in patients with normal or near-

normal renal function. When ACE-inhibitor renography is performed in patients with ischemic nephropathy or a small, poorly functioning kidney, as many as 50% of the studies may have an indeterminate probability scan. Moreover, asymmetry of blood flow in patients, even those with patent renal arteries as demonstrated by 133 xenon washout techniques, may result in false-positive results on renal scintigraphy. It is not a test for detecting the presence or absence of renal artery stenosis [30-32].

### **Magnetic Resonance Angiography**

Magnetic resonance angiography (MRA) is suited for noninvasive workup of renal artery stenosis and has been widely applied for clinical practice. The reliability of MRA is not affected by the presence of bilateral renovascular disease. It is unnecessary to hydrate the patients or to stop diuretics before the examination. Currently 3D contrast-enhanced MRA with an intravenous injection of gadolinium-based contrast agent forms the backbone of MRI examination of renal arteries.

Several investigators report using angiography as the standard of reference, with sensitivity ranging from 88%-100% and specificity ranging from 71%-100% [33-35]. In a meta-analysis of 39 studies, 25 of which met the inclusion criteria [36], the sensitivity and specificity of gadolinium-enhanced MRA were 97% and 85%, respectively. With the use of high-spatial-resolution small-field-of-view MRA techniques it is now possible to evaluate not only the main renal arteries but also the accessory renal arteries and distal stenosis. The recent introduction of improved gradient hardware and parallel imaging techniques has reduced the acquisition time and improved spatial resolution.

Most MRI techniques rely solely on the morphologic assessment of the vasculature. To assess the hemodynamic consequences of a particular arterial lesion, additional functional tests are sometimes required. Although still investigational, cine phase-contrast MRI flow quantification techniques in combination with 3D gadolinium-enhanced MRA appear to be feasible for detecting and determining the degree of renal artery stenosis. A combination of cine phase-contrast MRI renal flow and parenchymal volume measurements enables identification of patients who may benefit from percutaneous transluminal angioplasty and stent placement [37-42].

Initially, gadolinium-based MRI contrast agents were widely believed to be well tolerated and non-nephrotoxic, even when used in patients with impaired renal function. However, exposure to gadolinium contrast agents in patients with renal failure and those maintained on dialysis has recently been linked with the development of nephrogenic systemic fibrosis (NSF) [43-45]. Further studies are necessary to determine this exact relationship. Until then, as detailed in the ACR guidance document for safe MRI practices which was just recently published, for all patients with moderate to end-stage kidney disease (estimated GFR of  $<60$  mL/min/1.73m<sup>2</sup>) and those with acute renal injury, it is recommended that one consider

refraining from administering gadolinium contrast agents unless a risk-benefit assessment for that particular patient indicates the benefit clearly outweighs the potential risk(s) [43].

### **Computed Tomographic Angiography**

Computed tomographic angiography (CTA) involves the process of rapidly acquiring volumetric images by moving the beam continuously in a helical manner across a region of interest during a single bolus infusion of intravenous contrast, usually 130-150 ml. This volume of contrast raises the risk of nephrotoxicity in patients with pre-existing renal failure. A prospective randomized study comparing intra-arterial digital subtraction angiography (IADSA) to CTA demonstrated no increased risk for contrast nephropathy despite a greater dose of contrast media [46].

Sophisticated methods of image processing allow 3D displays of the aorta and renal vasculature that are remarkably clear, and the main value of CTA currently is in evaluating renal donors preoperatively.

Two studies comparing CTA with digital renal arteriography have reported the sensitivity of CTA for detecting significant stenoses (greater than 50% narrowing) to be 88%-96% and the specificity 77%-98%, and in one study the accuracy was 89%. In diagnosing narrowing of only the main renal arteries, one study found the sensitivity and specificity to be 100% and 98%, respectively [47,48]. Normal results from CTA virtually rule out renal artery stenosis. Both maximum-intensity projection (MIP) and volume-rendering techniques are useful and complementary in CT evaluation of renal artery stenosis [49]. Secondary signs include poststenotic dilatation, renal parenchymal changes of atrophy, and decreased cortical enhancement. A threshold of 800 mm<sup>2</sup> for cortical area and 8 mm for mean cortical thickness seen on CT can be a useful morphologic marker of atherosclerotic renal disease.

Like MRA, CTA is more accurate in diagnosing proximal lesions. CTA can also be used to assess patency of renal stent grafts [50-52]. Improvements in both MRA and CTA techniques in the near future are likely to render catheter angiography unnecessary in the diagnosis of renal arterial disease. The introduction of multi-detector-row helical CT including recent 64-channel CT systems permit the acquisition of isotropic datasets that enable the reconstruction of high-resolution 2D and 3D images in any plane.

In a large multicenter study in the Netherlands, the validity of contrast-enhanced CTA and MRA was prospectively investigated in 356 patients with suspected renovascular hypertension from 1998-2001, using IADSA as the standard of reference [53]. The combined sensitivity and specificity were 64% and 92%, respectively, for CTA and 62% and 84%, respectively, for MRA. Possible explanations for the low sensitivity of CTA and MRA in this study are suboptimal technique, low overall disease prevalence, high proportion of

patients with fibromuscular dysplasia, and imperfect standard of reference [53].

### Summary

- Diagnostic imaging for hypertension depends on the index of suspicion for renovascular disease and on the patient's renal function. If clinical findings strongly suggest the possibility of renovascular disease, contrast-enhanced MRA or CTA should be performed. Duplex Doppler sonography or captopril scintigraphy could also be used if MRA is not desired or is contraindicated. CTA may be helpful in a select group of patients who are likely to have proximal renal artery stenosis. Conventional angiography and IADSA should be reserved for confirmation and for therapeutic reasons such as angioplasty and stent placement, especially with the recent advances in MR and CT techniques and their successful results [54,55].
- For patients with a high index of suspicion for renovascular disease who have normal renal function, contrast-enhanced MRA and CTA are the most accurate means to evaluate for renovascular disease. Captopril renography is also very adequate in these patients if MRA is not desired or is contraindicated. Duplex Doppler sonography also can be used in these patients if a dedicated team of technologists and radiologists is available and the technique has proven to be reliable in that medical center.
- For patients with a high index of suspicion for renovascular disease and diminished renal function, gadolinium-enhanced contrast MRA is best suited to evaluate renovascular disease. However, the recently reported association of exposure to gadolinium contrast agents in patients with renal failure with NSF warrants caution. Duplex Doppler sonography is also the preferred screening examination, especially in a medical center where the technique has proven to be reliable and where dedicated technologists and physicians are skilled in the examination and can perform it with a high degree of accuracy. Captopril renography is not a reliable test in patients with poor renal function. CTA may also be contraindicated secondary to renal insufficiency.
- Patients with hypertension and a low index of suspicion for renovascular disease most likely have “essential” hypertension that is usually easily controlled with medication. There is no need for diagnostic imaging in these patients.

### Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie,  $<30 \text{ mL/min/1.73m}^2$ ), and almost never in other

patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates  $<30 \text{ mL/min/1.73m}^2$ . For more information, please see the [ACR Manual on Contrast Media](#) [56].

### Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level*	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

\*RRL assignments are not included for some examinations. The RRL assignments for the NS (not specified) exams cannot be made because the RRL depends on the region of the body exposed to ionizing radiation, and the body part will vary as a function of the clinical situation.

### Supporting Document(s)

- [ACR Appropriateness Criteria® Overview](#)
- [Evidence Table](#)

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.