Current Advances in the Diagnosis and Treatment of Renal Artery Stenosis

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Renal artery stenosis (RAS) is a common condition associated with hypertension and renal insufficiency. The high prevalence of RAS patients with coronary and lower extremity vascular disease has been well established. Fibromuscular dysplasia in young females and atherosclerosis in patients over the age of 55 are the most common causes. Poorly controlled hypertension refractory to medical therapy, worsening of renal function, and flash pulmonary edema may point to underlying RAS. Duplex ultrasonography and magnetic resonance angiography have largely replaced captopril scanning for RAS screening. However, renal angiography still remains the gold standard to diagnose RAS. Treatment options include medical therapy, angioplasty, and surgery. In general, patients with a stenosis greater than 50%, a translesional systolic pressure gradient greater than 15 mm Hg, and difficult-to-control hypertension and/or worsening renal insufficiency are candidates for renal revascularization. Percutaneous transluminal revascularization has evolved to become the preferred revascularization therapy because it is a less invasive and more cost-effective alternative to surgery and is associated with high technical success, as well as a low complication rate. The natural history of RAS is to progress over time, leading to renal artery occlusion, loss of renal mass, worsening of renal function, and, ultimately, end-stage renal disease. It is therefore important to aggressively screen, recognize, and treat the entity early in its course.
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Key words: Renal artery disease • Renal insufficiency • Hypertension

Although a definition of renal artery stenosis (RAS) has not been clearly established, it is generally defined as having at least 1 main renal artery with a stenosis greater than 50%.[1–4] Other factors that have been taken into consideration are a translesional systolic pressure gradient (TSPG) greater than 15 mm Hg or clinical evidence of a possible adverse effect, such as difficult-to-control hypertension or worsening renal insufficiency.[5]

Epidemiology

Atherosclerosis is a systemic illness that often affects multiple vascular trees in a given patient. The true epidemiology, including the incidence and the prevalence of renal artery disease, is less well known. The most likely reason is that the majority of epidemiological data has been derived from studies of patients undergoing other procedures, such as cardiac catheterization. The prevalence of RAS in an elderly cohort has been reported to be 6.8%.[6] A high prevalence of RAS in association with coronary and lower extremity vascular disease has been well established.[7–14] RAS coexists in approximately 15%–23% of coronary disease, 28%–38% of aorto-iliac disease, and 45%–59% of lower extremity vascular disease.[15] An autopsy study of more than 2000 patients who died from stroke revealed that 10% of the cases had at least 1 RAS of more than 75%.[16,17] The prevalence of RAS increases with age and it is found in 7% of patients over the age of 65.[18]

Renal ischemia due to RAS is an important cause of reversible hypertension and renal insufficiency. RAS exists in 1%–5% of the 60 million Americans with hypertension.[19–21] Atherosclerotic RAS accounts for 67% of renovascular hypertension patients.[22] Renovascular hypertension leads to malignant hypertension in 10%–45% of patients, and represents 10%–20% of end-stage renal disease and 5%–15% of renal failure patients over 50 years of age.[22] In 2000, the annual incidence of end-stage renal disease was estimated to be approximately 100,000 and prevalence was estimated to be 372,407 and increasing rapidly. It is estimated that by 2010, approximately 700,000 patients will be on hemodialysis, with 10%–15% secondary to RAS. By 2010, it is estimated that there will be more than 650,000 cases of end-stage renal disease in the United States. It has been suggested that 2.1% of all new cases of end-stage renal disease are due to RAS.[23] In addition, irrespective of how renal disease severity is classified (degree of albuminuria or proteinuria, estimated glomerular filtration rate, or presence of end-stage renal disease), 10-year mortality for severe renal abnormalities is extraordinarily high (107/1000 person-years) compared with that predicted by the Framingham data with multiple risk factors (25/1000 person-years).[24]

Ethnic variations in chronic kidney disease are well established. African Americans are more likely to have end-stage renal disease secondary to hypertension[25] and develop end-stage renal disease a decade earlier than their white counterparts.[26] They are less likely to have RAS[23] or to undergo peritoneal dialysis and renal transplantation.[27] Dialysis is likely to be initiated later for Asian Americans and Hispanic Americans with end-stage renal disease than for whites.[28] However, once dialysis is initiated, whites have a higher mortality rate than their African American or Asian American counterparts.[29,30]

Pathophysiology

Atherosclerosis involves a number of highly interrelated processes, including dyslipidemia, platelet activation, thrombosis, endothelial dysfunction, inflammation, oxidative stress, vascular smooth muscle activation, altered matrix metabolism, remodeling, and genetic factors.[31] RAS decreases blood flow to the affected kidney, inducing ischemia followed by an activation of the renin-angiotensin system. Subsequently, endothelin, angiotensin II, and oxidative stress lead to vascular remodeling due to fibrogenic cytokines and ultimately result in renovascular hypertension and irreversible tissue damage.[32]

In general, more than 90% of RAS cases are due to atherosclerosis involving the ostial or proximal renal artery with plaque extending into the perirenal aorta.[33] Most of these patients are men and have a history of smoking. Half the patients have dyslipidemia and 1 in 5 suffers from diabetes.[16] Fibromuscular dysplasia, with a characteristic beaded angiographic appearance involving the distal two-thirds of the main renal artery, accounts for 10% of RAS cases, mainly in young females (15–50 years of age). The risk factors for developing RAS are essentially the same as for other atherosclerotic vascular diseases, including age, hypertension, diabetes mellitus, and dyslipidemia. Predictive variables include age, reduced high-density lipoprotein, and an increased systolic blood pressure.[18]

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Clinical Features

Most patients remain clinically asymptomatic because of the large functional kidney reserve, which permits normal serum creatinine levels despite a marked deterioration in total glomerular filtration rate. There is little or no change in renal function even if half the nephrons of a normal kidney are destroyed. Incidental RAS is commonly identi-

Table 1
Clinical Manifestations of Renal Artery Stenosis

- Asymptomatic
- Poorly controlled hypertension refractory to medical therapy
- Worsening renal function
- Flash pulmonary edema
- Cardiac disturbance syndrome

fied during imaging of other locations, such as coronary (18%–24%) and peripheral vascular (44%–50%) angiography.[6] However, RAS may have serious sequelae such as progressive loss of renal function and dialysis if undetected.[3,34–36]

RAS has 2 principal clinical manifestations: renovascular hypertension as a result of renin-angiotensin-aldosterone pathway activation, and ischemic nephropathy as a consequence of reduced glomerular filtration and renal mass loss. Clinical features suggesting RAS are abrupt onset of hypertension in persons over 50 years of age, an accelerated or marked rise in previously adequately controlled blood pressure, malignant hypertension, or hypertension refractory to 3 or more antihypertensive agents (Table 1). Presence of a flank bruit, unexplained congestive heart failure, atherosclerotic disease affecting other vasculature, and unexplained hypokalemia may be the supportive findings. Ischemic nephropathy manifests as worsening serum creatinine level, a rise in creatinine after institution of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB), and a small kidney size identified during imaging. Patients at a higher risk of having RAS often have 1 or more of the following conditions: multivessel coronary artery disease, peripheral vascular disease, unexplained azotemia, azotemia with ACEI/ARB therapy, malignant or resistant hypertension, onset of hypertension at 55 years of age, flash pulmonary edema, and the presence of hypertensive heart disease.[5]

Diagnosis

Diagnostic evaluation of RAS can be broadly categorized into physiologic and imaging assessment (Table 2). Physiologic tests include peripheral plasma renin activity (PRA), captopril-stimulated PRA, and captopril renal scintigraphy. The PRA has a low predictive value, whereas captopril scintigraphy has sensitivity and specificity of 90%.[37,38] However, captopril renal scintigraphy may be influenced by renal parenchymal disease and obstructive uropathy.

In situations of high clinical suspicion, an imaging modality should be used to establish the diagnosis of RAS. A variety of noninvasive tests are available for the diagnosis of RAS, including duplex ultrasonography, computed tomography (CT), and magnetic resonance imaging and magnetic resonance angiography (MRI/MRA).[39–44] Renal artery duplex ultrasonography has emerged as an inexpensive but valuable diagnostic tool that can diagnose RAS with precision, as well as exclude patients without the disease if performed by an experienced technician.[45,46] A renal-to-aortic ratio (RAR) greater than or equal to 3.5 and peak systolic velocity (PSV) greater than 200 cm/s correspond with a stenosis of 60%–99%. In one prospective study, renal duplex ultrasonography demonstrated 98% sensitivity and 99% specificity.[47] When compared to angiography, renal duplex ultrasonography demonstrated a sensitivity and specificity of 84%–98% and 62%–99%, respectively.[48] Renal duplex may also be used to predict a response in blood pressure control or renal function after revascularization. If resistance within the renal circulation, measured as resistive index (RI), is greater than 80, the chances of improvement are unlikely.[49,50] No remarkable improvement in blood pressure (97% of the patients) or renal function (80% of the patients) was noted if the baseline RI was greater than or equal to 80.[50] Renal duplex ultrasonography is also utilized to determine the adequacy of renal artery stent revascularization and can image the entire artery despite metallic endoprosthesis. However, it has its own inherent limitations, such as a steep learning curve, operator dependency, difficulty in obese patients, and lack of sensitivity and specificity in identifying accessory renal arteries.[51]

Computed tomographic angiography (CTA) has a sensitivity of 89%–100% and a specificity of 82%–100% for the detection of RAS.[52–58] Because CT requires larger

Table 2
Diagnostic Modalities Used to Diagnose Renal Artery Stenosis

Serial Number	Test	Sensitivity (%)	Specificity (%)
1	Captopril scan	85–90	90
2	Renal duplex	98	99
3	CT	89–100	82–100
4	MRI/MRA	91–100	71–100
5	Angiography	98	100

amounts of contrast, its use in azotemic patients has been somewhat limited. However, the newer 16-slice CT scanners, which can acquire better and clearer images in a shorter time with less contrast, are gaining popularity. Renal duplex or MRA may be the preferred modality in patients with impaired renal function. Abdominal MRA is increasingly being used to evaluate the renal arteries (Figure 1). Magnetic resonance angiography has a sensitivity of 91%–100% and a specificity of 76%–94%.[59–67] Gadolinium-enhanced MRA provides better quality images than the non-contrast–enhanced studies. Magnetic resonance angiography can also identify the accessory renal arteries approximately 80% of the time.[68] However, renal MRA is not useful in monitoring patients after renal artery stenting due to the artifact produced by the stent; however, the new cobalt-chromium stents are reportedly MRA compatible.

Renal angiography still remains the gold standard for diagnosing RAS with minimal risks. It should not replace appropriate noninvasive tests, but in many cases angiography is the first test performed because patients who have clinical evidence of RAS may need angiography of other vascular beds. Nonselective renal angiography can be safely and effectively performed at the time of cardiac catheterization using a small amount of contrast and nontraumatic, end-hole catheters for an accurate gradient measurement (Figure 2). Renal angiography should not be performed, however, without clinical indications and "drive-by" angiography should be avoided. RAS can be confirmed via angulated, 20° left and right anterior oblique views. Ostial disease involving the aorta, proximal or bifurcation location, and an increased incidence of bilateral disease with advancing age are the characteristics of RAS.[33] Nonnephrotoxic agents such as carbon dioxide and gadolinium may be beneficial in patients with renal insufficiency. Digital subtraction angiography (DSA) significantly improves the quality of renal artery angiography. Selective renal angiography is guided by the identification of vertebral bony landmarks. It is important to look for accessory renal arteries (Figure 3).

Although angiography identifies RAS, what constitutes significant stenosis is not clear. A TSPG, measured by an end-hole catheter, of 15 mm Hg to 20 mm Hg is considered to be clinically significant but has its own inherent limitations, such as lack of correlation with the angiographic degree of stenosis and artifactual overestimation of the extent of the disease.[69–71] The role of measuring the fractional flow reserve (FFR) using a 0.014" pressure-sensing guide wire in determining the significance of the lesion severity, reported in one study,[49] has not been well established.[72]

Treatment

Treatment decisions for the management of RAS should consider relative benefits and risks involved and must take into account the likelihood of blood pressure reduction, renal mass preservation, or both. In general, medical therapy is considered over revascularization in patients with underlying advanced nephropathy

Figure 1. *Magnetic resonance angiography (MRA) showing bilateral renal artery stenosis.*

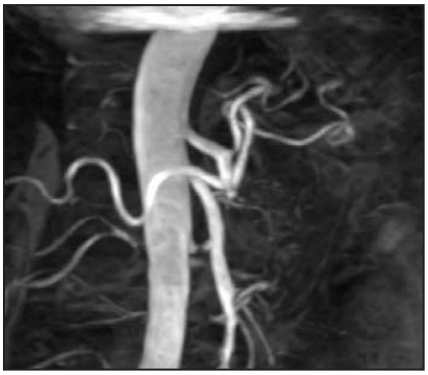


Figure 2. *Nonselective renal artery angiography performed by placement of a catheter in the suprarenal aorta using digital subtraction angiography (DSA) revealed patent bilateral renal arteries.*

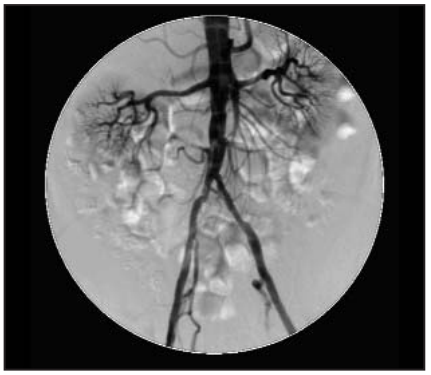


Figure 3. *Renal angiography showing accessory renal arteries supplying the upper* **(A)** *and the lower* **(B)** *poles of the left kidney.*

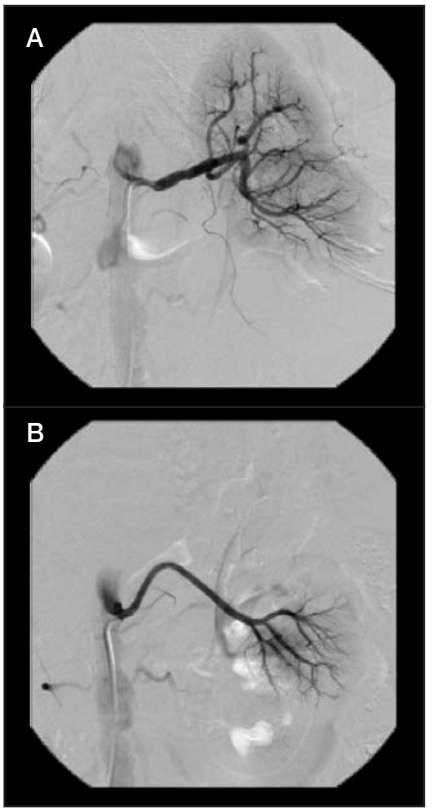


Table 3
Indications for Renal Artery Revascularization

≥ 50% stenosis
Translesional systolic pressure gradient ≥ 15 mm Hg
Difficult-to-control hypertension
Worsening renal function
Nonischemic pulmonary edema

manifested by unilateral RAS and a serum creatinine level greater than 2.5 mg/dL, renal length less than 7 cm, proteinuria greater than 1 g/d, severe diffuse intrarenal vascular disease, and target kidney RI greater than 80. Revascularization is favored in patients with bilateral RAS and a serum creatinine level greater than or equal to 1.5 mg/dL, unilateral RAS and fractional glomerular filtration rate less than or equal to 40%, ACEI-induced renal failure, hypertensive crisis, and nonischemic pulmonary edema (Table 3).

The ideal therapy after revascularization of the RAS is not well known. The treatment options for RAS include medical therapy, balloon angioplasty/stenting, and surgery. Aggressive risk-factor stratification is an essential component of RAS therapy. Anti-hypertensive, anti-cholesterol, and anti-platelet agents have not shown any effect on artery patency or progression of disease in the contralateral kidney.[17] A randomized trial (the STAR study) is underway to determine the effects of statins and anti-hypertensive and anti-platelet agents (with or without stent placement) upon the progression of renal dysfunction due to atherosclerotic RAS.[73] ACE inhibitors and ARBs have been shown to slow the progression of renal function deterioration due to unilateral renal artery disease both in diabetic and nondiabetic patients.[74–77] Additional agents to achieve a target blood pressure goal may be used. However, progression or worsening of RAS occurs in 10% of patients irrespective of medical treatment, leading to renal artery occlusion and irreversible renal function loss.[78,79] In addition, it is important to note that the drugs that interfere with the renin-angiotensin system may decrease perfusion and filtration of the kidney affected by the RAS. Patients with bilateral renal artery stenosis may develop renal insufficiency with ACEI/ARB therapy because the filtration of both kidneys may deteriorate. Serial renal function evaluation and duplex ultrasonography should be undertaken in patients with known RAS.

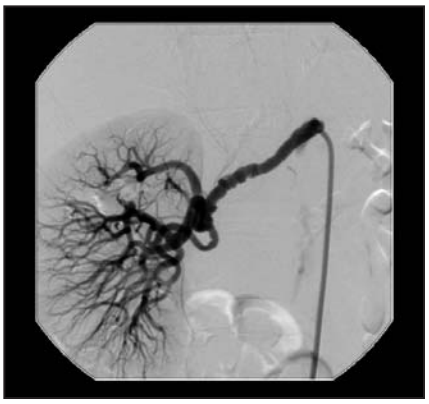
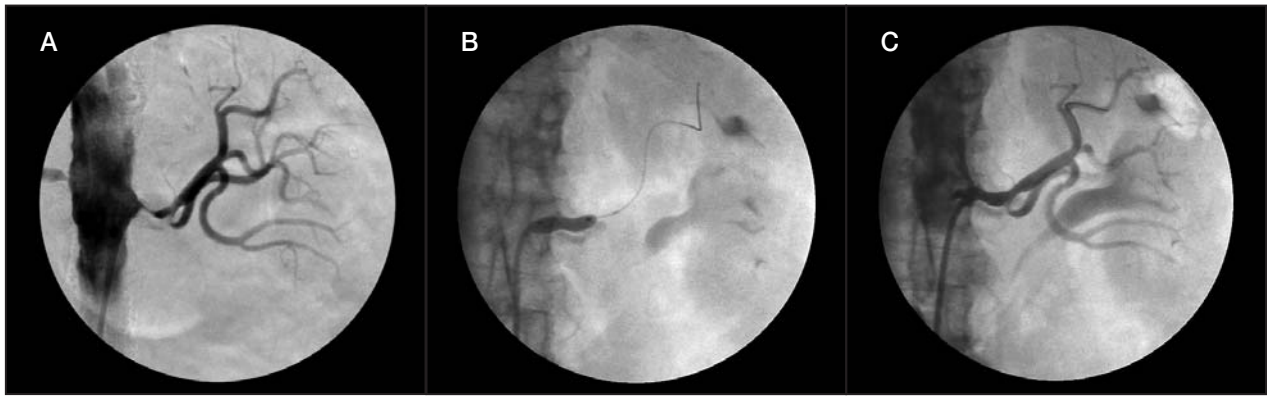


Figure 4. *Selective renal artery angiography demonstrating fibromuscular dysplasia of the right renal artery in a young female with hypertension.*

The treatment options for RAS include medical therapy, balloon angioplasty/stenting, and surgery.

Percutaneous transluminal angioplasty (PTA) or revascularization has evolved as a less invasive and more

Figure 5. *Left renal artery stenosis* **(A)** *successfully treated with renal artery stenting* **(B)**. *Repeat angiography showed a 0% residual stenosis* **(C)**.



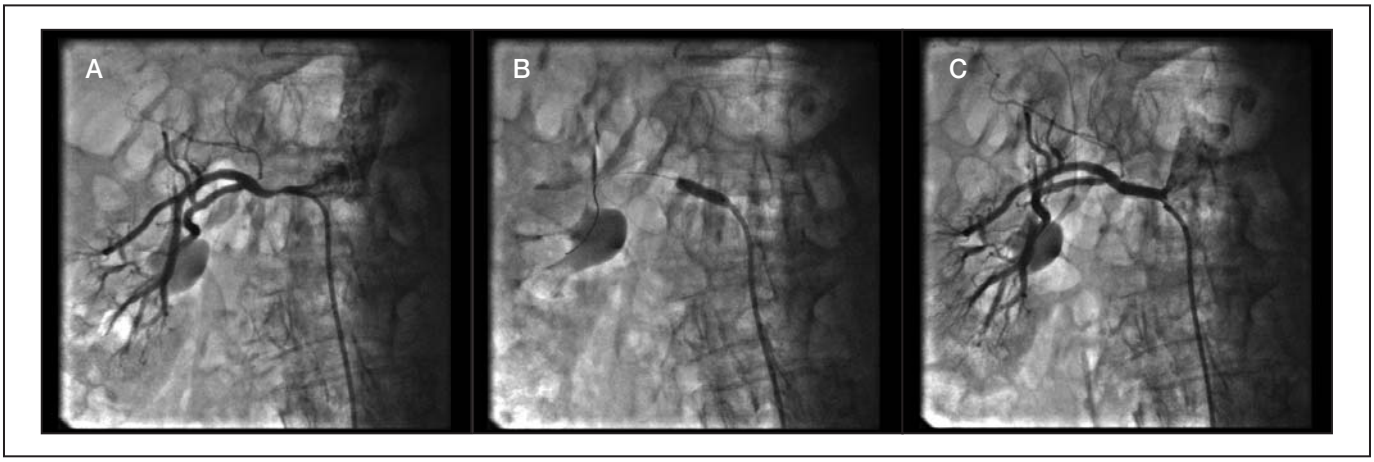
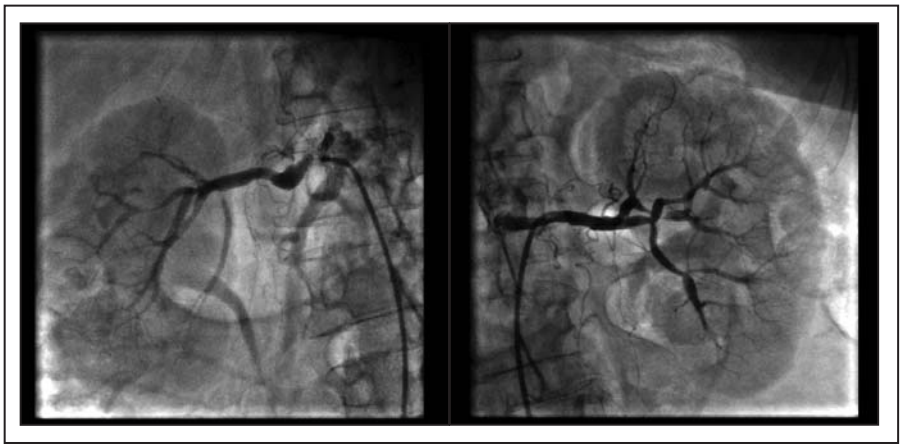


Figure 6. *Right renal artery stenosis* **(A)** *successfully treated with renal artery stenting* **(B)**. *Repeat angiography showed a 0% residual stenosis* **(C)**.

cost-effective alternative, typically associated with high technical success as well as low complication rates.[14] PTA is the treatment of choice for patients with fibromuscular dysplasia (Figure 4). The procedural success rates of renal artery revascularization have been reported as high as 98%–100%, with a low complication rate and excellent long-term patency rates of 85%–98%.[14,80–82] Success of percutaneous renal revascularization is defined as less than 50% residual stenosis after PTA, less than 10% residual stenosis after stenting, a 70% improvement in clinical symptoms, and a 50% decrease in angiographic stenosis.[83,84] Successful renal PTA has been shown to improve blood pressure in 38%–58% of patients and cure 3%–19% of patients with hypertension.[85–87] However, in some cases no improvement in blood pressure is encountered, most likely due to underlying essential hypertension, intrarenal vascular disease, or renal parenchymal disease. Renal artery stenting has been shown to effectively salvage deteriorating renal function (Figures 5 and 6).[88,89] Unfortunately, most studies suggest that renal artery revascularization rarely cures hypertension, although hypertension is improved in the majority of patients. The cure rates of PTA, stenting, and surgery range from 6%–21%.[90,91]

Surgical or percutaneous revascularization may improve hypertension and renal function, but 30%–40% of patients have no obvious benefit.[92–94] Postprocedural deterioration of renal function has been reported after renal PTA.[95–97] Renal artery revascularization, however, should not be expected to improve essential hypertension or renal parenchymal disease. The Dutch Renal Artery Stenosis Intervention Cooperative Study Group (DRASTIC) trial, a prospective, randomized study of medical therapy versus balloon angioplasty in 106 patients, demonstrated that renal artery PTA, in patients with unilateral RAS with serum creatinine less than 2.0, compared to medical therapy, had no effect on blood pressure. The study did, however, require a lesser number of medications to control blood pressure in the PTA group.[91] In addition, the study had many limitations, such as the inclusion of angioplasty as the only form of revascularization. In addition, no stenting was performed. A large number of patients

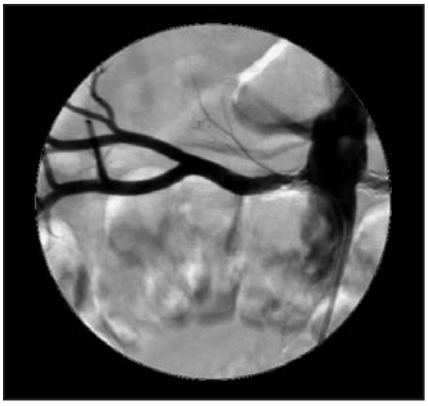
Figure 7. *In a patient with hypertension, chronic renal insufficiency, and elevated resistive indices revealed by duplex ultrasonography, renal angiography demonstrated severe main and peripheral renal artery atherosclerotic disease, making the patient an unsuitable revascularization candidate.*



had a crossover (44%) to the PTA arm due to failed medical therapy within 3 months. A renal artery occlusion rate of 16% in the medically treated patients versus 0% in the PTA group, showing at least an anatomical superiority of the treatment, was not included as a variable in the final analysis. Other possible explanations of variable response to revascularization include selection of patients with noncritical stenosis, presence of irreversible renal injury, distal embolization related to revascularization procedure, and coexisting primary hypertension (Figure 7).[50] In patients with underlying renal insufficiency, one-third experience stabilization whereas one-third have improvement in their renal function.[92]

Renal stenting in selected patients may slow the progression of renal failure and delay the need for renal replacement therapy.[93] A meta-analysis of 14 studies revealed renal artery stenting to be associated with high technical success rates (98%), low complication rates, and decreased in-stent restenosis rates (17%; Figure 8).[14] Hypertension was cured in 20% and improved in 49% of patients, whereas renal function improved in 30% and stabilized in 38% of patients treated with renal artery stenting. Technically, the shortest stent that covers the lesion adequately should be used. The stent must extend 1 mm to 2 mm into the aorta when treating ostial RAS. Optimal stent expansion should be ensured. Long-term results from a prospective registry have demonstrated recently that stenting of atherosclerotic RAS not only improves the mean arterial blood pressure significantly, with the effect seen immediately after the intervention, but also preserves renal function.[98] Baseline serum creatinine and left ventricular function have been shown to be independent predictors of improved renal function, whereas female gender, elevated baseline mean arterial blood pressure, and normal renal parenchymal thickness were independent predictors for a decrease in blood pressure after renal artery stenting.[99]

Figure 8. *In-stent restenosis of the right renal artery.*



The role of surgery in the treatment of RAS has been diminished due to recent advances in renal artery percutaneous interventions. After surgical revascularization, serum creatinine remains stable or improves in more than 70% of patients and deteriorates in the remainder.[100,101] However, renovascular surgery is associated with significant morbidity and mortality, especially in azotemic patients.[102] Surgery should be reserved for patients with comorbidities such as concurrent abdominal aortic aneurysm dissection, renal artery aneurysm, or failed PTA/stenting.[103]

Potential complications of renal artery revascularization include dissection, atheroembolic shower (< 3%), symptomatic systemic embolization (< 1%–8%), cholesterol embolization, artery occlusion leading to renal infarction (1.5%) and renal failure, and access site complications.[14,96,99,104] However, 30-day mortality rate is 0.5%–1% and only less than 1% of the patients need surgical salvage. The role of distal embolic protection with GuardWire™ (Medtronic, Minneapolis, MN) and FilterWire™ (Boston Scientific, Natick, MA) devices has been less well established.[105–108] Restenosis rates of 11%–30% have been cited with female gender, age greater than 65 years, smoking, and less than 6-mm dilation being the documented risk factors.[96] Vascular brachytherapy has shown some promise in small studies and case reports.[109–111]

Prognosis

An awareness of natural history is critically important in the subsequent management of patients with RAS. The natural history of RAS is to progress over time leading to renal artery occlusion, loss of renal mass, and worsening of renal function. Risk factors associated with a more rapid deterioration include hypertension, proteinuria, dyslipidemia, severity of renal impairment at the time of diagnosis, resistive index greater than or equal to 80, male gender, and age.[112] It has been reported that progression of RAS occurs at 7% annually[113] whereas duplex-ultrasonography–defined renal atrophy occurs in 20.8% of kidneys with RAS greater than 60%.[114] The rate of progression ranges from 36%–71%.[115] Arteries with most severe stenoses result in total occlusions in 16% of cases.[1,46,113,115] Presence of RAS, even before the development of end-stage renal disease, heralds a poor prognosis.

Despite successful treatment of RAS, it is associated with high mortality.[95,116] One study reported a 2-year survival in patients with end-stage renal disease due to renal artery stenosis of 56%.[117] The overall survival for patients on hemodialysis is 10% if they suffer myocardial infarction, 18 months if they have congestive heart failure, and is equal to colon cancer if they are 65 years of age or older. In patients with RAS

Table 4
Renal Artery Revascularization Options

Sr No	Options	Success Rate (%)	Complication Rate (%)	Cost (US $)
1	Percutaneous transluminal angioplasty/Stent	98–100	13–16	1402–2573
2	Surgery	97	38	15,393

treated with stent deployment, baseline serum renal insufficiency is independently associated with a higher incidence of adverse events and decreased survival. In addition, improvement in renal function is associated with an improved survival.[118] Survival is linearly correlated to serum creatinine levels.[119] Two-year survival rates of 96% for patients with unilateral RAS, 74% for patients with bilateral RAS, and 47% for patients with stenosis of a solitary kidney have been reported.[36] In a cohort of 4000 patients undergoing catheterization, the 4-year mortality was reported to be 43% in patients with severe RAS (defined as > 75% stenosis) versus 11% in those without RAS.[120] RAS was found to be an independent predictor of cardiovascular mortality. Renal disease was found to be an independent and strong predictor of increased in-hospital as well as 1-year mortality after percutaneous coronary intervention.[121]

Cost Effectiveness

It has been shown that angioplasty, stent, and bypass grafting for RAS have similar success rates with equal efficacy for the treatment of renovascular hypertension. However, the two percutaneous treatments cost significantly less than even an uncomplicated surgical bypass (Table 4). Initial treatment costs were $1402, $2573, and $15,393 for angioplasty, stenting, and surgery, respectively. The renal artery bypass graft had higher complication rates (38%) compared to the percutaneous modalities (13%–16%). In addition, a major portion of cost for bypass grafting is attributable to expected complications and unavoidable postoperative hospitalization.[122]

Conclusions and Recommendations

It is highly likely that the incidence of chronic kidney disease caused by atherosclerosis will increase as the epidemics of obesity and diabetes increase and the level of hypertension control remains low (27%).[123] This projection is supported by a study of young adults with childhood-onset chronic renal failure demonstrating high prevalence of coronary and carotid abnormalities measured by noninvasive techniques, which correlate significantly with the duration of renal disease.[124] A high incidence of RAS in patients undergoing coronary angiography has been reported.[2,125–128] Despite a well-established relationship between RAS and coronary artery disease and peripheral vascular disease, it is less well understood by physicians, including cardiovascular specialists, that the presence of asymptomatic RAS may have serious consequences, such as progressive loss of renal mass and function and even dialysis. Given the high incidence and prevalence of RAS, it is therefore extremely

Figure 9. *Renal artery stenosis management algorithm.* www.medreviews.com

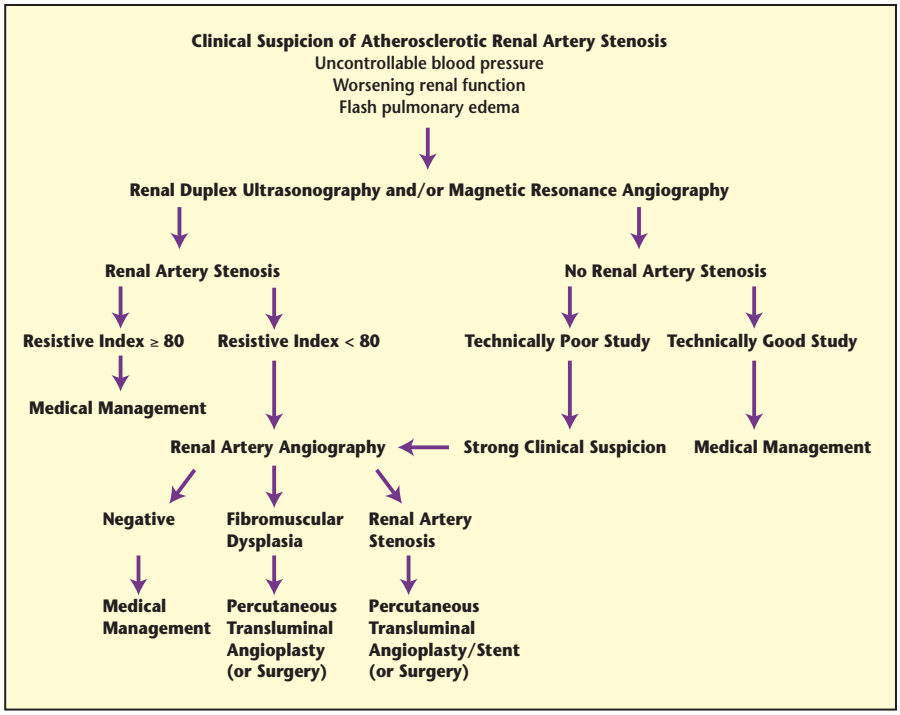


Table 5
Recommendations for the Management of Renal Artery Disease

Aggressive screening, recognition, and early treatment
Monitor blood pressure and serum creatinine every 3 months
Discontinue ACEI/ARB therapy if renal function deteriorates
Evaluate kidney size and renal artery patency annually by ultrasonography
Consider revascularization early if blood pressure control becomes inadequate or if renal atrophy > 1 cm is suggested by ultrasound

important for physicians to recognize and treat it using an endovascular modality early in its course. Patients with suspected RAS, such as those with refractory hypertension and flash pulmonary edema, should be referred to a cardiac catheterization laboratory (Figure 9).

In patients with known RAS, blood pressure and serum creatinine should be monitored every 3 months (Table 5). ACE inhibitors/ARB therapy should be discontinued if worsening of renal function is encountered within the first 4 weeks of the institution of therapy. Kidney size and renal artery patency should be evaluated with ultrasonography annually, and every 6 months in patients with greater than 60% or bilateral stenosis on medical therapy. Angiography and revascularization should be considered early if blood pressure control becomes inadequate, renal function deteriorates, or if renal atrophy greater than 1 cm is suggested by ultrasonography.

At present, there are a number of questions and controversies involving RAS. Renal artery stenting is not yet approved by the US Food and Drug Administration. Which patients will respond to revascularization is not clear. The role of distal embolic protection devices to reduce the incidence of atheromatous embolization is being investigated. Whether drug-eluting stents have a similar impact on RAS is unknown. The mechanism of congestive heart failure in patients with bilateral RAS or a single functioning kidney remains unclear. Last but not least, the effect of revascularization on the survival rates in patients with atherosclerotic RAS has not been well established. Therefore, large, multicenter, randomized, prospective trials are warranted to address the controversies surrounding RAS and to assess the safety, efficacy, and clinical outcomes of the emerging and rapidly evolving treatment technologies. ■

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Main Points

- Renal ischemia due to renal artery stenosis (RAS) is an important cause of reversible hypertension and renal insufficiency.
- Atherosclerosis involves a number of highly interrelated processes, including dyslipidemia, platelet activation, thrombosis, endothelial dysfunction, inflammation, oxidative stress, vascular smooth muscle activation, altered matrix metabolism, remodeling, and genetic factors.
- RAS has 2 principal clinical manifestations: renovascular hypertension as a result of renin-angiotensin-aldosterone pathway activation, and ischemic nephropathy as a consequence of reduced glomerular filtration and renal mass loss.
- Diagnostic evaluation of RAS can be categorized into physiologic and imaging assessment. Physiologic tests include peripheral plasma renin activity (PRA), captopril-stimulated PRA, and captopril renal scintigraphy. In situations of high clinical suspicion, an imaging modality should be used to establish the diagnosis of RAS. A variety of noninvasive tests are available for the diagnosis of RAS, including duplex ultrasonography, computed tomography, and magnetic resonance imaging and magnetic resonance angiography.
- Treatment decisions for the management of RAS should consider relative benefits and risks involved and must take into account the likelihood of blood pressure reduction, renal mass preservation, or both.
- The natural history of RAS is to progress over time leading to renal artery occlusion, loss of renal mass, and worsening of renal function. Risk factors associated with a more rapid deterioration include hypertension, proteinuria, dyslipidemia, severity of renal impairment at the time of diagnosis, resistive index greater than or equal to 80, male gender, and age.
- Given the high incidence and prevalence of RAS, it is extremely important for physicians to recognize and treat RAS using endovascular modality early in its course in patients with suspected RAS, such as those with refractory hypertension and flash pulmonary edema referred to cardiac catheterization.

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