Renal Artery Stenosis

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KEYWORDS

• Renal artery stenting • Renal fractional flow reserve • Renovascular hypertension
• Ischemic nephropathy • Flash pulmonary edema • Chronic kidney disease • Renal atherosclerosis

KEY POINTS

- Screening for renal artery stenosis can be done with Doppler ultrasonography, CT angiography, and magnetic resonance angiography.
- Patients with medically controlled renovascular hypertension should not undergo renal stenting, because there is no added benefit of revascularization.
- Patients with (1) uncontrolled renovascular hypertension having failed 3 maximally tolerated antihypertensive medications (one of which is a diuretic), (2) ischemic nephropathy, and (3) cardiac destabilization syndromes with hemodynamically severe renal artery stenosis are likely to benefit from renal artery stenting.
- Physiologic measurements, including fractional flow reserve with hyperemic/resting translesional gradients, may be performed to select patients who should undergo renal artery revascularization.
- Patients should have routine 30-day, 3-month, 6-month, 12-month, and annual clinical, laboratory, and imaging follow-up for surveillance of in-stent restenosis.

INTRODUCTION

Renal artery stenosis (RAS), the single largest cause of secondary hypertension affecting 25% to 35% of the patients with secondary hypertension,[1,2] is associated with progressive renal insufficiency and causes cardiovascular complications such as refractory heart failure and flash pulmonary edema.[3–5] An understanding of the underlying pathophysiologic mechanisms, clinical manifestations, and medical and interventional treatment strategies is paramount in optimizing the care of patients with RAS. A critical issue is the appropriate patient selection for interventional procedures.

CAUSE AND PREVALENCE

RAS is caused by a heterogeneous group of conditions, including atherosclerosis, fibromuscular dysplasia (FMD), vasculitides, neurofibromatosis, congenital bands, and extrinsic compression of the renal artery. Atherosclerosis accounts for approximately 90% of the flow-limiting lesions of the renal arteries.[6]

ARAS typically involves the ostium and proximal portion of the renal artery and is frequently in continuity with atherosclerotic disease in the abdominal aorta. Patients with RAS frequently have associated atherosclerosis of multiple vascular beds, including coronaries, carotids, and peripheral vessels. Screening renal duplex ultrasonography (DUS) studies demonstrated RAS (>60% stenosis) in 6.8% of subjects in a "healthy" Medicare population with a mean age of 77 years.[7] There were almost twice as many men (9.1%) as women (5.5%, $P = .053$), and there were no racial differences (Caucasian = 6.9% and African American = 6.7%) in the prevalence of RAS.

An autopsy series found RAS (≥50% stenosis) in 27% of patients older than 50 years, and in 53% of

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those with a history of diastolic hypertension (>100 mm Hg).[8] RAS is the cause of end-stage renal disease (ESRD) in 10% to 15% of patients starting dialysis[9]; approximately 25% of elderly patients with renal insufficiency (creatinine >2.0 mg/dL) have undiagnosed RAS.[5] RAS is present in 30% to 40% of patients with peripheral artery disease or abdominal aortic aneurysm.[10]

PATHOPHYSIOLOGY OF RENAL HYPOPERFUSION

Several processes contribute to the pathophysiologic process of RAS.[11] Renal hypoperfusion is a strong stimulus for renal neurohormonal activation, resulting in renin and subsequent angiotensin II release. Renin-angiotensin-aldosterone system (RAAS) activation occurs with both unilateral and bilateral (or solitary) renal hypoperfusion.[12]

In unilateral RAS, the ischemic kidney secretes renin, which leads to increased angiotensin formation and, hence, elevated blood pressure. As blood pressure rises, sodium excretion by the contralateral normal kidney increases; therefore, there is no sodium retention or subsequent volume overload. This mechanism for the hypertensive hyponatremia syndrome is seen in unilateral RAS.[13]

With bilateral (or solitary) RAS, the lack of compensation from a normal kidney in terms of sodium excretion leads to fluid retention, loss of kidney function, and congestive heart failure (CHF).[14] Angiotensin is also a potent stimulator of reactive oxygen species (ROS) generation. ROS are direct vasoconstrictors and produce multiple vasoactive and fibrogenic factors, which contribute to hypertension and renal dysfunction.[15] Apoptosis, possibly induced by ROS, may also contribute to loss of vascular cells by promoting inflammation and tissue injury.

In patients with moderate RAS, despite reduced renal blood flow (RBF), cortical and medullary oxygenation is preserved because of compensatory mechanisms that decrease oxygen consumption. However, compensation for impaired RBF is limited in patients with severe RAS, which results in significant decreases in cortical oxygenation.[16]

CLINICAL SYNDROMES ASSOCIATED WITH RENAL HYPOPERFUSION

The main clinical syndromes associated with hemodynamically significant RAS include renovascular hypertension, ischemic nephropathy, and cardiac destabilization syndromes.

Renovascular Hypertension

Resistant hypertension is defined as blood pressure higher than goal on 3 different classes of antihypertensive medications, ideally including a diuretic drug.[17,18] Patients with resistant hypertension should be evaluated for secondary causes of hypertension. Studies of refractory hypertension commonly reveal a high prevalence of previously unrecognized renovascular disease, particularly in older patient groups. In patients older than 50 years of age who were referred to a hypertension center, 13% had a secondary cause of hypertension, the most common of which was renovascular disease.[19]

RAS is a common finding in hypertensive patients undergoing cardiac catheterization to assess coronary artery disease. In a population of veterans with hypertension referred for coronary angiography, greater than 20% of patients were found to have hemodynamically significant atherosclerotic RAS (ARAS) (>70%).[20]

Ischemic Nephropathy

RAS is a potentially reversible form of renal insufficiency. However, if unrecognized, it can lead to ESRD. Some studies suggest that as much as 11% to 14% of ESRD is attributable to chronic ischemic nephropathy from ARAS.[21] Favorable predictors of improved success with intervention include a rapid recent increase in serum creatinine concentration, decrease in glomerular filtration rate (GFR) during angiotensin-converting-enzyme (ACE) inhibitor or angiotensin II receptor blockers (ARB) treatment, absence of glomerular or interstitial fibrosis on kidney biopsy, and kidney pole-to-pole length greater than 8.0 cm.[22] In 73 patients with chronic renal failure (creatinine clearance >50 mL/min) and clinical evidence of renal vascular disease and a mean follow-up of 2 years, renal function improved in 34 of 59 patients (57.6%). The most important predictor of improvement was the slope of the reciprocal serum creatinine plot before revascularization, suggesting that rapidly progressive renal failure is associated with a more favorable response on renal failure progression after revascularization in patients with vascular nephropathy and RAS.[23]

Cardiac Destabilization Syndromes

Exacerbations of coronary ischemia and CHF caused by increased vasoconstriction and/or volume overload can be attributed to RAS. The most widely recognized example of a cardiac destabilization syndrome is “flash” pulmonary or Pickering syndrome.[3,24] Renovascular disease may also complicate the treatment of patients with heart failure by preventing the administration of angiotensin antagonist therapy.