American College of Radiology
ACR Appropriateness Criteria®
Renovascular Hypertension

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

Radiologic Procedure	Rating	Comments	RRL*
MRA abdomen without and with IV contrast	8		O
CTA abdomen with IV contrast	8		☢☢☢
US duplex Doppler kidneys retroperitoneal	7		O
MRA abdomen without IV contrast	5		O
ACE-inhibitor renography	5		☢☢☢
Arteriography kidney	3		☢☢☢
Venography with renal vein sampling	3		Varies
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Variant 2:   **High index of suspicion of renovascular hypertension. Decreased renal function, eGFR <30 mL/min/1.73 m^2.**

Radiologic Procedure	Rating	Comments	RRL*
US duplex Doppler kidneys retroperitoneal	9		O
MRA abdomen without IV contrast	7		O
CTA abdomen with IV contrast	5		☢☢☢
MRA abdomen without and with IV contrast	3		O
ACE-inhibitor renography	3		☢☢☢
Arteriography kidney	3		☢☢☢
Venography with renal vein sampling	3		Varies
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

RENOVASCULAR HYPERTENSION

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Summary of Literature Review

Introduction/Background

Hypertension is a common condition, affecting approximately 20% of adults. Secondary hypertension (ie, hypertension with a demonstrable cause) accounts for only 5% to 10% of all cases of hypertension, with the remaining cases considered primary hypertension or essential hypertension. Renovascular hypertension is the most common type of secondary hypertension and is estimated to have a prevalence between 0.5% and 5% of the general hypertensive population, and it has an even higher prevalence among patients with severe hypertension and end-stage renal disease, approaching 25% in elderly dialysis patients [1]. There are varied causes of reduced renal perfusion with resultant renovascular hypertension, the most common being renal artery stenosis (RAS) secondary to either atherosclerotic disease (90%) or fibromuscular dysplasia (10%) [2]. Less common etiologies include vasculitis, embolic disease, dissection, post-traumatic occlusion, and extrinsic compression of a renal artery or of a kidney [3]. Clinical features associated with an increased likelihood of renovascular hypertension include an abdominal bruit, malignant or accelerated hypertension, significant (diastolic pressure >110 mm Hg) hypertension in a young adult (<35 years of age), new onset after 50 years of age, sudden development or worsening of hypertension, refractory hypertension, deterioration of renal function in response to angiotensin-converting enzyme inhibitors, and generalized arteriosclerotic occlusive disease with hypertension.

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 RAS has varied. Most investigators consider a 50% to 60% stenosis to be significant, yet perfusion pressure in a large artery is generally not reduced until stenosis exceeds 70% to 75%. 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.

Testing for RAS is not appropriate for patients who have a low likelihood of renovascular hypertension. Investigation for renovascular hypertension is appropriate when the clinical presentation suggests secondary hypertension rather than primary hypertension, when there is not another known cause of secondary hypertension, and when intervention would be carried out if a significant RAS were identified. Recent investigation has directed the appropriateness of investigation for RAS. Specifically, the Cardiovascular Outcomes in Renal Atherosclerotic Lesions trial—a randomized controlled trial of 947 patients from 113 centers published in 2013—showed no difference in multiple end points between medical therapy and renal stenting in patients with atherosclerotic RAS and hypertension or chronic kidney disease [4]. The conclusion derived from this trial is that testing for RAS is not typically warranted for patients whose hypertension is well managed with medical therapy. Scenarios where testing for RAS may be warranted include new-onset hypertension, failure of antihypertensive medical therapy, progressive renal insufficiency suspected to be attributable to renovascular disease, episodes of flash pulmonary edema, and young patients with suspected fibromuscular dysplasia (for whom renal artery angioplasty may be

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preferable to long-term medical therapy) [3,5]. Given the limited scenarios in which testing for renovascular hypertension is considered appropriate, the decision to perform diagnostic imaging to identify RAS should ideally be based on a multidisciplinary assessment of an individual patient's clinical presentation and comorbidities, and the likelihood of response to intervention [5].

Overview of Imaging Modalities

Ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), scintigraphy, and angiography all may be utilized in the diagnosis of RAS. Intravenous urography for RAS is of historical note [6] and is no longer used as a screening test. US can be utilized regardless of level of renal function. Contrast-enhanced CT angiography (CTA) and MR angiography (MRA) are both effective modalities for diagnosis of RAS, though both have been associated with potential morbidity in the setting of impaired renal function—nephrogenic systemic fibrosis (NSF) in the case of MRI and contrast material–induced nephropathy (CIN) in the case of CT [7]. Noncontrast MRI protocols are an alternative in patients with impaired renal function. The association between intravenous contrast material for CT and development of acute kidney injury has come under question, and recent data indicate that there is a much lower risk of CIN than was previously thought [8]. In addition to identification of RAS, CT, MRI, and, to a lesser extent, US can also assess for aortic disease, accessory renal arteries, some forms of renal parenchymal disease, and other causes of secondary hypertension such as pheochromocytomas. Renal scintigraphy also can be utilized for the diagnosis of RAS but has decreased accuracy in patients with bilateral RAS or impaired renal function. Angiography is predominantly used for confirmation and intervention rather than screening for RAS.

Discussion of Procedures by Variant

Variant 1: High index of suspicion of renovascular hypertension. Normal renal function.

US

Duplex Doppler US is an attractive technique as a noninvasive screening test in that it does not require intravenous contrast material 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.

Two of the most frequently used parameters are peak systolic velocity (PSV) in the main renal artery and renal artery to aortic systolic ratio (RAR), both of which depend on a direct evaluation of elevated velocity in a stenotic segment of the renal artery. PSV cutoff values ranging from 180 cm/s to 300 cm/s have been proposed in various studies. Hua et al [9] showed a PSV of 200 cm/s to have a sensitivity of 91% and a specificity of 75%, whereas Motew et al [10] reported a PSV of 200 cm/s to have a sensitivity of 91% and a specificity of 96% and AbuRahma et al [11] reported a PSV of 200 cm/s to have a sensitivity of 73% and specificity of 82% for stenosis ≥60%. To improve specificity, some authors recommend a higher PSV threshold of 300 cm/s [3].

An elevated RAR value is also a useful criterion for identifying stenosis, because PSV may be elevated on the basis of hypertension without underlying RAS. The suggested RAR cutoff value also varies between authors, though an RAR of 3.5 is a commonly reported threshold value [12]. It is noted that identification of elevated PSV and RAR depends on adequate visualization of a stenotic segment of the renal artery, which may be impeded by patient body habitus, obscuring bowel gas, dense atherosclerotic plaques, and presence of accessory renal arteries. In these cases, distal criteria may be useful as an indirect indicator of stenosis. A parvus-tardus intrarenal waveform, with a small peak and a slow upstroke, is highly suggestive of a proximal stenosis [13]. This is reflected by an acceleration time of >70 milliseconds and loss of the early systolic peak. Though an elevated resistive index (RI), defined as $(\text{PSV} - \text{end-diastolic velocity})/\text{PSV}$, is not a specific indicator of RAS, an RI >0.80 has been reported to be a negative prognostic sign for response to revascularization [14,15]. However, other studies have not confirmed a significant difference in revascularization outcomes according to RI and have argued against using an elevated RI as a contraindication to revascularization [16,17].

Doppler US can also be used for detection of significant renal artery in-stent restenosis, though studies have shown that compared with native renal arteries, higher PSV and RAR values are indicative of stenosis in stented arteries. Chi et al [18], in a study of 67 patients with renal artery stents, found that a PSV of at least 395 cm/s or RAR of at least 5.1 was most predictive of significant in-stent stenosis. Similarly, Del Conde et al [19], in a study of 132 stented renal arteries, reported a mean PSV of 382 cm/s and RAR of 5.3 in arteries with >60% stenosis.

Although Doppler US is a preferred screening tool for RAS, it is time-consuming and highly operator dependent, and MRI or CT may be more reliable modalities for operators who are less experienced with US for RAS.

Nuclear Medicine
Renal scintigraphy was first used for evaluating renal function in the late 1950s. Initial attempts to use renography specifically for evaluating renovascular hypertension had a high rate of false-positive and false-negative results. Captopril was later added to the examination in an attempt to improve the accuracy of the test for diagnosing renovascular hypertension and for predicting blood pressure reduction after surgery or angioplasty. Administration of an angiotensin-converting enzyme inhibitor such as captopril leads to a decrease in glomerular filtration pressure, prolonged transit time of tubular agents such as Tc-99m-MAG3, and decreased uptake of glomerular agents such as Tc-99m-diethylenetriaminepentaacetic acid.

Captopril renal scintigraphy analysis is based on characterization of renal function deterioration when compared with a baseline study, with decreased glomerular filtration rate reflected in time-activity curves. Captopril renography is therefore a functional assessment of renal perfusion and function rather than a method of directly visualizing the vasculature. The sensitivity and specificity of this examination are decreased in patients without clinical features of renovascular hypertension and are also decreased in patients with bilateral RAS, impaired renal function, and urinary obstruction [20]. The reported sensitivity of captopril renal scintigraphy for renovascular hypertension ranges from 34% to 93%, with a meta-analysis of 14 studies between 1990 and 2000 by Vasbinder et al [21] showing a mean sensitivity of approximately 81%. There have also been inconsistent results regarding the predictive value of captopril renal scintigraphy in identifying patients who will respond to revascularization. High correlation between a positive result on captopril renal scintigraphy and reduction in blood pressure after intervention has been reported in some studies [22]. However, the predictive value has been dismissed in other studies, with reported positive predictive values as low as 51% [23-26].

In summary, captopril renal scintigraphy has decreased sensitivity and specificity in patients with bilateral stenosis and impaired renal function, but it can be a useful tool for detecting renovascular hypertension in appropriately selected patients. As a functional evaluation of renal perfusion and function, captopril scintigraphy can be useful to determine the physiologic sequence of a known stenosis and to assess the relative function of each kidney before intervention [27,28].

MRA
MRA is suited for noninvasive workup of RAS and has been widely applied in 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. Three-dimensional contrast-enhanced MRA with an intravenous injection of gadolinium-based contrast agent has been the backbone of MRI examinations of renal arteries, but noncontrast MRA with steady-state free precession (SSFP) and arterial spin labeling techniques has also been used for evaluating the renal arteries.

Several investigators report using angiography as the standard of reference, with the sensitivity of MRA ranging from 88% to 100% and the specificity ranging from 71% to 100% [29-31]. In a meta-analysis of 25 studies [32], the sensitivity and specificity of gadolinium-enhanced MRA were 97% and 85%, respectively. Solar et al [33] compared contrast-enhanced MRA with Doppler US using angiography as the reference and found contrast-enhanced MRA to be superior, with a sensitivity of 93% and a specificity of 93%, compared with US, with a sensitivity of 85% and a specificity of 84%. With the use of high-spatial-resolution small-field-of-view contrast-enhanced MRA techniques, it is possible to evaluate not only the main renal arteries but also the accessory renal arteries and distal stenosis. Improved gradient hardware and parallel imaging techniques have reduced acquisition times and improved spatial resolution. Another MR technique currently being investigated, blood oxygen level–dependent MRI, is able to assess renal oxygenation, which may allow for functional assessment in patients with RAS [34-36]. MRA may be used to evaluate in-stent stenosis and has been especially successful when nonferromagnetic stents such as platinum, nitinol, or cobalt-chromium are used, as compared with stainless steel stents [37-39].

CTA
Contrast-enhanced CTA provides accurate anatomic images of the renal arteries with isotropic data sets that enable the reconstruction of high-resolution images in any plane. As with conventional angiography, the disadvantages of this technique are its ionizing radiation and its use of nephrotoxic contrast material. Advantages compared with arteriography include less invasiveness, faster acquisitions, and multiplanar imaging [40]. Two

studies comparing CTA with digital renal arteriography have reported the sensitivity of CTA for detecting stenoses (>50% diameter) to be 88% to 96% and the specificity to be 77% to 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 [41,42]. Normal results from CTA virtually rule out RAS. Both maximum-intensity projection and volume-rendering techniques are useful and complementary in CT evaluation of RAS [43]. Secondary signs include poststenotic dilatation, renal atrophy, and decreased cortical enhancement. A threshold of 800 mm^2 for cortical area and 8 mm for mean cortical thickness seen on CT can be useful morphologic markers of atherosclerotic renal disease [44].

Like MRA, CTA is more accurate in diagnosing proximal rather than distal lesions, though in general CTA provides better depiction of branch renal arteries than MRA [45]. CTA can also be used to assess patency of renal stents [44,46,47]. Steinwender et al [48] described CTA evaluation of 95 renal artery stents in which 98% of the stents were assessable on CTA, and there was 100% sensitivity and 99% specificity for detecting in-stent stenosis.

Arteriography
Intra-arterial digital subtraction angiography (IADSA) is considered the reference standard for demonstrating RAS and is an integral part of angioplasty and stenting procedures. Angiography has high spatial resolution for evaluating the main renal arteries as well as the branch renal arteries. There is high interobserver agreement for identification of severe stenoses by angiography [49], but there is reported substantial interobserver variability in visual estimation of moderate RAS. IADSA allows for measurement of pressure gradients across a stenosis, providing assessment of its hemodynamic significance before intervention. A pressure gradient >20 mm Hg, or >10% of mean arterial pressure, is considered to be an indicator of hemodynamic significance [50,51].

Smith et al [52], in a small study of 19 patients, reported the sensitivity and specificity of intravenous digital subtraction angiography (IVDSA) to be as high as 87%. However, false-positive rates ranged from 26% to 37%, which they attributed to limited spatial resolution, subtraction artifacts, and quantum noise. Other reported limitations of this technique have included obscuration of renal artery stenoses by overlap with opacified mesenteric vessels and also suboptimal evaluation of fibromuscular lesions [53-55]. Wilms et al [55], in a study of 45 patients, found fewer false-positives, which they attributed to technical advances and software improvements. They also reported that IVDSA grading of stenosis was accurate in 94% of cases of atherosclerotic RAS but in only 56% of fibromuscular stenosis cases. Dunnick et al [56], in a prospective study of 94 patients, reported 100% sensitivity and 93% specificity for RAS, though the 100% sensitivity was achieved in part by including inadequate examinations as positive, and the authors acknowledged the limitations of IVDSA for evaluating vessels affected by fibromuscular dysplasia. Although good results can be achieved with IVDSA, its resolution is inferior compared with that of IADSA, and it is less sensitive than IADSA for evaluating fibromuscular dysplasia and atherosclerotic stenosis of branch vessels. In addition, the contrast dose is often substantially higher than in arteriography and requires central injection in the inferior vena cava or right atrium. For these reasons, IVDSA is not utilized as a screening examination for renovascular hypertension.

Venography
In patients with unilateral RAS, the ischemic kidney secretes increased renin, and there is relative suppression of renin release by the contralateral kidney. This results in asymmetry in renal vein renin levels. With bilateral RAS, there is also lateralization of renin secretion, with higher renal vein renin for the kidney with the greater degree of stenosis. This is the basis for renal vein renin assays for evaluation of renovascular hypertension. Various parameters have been described, including renal vein–to–inferior vena cava ratios and right renal vein–to–left renal vein ratios. Renal vein renin assays were initially considered the best means to predict response to revascularization in patients with suspected renovascular hypertension, with the majority of studies before 1980 supporting the validity of this procedure. However, later studies have shown a high rate of false-negative and false-positive results. Sellars et al [57] reviewed 37 cases and found a false-positive rate of 39% and a false-negative rate of 71%. Luscher et al [58], in a study involving 95 patients, reported a high sensitivity of 92% for a positive renal vein renin assay but a low specificity of 42% and a high number of both false-positive and false-negative results. Roubidoux et al [59] measured captopril-stimulated renal vein renin ratios in 133 patients and found a sensitivity of 65%, a false-positive rate of 47.8%, a positive predictive value of 18.6%, and a negative predictive value of 89.3%. Postma et al [25], in a retrospective study of 25 patients with documented RAS, found that a positive renal vein renin assay had a sensitivity of 72% and a specificity of only 29%. In general, the high rates of false-negative and false-positive studies limit the use of renal vein renin assays as screening tests for renovascular hypertension.

Variant 2: High index of suspicion of renovascular hypertension. Decreased renal function, eGFR <30 mL/min/1.73 m².

The selection of imaging modality and technique for evaluation of RAS may vary in the setting of decreased renal function primarily because of the risk of CIN with iodinated contrast material for CT and the risk of NSF with gadolinium-based contrast agents for MRI.

US

For patients with a high index of suspicion for renovascular disease and diminished renal function, duplex Doppler US is a preferred screening examination, especially at a site 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. The technical details of the examination and the threshold criteria are similar to those used for patients with normal renal function (see variant 1).

CTA

Depending on the degree of impaired renal function, contrast-enhanced CTA has been considered to be precluded because of potential nephrotoxicity of contrast material. However, the causal relationship between contrast material for CT and acute kidney injury has been disputed, and recent data suggest a low risk of clinically relevant CIN. Cutoff values for serum creatinine and estimated glomerular filtration rate (eGFR) beyond which iodinated contrast material would not be administered vary by institution, though eGFR is recognized to be a better indicator of baseline renal function than serum creatinine. Recent large studies from Davenport et al in 2013 and McDonald et al in 2014 indicate that intravenous iodinated contrast material is not an independent nephrotoxic risk factor in patients with a stable baseline eGFR of >45 mL/min/1.73 m² and that iodinated contrast material is rarely nephrotoxic in patients with a stable baseline eGFR of 30 to 44 mL/min/1.73 m² [60-63]. Conflicting results were obtained for patients with more severe renal dysfunction with an eGFR of <30 mL/min/1.73 m², with the 2013 Davenport et al study reporting an excess of acute kidney injury in these patients receiving intravenous contrast material versus controls but with the 2014 McDonald et al study showing no significant difference in acute kidney injury for contrast material recipients versus control patients with this baseline eGFR [8,60-63]. The ACR *Manual on Contrast Media* notes that if a threshold for CIN risk is used, an eGFR of 30 mL/min/1.73 m² has the greatest level of evidence [7]. Reduced iodine dose should be considered in patients with borderline renal function, but other parameters are similar to patients with normal renal function. Unenhanced CT does not provide useful diagnostic information regarding RAS.

MRA

Contrast-enhanced MRA may be precluded because of the risk of NSF with eGFR <30 mL/min/1.73 m². In these patients, unenhanced MRA techniques are available as an alternative to contrast-enhanced MRA to avoid the risk of NSF. Utsunomiya et al [64], comparing unenhanced SSFP MRA with CT or IADSA in 26 patients, found a sensitivity, specificity, positive predictive value, and negative predictive value of 78%, 91%, 64%, and 96%, respectively. Mohrs et al [65], comparing an SSFP technique with contrast-enhanced MRA in 45 patients, found a sensitivity, specificity, positive predictive value, and negative predictive value of 75%, 99%, 75%, and 99%, respectively, for detecting renal artery stenoses >50%. Braidy et al [66] compared an unenhanced SSFP technique to contrast-enhanced MRA with a sensitivity, specificity, positive predictive value, and negative predictive value of 85%, 96%, 94%, and 96%, respectively, but emphasized that when stenosis is found, other modalities should be employed for better estimation. Albert et al [67], in a report of a multicenter trial of 75 patients, compared an unenhanced MRA technique to contrast-enhanced CT with a sensitivity of 74% and specificity of 93% for >50% stenosis.

Arteriography and Venography

Impaired renal function may also limit the use of iodinated contrast material for angiography-based interventional procedures. Carbon dioxide, supplemented by limited use of gadolinium-based agents when mild to moderate decreased function allows, have both been used as alternatives to iodinated contrast in patients for whom iodinated contrast is contraindicated, though images obtained with these alternative contrast agents are less desirable when compared with those obtained with iodinated contrast material [68,69].

Nuclear Medicine

Captopril renal scintigraphy is not a reliable test in patients with poor renal function.

Summary of Recommendations

- Given the limited scenarios in which testing for RAS is considered appropriate, the decision to perform diagnostic imaging to identify RAS should ideally be based on a multidisciplinary assessment of an individual patient's clinical presentation, comorbidities, and likelihood of response to intervention.
- For patients with normal renal function, contrast-enhanced CTA and MRA are preferred modalities. US is also an effective modality.
- For patients with decreased renal function with eGFR <30 mL/min/1.73 m^2, US is a preferred screening examination. Unenhanced MRA techniques are available as an alternative to contrast-enhanced MRA to avoid the risk of NSF in these patients.

Summary of Evidence

Of the 70 references cited in the *ACR Appropriateness Criteria® Renovascular Hypertension* document, 2 are categorized as therapeutic references including 1 well-designed study. Additionally, 66 references are categorized as diagnostic references including 5 well-designed studies, 15 good-quality studies, and 16 quality studies that may have design limitations. There are 31 references that may not be useful as primary evidence. There are 2 references that are meta-analysis studies.

The 70 references cited in the *ACR Appropriateness Criteria® Renovascular Hypertension* document were published from 1964 to 2017.

Although there are references that report on studies with design limitations, 21 well-designed or good-quality studies provide good evidence.

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. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [70].

Relative Radiation Level Designations		
Relative Radiation Level*	**Adult Effective Dose Estimate Range**	**Pediatric Effective Dose Estimate Range**
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies".		

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

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