

INTRODUCTION

Renovascular hypertension (RVH) is the most important cause of secondary hypertension and it is often due to occlusive lesion of renal arteries. RVH is precipitated by a hemodynamically significant stenosis of a renal artery or arteries (that is, a stenosis greater than 75% of the vessel lumen or 50% with post-stenotic dilation). The frequency of renovascular hypertension is less than 1% in patients with mild to moderate elevation of blood pressure but in contrast the prevalence is much higher (10-25%) in patients with acute, severe or refractory hypertension. RVH is a potentially curable cause of hypertension and major advances in vascular imaging has lead to early and easy non invasive identification of vascular lesions. Effective and well tolerated antihypertensive drug therapy has lead to satisfactory medical management of RVH. Selected patients may need angioplasty, stenting or both.

AETIOLOGY

Atherosclerotic renal artery stenosis and fibromuscular dysplasia are the major causes of renovascular hypertension.

Atherosclerotic renal artery stenosis (ARAS) is the most common cause of renal arterial compromise accounting for 70-90% of cases of renal artery stenosis. ARAS usually involves the ostium or proximal renal arteries. It is more common in older patients, patients with other CV risk factors and has poor prognostic implications.

Fibromuscular dysplasia (FMD) on the other hand is not as common as ARAS and accounts for 10-30% cases. It is more common in young women. It affects the distal 2/3 of renal arteries and its branches. It may involve the intima, media or adventitia but most commonly involves the media. Genetic factors play a role. It is usually associated with good prognosis and progressive disease with total occlusion is rare.

Other nonatherosclerotic causes include aneurysms, congenital or traumatic arteriovenous fistulas, polyarteritis nodosa, takayasu arteritis, neurofibromatosis, trauma, acute arterial thrombosis or embolism, aortic/renal artery dissection, hypercoagulable states, congenital bands and radiation induced fibrosis. Transplant renal artery stenosis is the most common vascular complication following renal transplant and contributes to transplant failure.

PATHOPHYSIOLOGY

The chief mechanism underlying renovascular hypertension involves two factors: 1) Activation of Renin Angiotensin Aldosterone System 2) Presence or absence of contralateral kidney.

In unilateral renal artery disease, the ischemic kidney initiates hypersecretion of renin, which in turn accelerates conversion of angiotensin I to angiotensin II and there is aldosterone induced sodium and water retention. On the other hand, there is renin suppression and pressure diuresis by the non stenotic kidney, precluding volume retention from contributing to the angiotensin II mediated hypertension. By contrast, a solitary ischemic kidney or bilateral disease has little or no capacity to excrete sodium and water thus leading to volume retention playing an additive role in the hypertension.

WHEN TO SUSPECT FOR RENOVASCULAR HYPERTENSION

The clinical clues which suggest the presence of renal arterial disease as the cause of hypertension and CKD include

- Age at onset of hypertension <30 years or >55years
- Abrupt onset of hypertension
- Acceleration of previously well controlled hypertension
- Refractory hypertension
- Accelerated hypertensive retinopathy
- Malignant hypertension
- Systolic diastolic abdominal bruit
- Flash pulmonary edema
- Evidence of generalised atherosclerosis obliterans
- Asymmetry in kidney size on imaging studies
- Acute kidney failure on treatment with an ACE inhibitor or ARB.

Because of the potential risks of invasive procedures, only those patients who have a high likelihood of getting benefit from the procedure should be tested for RAS which include severe hypertension with progressive renal insufficiency, refractory hypertension, accelerated or malignant hypertension, unexplained recurrent flash pulmonary oedema, hypertension with ACEI or ARB induced acute renal failure and severe hypertension with asymmetry of renal size.

Table 1: Computed tomographic angiography and Magnetic resonance angiography

CTA	MRA
Sensitivity 94%	90%
Specificity 60-90%	100%
Can detect small accessory renal arteries	No iodinated contrast medium
Can be used in implanted devices	Cannot be used in those with implanted devices
Can cause contrast induced nephropathy in those with impaired renal function	Gadolinium based contrast medium may lead to nephrogenic systemic fibrosis in those with moderate to end stage renal failure
Images difficult to interpret in heavily calcified arteries	No calcification artefact
Contraindicated in patients with contrast allergy	

INVESTIGATIONS

Investigations should include tests which define the structural abnormalities like Duplex Doppler ultrasonography, computed tomographic angiography (CTA), magnetic resonance angiography (MRA) and conventional angiography and those that define functional status of the kidneys like captopril renography, renal vein renin levels and ^{99m}Tc-DTPA renography. Renal arteriography which is an invasive procedure is the gold standard for the diagnosis of renal artery stenosis. Commonly employed non invasive procedures include Doppler ultrasonography, CTA and MRA (Table 1). Other procedures are not usually used as a screening test due to their low sensitivity and specificity.

Duplex Doppler ultrasonography is safe, inexpensive and easily available and forms the first line of investigation in most patients with renal artery stenosis. It aids in direct visualization of the main renal arteries (B-mode imaging) which is combined with measurement (Doppler) of a variety of hemodynamic factors. Stenotic lesions can be detected by comparing the systolic flow velocity in the renal artery to that in the aorta, since the velocity of flow increases as an artery narrows; end-diastolic velocity also may be increased distal to a stenotic lesion. But the result is operator dependent with an accuracy of 60-90% and the sensitivity and specificity of ultrasonography in detecting hemodynamically significant ARAS was 85% and 92% respectively.

Renal arteriography: ARAS typically involves the proximal 1/3 of the renal artery at or near the renal artery ostium. Lesions may be either concentric or eccentric within the renal artery. Regarding FMD, medial hyperplasia is the commonest form and is characterised

by 'string of beads' appearance in angiography (Figures 1, 2 & 3). It involves the middle to distal portion of the artery in contrast to ARAS. Renal arteriography helps to determine the translesional pressure gradient across areas of stenosis thus estimating the hemodynamic significance before performing invasive therapeutic procedures like percutaneous transluminal renal angioplasty (PTRA) or stenting. It was found that those with a translesional gradient >20 mmHg were associated with a significant improvement in hypertension following therapeutic procedure (Figures 4, 5, 6, 7 & 8).

MANAGEMENT

Optimal antihypertensive therapy and reducing CV risk is the initial step in the management of RVH. Blockade of renin-angiotensin system with ACE Is and ARBs is the most essential part in the treatment of RVH. If blood pressure control and renal function can be maintained with optimal medical therapy, little more is gained by elaborate diagnostic procedures. On the contrary, failure of medical therapy points to a potential benefit of improvement with interventional procedures.

Indications for invasive treatment of ARAS are controversial. Intervention should be done based on patient's clinical symptoms and for hemodynamically significant stenosis defined as 1) Greater than 50% diameter stenosis or greater than 75% reduction in cross sectional area and 2) Systolic pressure gradient greater than 10% of systolic pressure or a pressure gradient of 20 mmHg. While stenting is superior to percutaneous renal artery transluminal angioplasty (PRTA) in ARAS, PRTA is the preferred treatment in FMD.

MANAGEMENT OF RENOVASCULAR HYPERTENSION

1. Antihypertensive Drug Therapy
 - Blockade of the Renin-Angiotensin System using ACEIs, ARBs
 - Direct Renin Inhibitors (Aliskiren)
 - Calcium Channel Blocking Agents
 - Diuretics
 - Mineralocorticoid Receptor Blockade
 - Additional Classes: Beta-Blockade, alpha-receptor blockade, sympatholytic agents, vasodilators
2. Cardiovascular Risk Reduction
 - Removal of tobacco use
 - Treatment of dyslipidemia
 - Treatment of obesity: obstructive sleep apnea
 - Management of glucose intolerance / diabetes
3. Renal Revascularization: Selected Cases
 - Endovascular revascularization
 - PTRA: primarily fibromuscular dysplasia
 - PTRA with stenting: Atherosclerotic disease



Fig. 1

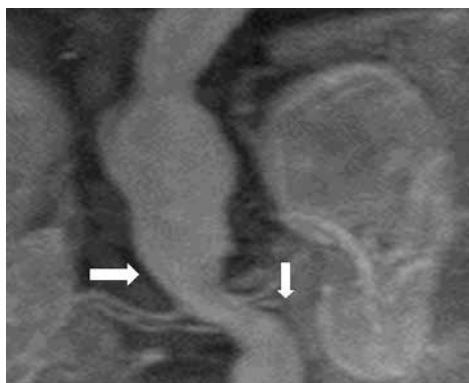


Fig. 2



Fig. 3

Fibromuscular Dysplasia: A 37 year old lady presented with hypertension, POVD with bilateral renal bruit. MRA showed string of beads appearance in left renal artery (Figure 1 & 2), with suprarenal aneurysmal dilatation of aorta and string of beads appearance in the other major arterial branches of aorta (Figure 3). Arterial biopsy from left dorsalis pedis was consistent with FMD. (Courtesy: Dr. Danish E, Department of Medicine, Government Medical College, Kozhikode)



Fig. 4: Tight stenosis at ostium of right renal artery



Fig. 5: Wire and distal protection device (to prevent embolization to distal end arteries)

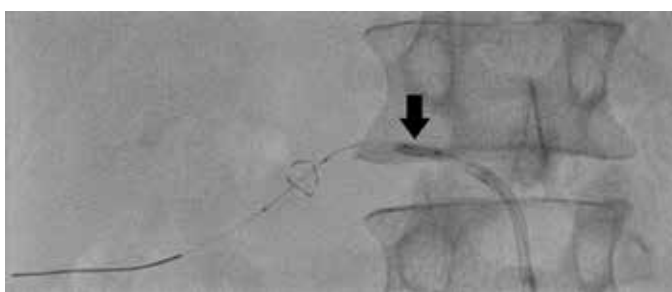


Fig. 6: Balloon dilatation of RAS



Fig. 7: Placing unexpanded stent at ostium



Fig. 8: After stent deployment

Figures 4 – 8: Percutaneous transluminal renal angioplasty (PTRA) with stenting in RAS (Courtesy: Dr. G. Rajesh, Department of Cardiology, Government Medical College, Kozhikode)

Surgical: Renal artery bypass / endarterectomy (now usually reserved for complex aorto-renal disease, aneurysmal disease, failed endovascular stent procedures)

CONCLUSIONS

Renovascular hypertension is the most important cause of secondary hypertension. It is generally due to renal artery stenosis caused by atherosclerotic arterial disease or fibromuscular dysplasia. It could be unilateral or bilateral. The evaluation should be restricted to high risk patients. Duplex Doppler ultrasound (US) is useful as a non-invasive screening test as it is a relatively inexpensive, that does not require contrast, and can be used in patients with any level of renal function, though it is operator dependent. The newer non-invasive imaging modalities

like CT or MR angiogram have made the evaluation easy though more expensive. Medical treatment remains the standard of care, which includes optimization of antihypertensive therapy along with CV risk reduction including lipid lowering and anti platelet therapy. Selected patients may need angioplasty, stenting or both. Surgical procedures are reserved for patients who have complex anatomical lesions of renal artery, for patients who require nephrectomy and those requiring surgery of aorta. As early recognition and treatment may result in reversal of the disease and control of blood pressure, a high index of suspicion is needed.

KEY WORDS

Renovascular hypertension (RVH), Atherosclerotic renal artery stenosis (ARAS), Fibromuscular dysplasia (FMD),

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