

# Imaging for Renal Artery Stenosis and In-Stent Restenosis

Duplex ultrasound, CTA, and MRA for the imaging diagnosis of renal artery disease.

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**R**enal artery stenosis (RAS) can cause a range of clinical disorders. Affected patients can present with uncontrolled hypertension despite taking multiple antihypertensive medications. Heart failure exacerbations and flash pulmonary edema episodes have been widely documented as signs of hemodynamically significant RAS.<sup>1-3</sup> In addition, renal insufficiency can occur as a result of RAS. Most importantly, the presence of RAS increases the risk of cardiovascular morbidities and mortality.<sup>1,2</sup> This likely reflects the overall atherosclerotic burden involving the aorta and its associated vascular beds.

The majority of RAS cases are due to atherosclerosis.<sup>2,3</sup> This process is associated with endothelial abnormality and dysfunction.<sup>3</sup> It is driven by inflammation via cellular

and cytokinetic pathways, resulting in vessel remodeling and luminal narrowing.<sup>3</sup> In severe cases, atherosclerosis may lead to vessel narrowing and occlusion, causing renal dysfunction. A subset of patients, predominantly young women with resistant hypertension, have RAS due to an abnormality of the muscular medial layer of the vessel, termed *fibromuscular dysplasia* (FMD).<sup>2,3</sup> It has a characteristic “string of beads” appearance on angiography as opposed to the luminal narrowing reflective of the atherosclerotic process and is noninflammatory in nature.<sup>2,3</sup>

Diagnosis of RAS begins with the clinical history. Clinical scenarios that include uncontrolled hypertension in a patient with a history of controlled blood pressure, new-onset hypertension in a young woman, presentation of unexplained renal insufficiency, unexplained flash pul-

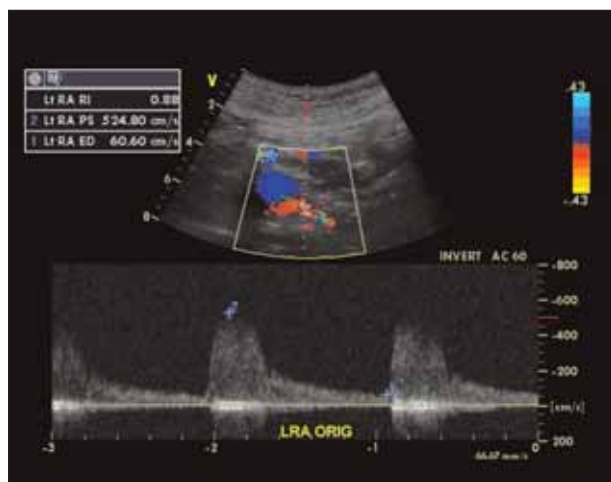


Figure 1. Color duplex ultrasound (DU) of the left renal artery with elevated peak systolic velocity (PSV) and color aliasing. The renal-to-aortic PSV ratio (RAR) was 6.8.



Figure 2. B-mode image of a left renal artery stent.

**TABLE 1. RENAL ARTERY STENOSIS: INDICATIONS FOR SCREENING**

- Hypertension age <30 or severe hypertension age >55
- Unexplained flash pulmonary edema
- Decline in renal function with ACEI or ARB therapy
- Unexplained renal size discrepancy >1.5 cm
- Accelerated, resistant, or malignant hypertension
- Multivessel coronary artery, peripheral arterial, and carotid diseases
- Unexplained renal dysfunction
- Unexplained congestive heart failure

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blockade.

monary edema, or worsening renal function after the initiation of angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers are highly suspicious for RAS. Patients with a history of atherosclerosis in multiple vascular beds, such as peripheral or carotid arterial disease, also have a higher incidence of RAS.<sup>2-5</sup> Moreover, significant RAS is present in up to one third of patients undergoing diagnostic coronary angiography.<sup>4</sup> Nonspecific laboratory findings present in RAS include an elevated serum creatinine level and a decreased urinary creatinine clearance. The urinalysis may exhibit proteinuria.<sup>3,4</sup> Common indications for RAS screening are highlighted in Table 1.

Proper diagnosis is essential to the treatment and follow-up of RAS. Clinical history and laboratory abnormalities suspicious for RAS require confirmation by imaging modalities. Regardless of the mechanism, medical management and/or percutaneous revascularization with/without stents are the standard of care. In patients who receive renal stent placement, imaging follow-up of stent patency remains crucial. Catheter-based angiography remains

**TABLE 2. ULTRASOUND CRITERIA FOR RENAL ARTERY STENOSIS**

Parameter	Degree of Stenosis
Peak systolic renal artery velocity to peak systolic aortic velocity ratio $\geq 3.5$	$\geq 60\%$
Peak systolic renal artery velocity >180 cm/s	$\geq 60\%$
End diastolic renal artery velocity >150 cm/s	$\geq 80\%$

**THE DOPPLER SHIFT EQUATION**

$$\text{Doppler shift} = 2fV\cos\Theta/C$$

f = transducer frequency

V = red cell velocity

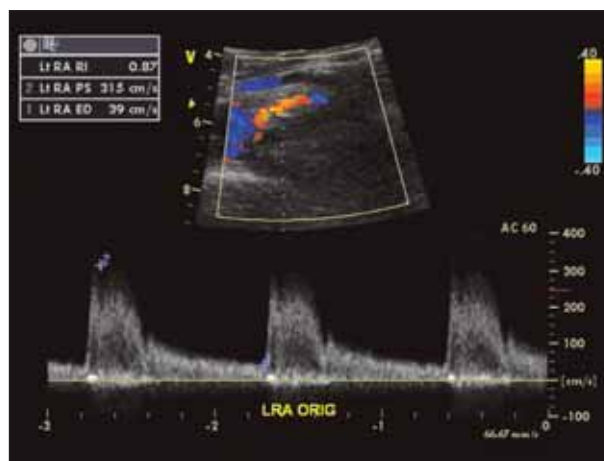
C = blood velocity constant

$\Theta$  = angle of insonation

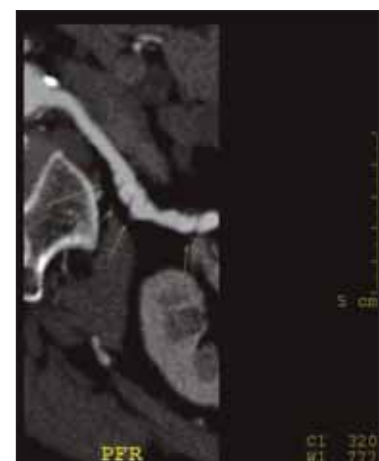
the gold standard for the confirmation of RAS and renal in-stent restenosis (ISR). However, noninvasive imaging techniques have now replaced invasive angiography as the screening test of choice for RAS and renal ISR.

**NONINVASIVE IMAGING****Duplex Ultrasound**

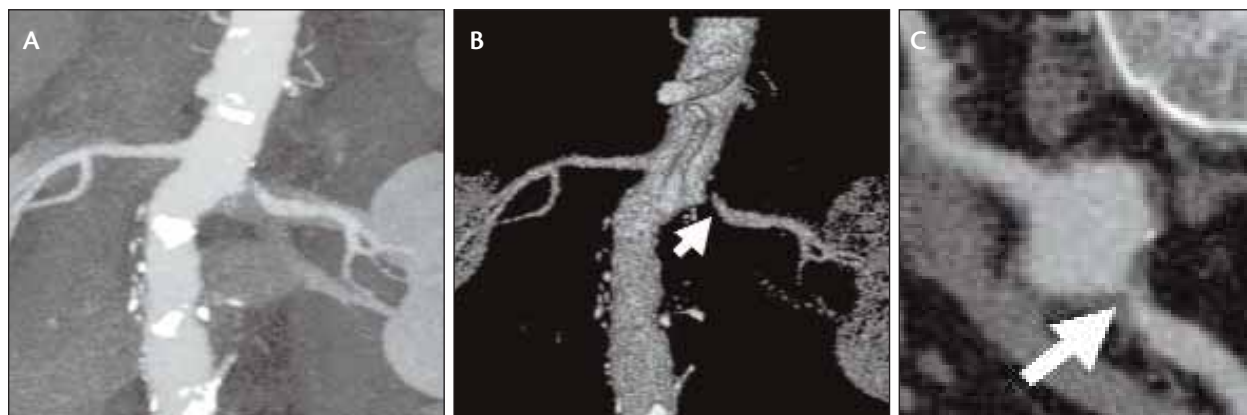
DU of renal arteries utilizes color Doppler with spectral analysis and has become one of the preferred screening modalities for RAS and renal ISR.<sup>6-9</sup> Ultrasound technology creates sound waves via the application of an electrical current to one or more piezoelectric elements located in the transducer. These waves propagate through tissue and may be absorbed, transmitted, scattered, and/or reflected. A portion of the reflected waves is captured by



**Figure 3.** Color US of the ISR in the left renal artery from Figure 2. Note the elevated PSV and turbulent spectral waveform.



**Figure 4.** Multiplanar CTA reconstruction of renal artery FMD.



**Figure 5.** CT angiography (CTA) reconstruction of the left RAS; the arrows point to the stenosis. Coronal maximum-intensity projection view (A). Coronal 3D rendering (B). Curve linear reconstructed view (C).

the ultrasound probe and processed into electrical signals, which are digitally encoded and can be translated into velocity measurements, grayscale (B-mode), and color (color Doppler) images (Figures 1 through 3). In renovascular imaging, a low-frequency (2–5 MHz) curved array transducer is typically used to insonate the aorta and renal vessels, ideally at a 60° angle.<sup>5</sup> The ultrasound machine provides erythrocyte flow velocity based on the Doppler shift equation (see The Doppler Shift Equation); as a result, PSV and end diastolic velocity (EDV) can be determined.

Typically, velocity information at the origin, proximal, mid, and distal segments of the renal artery is taken. Aortic velocity is taken at the level of the renal artery. Along with PSV, RAR—using the highest PSV in the renal arterial segment as the numerator and aortic PSV as the denominator—can also be used to determine the percent stenosis (Table 2). From published literature, PSV >180 cm/s and/or RAR  $\geq 3.5$  best determine  $\geq 60\%$  angiographic RAS.<sup>2,5</sup> EDV  $\geq 150$  cm/s is specific for detecting  $\geq 80\%$  angiographic stenosis.<sup>5</sup> The color Doppler images and waveforms



**Figure 6.** CTA of right renal artery stent ISR: curve linear reconstructed view; the arrow points to the area of ISR.



**Figure 7.** Magnetic resonance angiography (MRA) of left RAS in coronal view; the arrow points to the area of stenosis.



**Figure 8.** MRA of left RAS in oblique view; the arrow points to the area of stenosis.



**Figure 9.** MRA of renal artery FMD; the arrowhead points to the area of interest.

may demonstrate turbulent flow and abnormal signal morphology in the stenotic segments of the renal arteries, along with elevated velocity as described previously. Overall, using this information, DU is able to detect hemodynamically significant RAS with a positive and a negative predictive value of >90% and a 96% accuracy rate.<sup>5</sup>

Ultrasound imaging also allows for the measurement of kidney size. A kidney length of <8 cm typically represents severely impaired renal function and an organ unlikely response to renal revascularization.<sup>2</sup> A renal size discrepancy of 1.5 cm between the kidneys should raise suspicion for significant unilateral RAS.<sup>2</sup> The renal resistive index (RI), defined as  $(PSV - EDV) / PSV$  within renal parenchyma, is calculated and can provide important information on the success of renal revascularization.<sup>10</sup> Patients with an RI above 0.8 may receive less benefit from renal revascularization.<sup>2,5,10</sup>

In patients who have undergone stent placement, DU is also the test of choice for detecting hemodynamically significant renal ISR.<sup>6,7,11</sup> Renal angiography after stent placement has revealed 6- to 12-month ISR incidences of up to 39% in case reports; however, meta-analyses demonstrate an average ISR incidence of 16% to 17%.<sup>2,7-9,12,13</sup> Stents plated with carbon or gold have not been shown to reduce restenosis rates compared to bare-metal stents; however, drug-eluting stents have demonstrated higher patency rates.<sup>13-16</sup> Variable long-term success has been

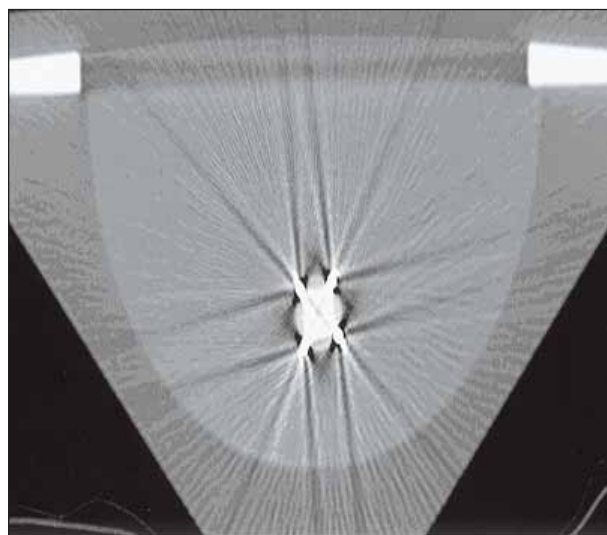
reported with brachytherapy for RAS.<sup>17,18</sup> ISR rates may be higher in patients with histories of smoking and stent diameters <6 mm.<sup>11,19,20</sup>

From the available literature, the velocity criteria developed for the native unstented renal arteries may not be applicable to the stented vessels because compliance changes after metal stent placement.<sup>6,7,21</sup> Both Napoli et al<sup>6</sup> and Bakker et al<sup>7</sup> have demonstrated that using the current velocity criteria for an unstented native renal artery may incorrectly estimate the true incidence of ISR, which may lead to unnecessary renal angiography and its associated cost and potential complications. Nonetheless, DU is still a viable tool to screen for renal ISR, but velocity criteria for ISR should be established and validated.

The disadvantages of renal DU include decreased reliability in a patient who is not fasting and/or is obese, a high level of operator dependence, and poor detail resolution.<sup>13</sup> The advantages of renal arterial duplex are its availability, safety, and lack of radiation or contrast exposure. Combined with the above, the high sensitivity of DU makes it the screening test of choice for RAS.

### Computed Tomographic Angiography

Computed tomography (CT) can be used to screen for RAS. CT technology involves the generation of x-rays, which pass through tissue in multiple cross-sectional planes around a central point and undergo variable absorption and/or transmission. A detector captures and converts the transmitted x-rays into a digital signal, which is processed by a computer and can be reconstructed into a two-dimensional (2D) or three-dimensional (3D) image of the area of interest. The use of intra-

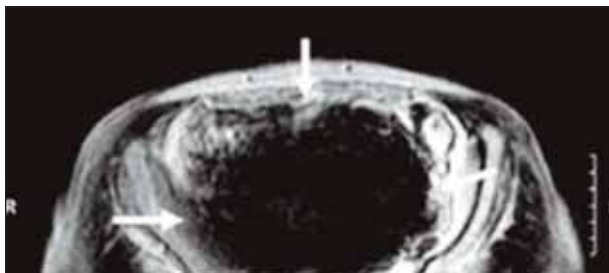


**Figure 10.** CTA of the stent with the x-ray beam hardening artifact.





**Figure 11.** The arrow points to the renal stent on MRA; the stent layout is not typically seen on MR due to the metal composition.



**Figure 12.** MRA of signal dropout from the metal stent.

venous contrast allows CT technology to distinguish vasculature from surrounding tissues with a resolution not available via ultrasound. A single-detector CT scanner initiated this cross-sectional image acquisition technique. Over the past 20 years, CT evolved from single-detector (SDCT) into multidetector (MDCT) imaging, yielding faster image acquisition and improved image resolution. CTA has been shown to detect hemodynamically significant stenoses with a sensitivity of 91% to 94% and a specificity of 93% to 97% compared to digital subtraction angiography (DSA).<sup>22</sup> The advancement of MDCT has also improved the visualization of distal renal arteries and has led to improved contrast efficiency and decreased radiation exposure. Single breath-hold image detection is a significant improvement with MDCT compared to the longer breath holds required for SDCT. Figures 4 through 6

demonstrate CTA images of RAS and renal ISR.

The main advantage of CTA is that it is less invasive, which eliminates puncture site complications that may be encountered with DSA.<sup>23</sup> Other advantages of CTA include high spatial resolution with excellent sensitivity and specificity profiles. It is also more widely available and less costly compared to DSA.<sup>22</sup> The disadvantages of CTA include the risk of contrast-induced nephrotoxicity, contrast allergies or anaphylaxis, and radiation exposure. Where indicated, patients with a history of shellfish allergies or iodinated contrast allergies may safely undergo CTA after premedication with steroids and histamine antagonists.<sup>22</sup>

### Magnetic Resonance Angiography

MRA is a viable alternative for noninvasive renal artery imaging. MRA uses the physics principle of nuclear magnetic resonance to detect radio signals emanating from hydrogen atoms that have been excited within a magnetic field.<sup>22</sup> A detector in the MR imaging machine processes the signals and is able to reconstruct a 2D or 3D representation of the anatomy. The vasculature has traditionally been rendered with time-of-flight or phased-contrast (PC) processing. Renal systolic velocity may be measured with electrocardiogram-gated 2D phased contrasted flow measurement, and 3D PC imaging may reveal evidence of turbulent flow at hemodynamically significant stenoses. The use of 3D gadolinium-enhanced MR (GEMR) imaging has improved visualization of the vasculature and shortened image acquisition time compared to traditional rendering techniques.<sup>24</sup> GEMR compares favorably with DSA for stenosis up to 1 to 2 mm, with sensitivities and specificities above 90%.<sup>22</sup> Figures 7 through 9 demonstrate MRA images of RAS.

The advantages of MRA include the lack of radiation exposure, the lack of iodinated contrast exposure, and superior renal parenchymal detail compared to CTA.<sup>24</sup> MRA also has a number of disadvantages, including its usefulness may be limited in patients with claustrophobia, metal implants, and unfavorable body habitus; it overestimates the degree of stenosis; the accuracy of findings are susceptible to motion artifacts; and gadolinium chelate is associated with the development of nephrogenic systemic fibrosis (NSS), an incurable systemic condition that is associated with disability and death.<sup>22,24-27</sup> This condition typically occurs in patients with acute or chronic azotemia with glomerular filtration rates  $\leq 30$  mL/min.<sup>26,27</sup> In the past, MRA was preferred over CTA in patients with renal insufficiency, but since the discovery of NSS, such a practice can no longer be recommended. Additional disadvantages of MRA include inadequate visualization of metal stents due to signal

**TABLE 3. IMAGING IN RENAL ARTERY STENOSIS**

Modality	Pros	Cons	Sensitivity <sup>2</sup>	Specificity <sup>2</sup>
Color duplex ultrasound	<ul style="list-style-type: none"> <li>• No radiation</li> <li>• No contrast exposure</li> <li>• Relatively low cost</li> </ul>	<ul style="list-style-type: none"> <li>• Technician dependent</li> <li>• May be limited by body habitus</li> <li>• Limited image resolution</li> </ul>	84%–98%	62%–99%
Multidetector CTA	<ul style="list-style-type: none"> <li>• Good three-dimensional resolution</li> </ul>	<ul style="list-style-type: none"> <li>• Caution with iodinated contrast exposure in patients with renal insufficiency</li> <li>• Radiation exposure</li> <li>• Cost</li> </ul>	91%–92%	99%
Magnetic resonance angiography	<ul style="list-style-type: none"> <li>• Good three-dimensional resolution</li> <li>• No radiation exposure</li> </ul>	<ul style="list-style-type: none"> <li>• Caution with gadolinium exposure in patients with renal insufficiency</li> <li>• Contraindicated with metal implants</li> <li>• Unreliable detection of stent restenosis with metal stents</li> <li>• Cost</li> </ul>	90%–100%	76%–94%

dropout because metal disrupts magnetic fields<sup>22</sup> and a prolonged testing time for MRA compared to CTA.<sup>22</sup> Relative strengths and weaknesses of the above noninvasive modalities are presented in Table 3.<sup>2</sup> Imaging modalities such as captopril scintigraphy and renal vein renin measurement are no longer recommended for RAS screening.

#### CTA and MRA Imaging of a Renal Stent

Metal vascular stents are known to cause artifacts that can partially or totally obscure the stented vessel lumen on earlier generations of CTA and MRA.<sup>28,29</sup> On CTA, stents cause artifacts that are characterized by an arti-

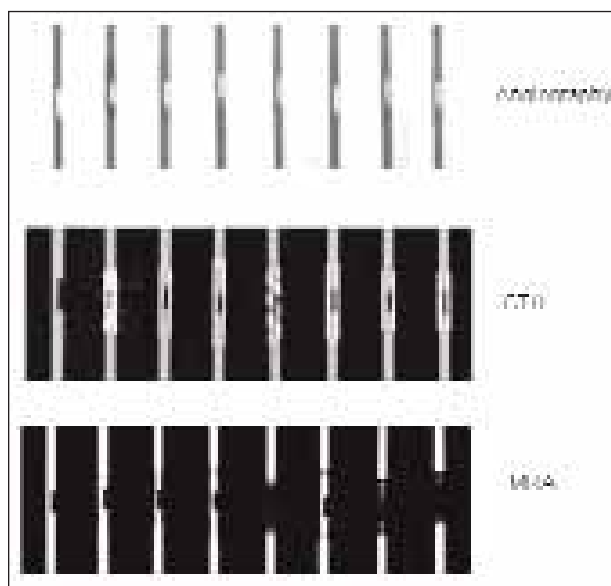
cial luminal narrowing and decreased intraluminal attenuation values.<sup>29</sup> These artifacts are caused by hardening of the x-ray beam (Figure 10). With the advent of MDCT, many of the imaging obstacles were overcome. Maintz et al<sup>30</sup> have demonstrated that MDCT is able to detect stenosis >50% with great accuracy in most commercially available stent compositions, including stainless steel, nitinol, and cobalt-based alloys except for tantalum.

On MRA, metal intravascular stents can cause susceptibility artifacts that lead to an intraluminal signal decrease or a signal loss (Figures 11 and 12).<sup>28</sup> These artifacts are mainly caused by susceptibility gradients around the stent material from the shielding effects of the conductive stent material, eddy currents, and, less importantly, flow.<sup>31</sup> According to published studies,<sup>30,32</sup> nitinol stents cause smaller artifacts when compared to those caused by stainless steel stents, but even nitinol stents do not allow artifact-free visualization on MR images (Figure 13).

#### CONCLUSION

Color DU, CTA, and MRA—which carry sensitivities of up to 96% to 100%—have become the preferred screening tests for patients with suspected RAS. These noninvasive modalities eliminate the risk of access site complications from DSA and may provide additional functional information about the condition of the kidneys. The benefits and risks of screening with one modality over another should be considered for each patient. When these tests are nondiagnostic, DSA may be performed. ■

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**Figure 13. Stent composition and imaging modality.**

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