Renovascular Disease

Synonyms: renovascular occlusive disease, renal vascular disease, renal artery stenosis, ischaemic nephropathy

Renovascular disease is the term given to the impairment of renal perfusion caused by disease affecting the arterial supply of the kidney(s). Renal hypoperfusion leads to hyperactivation of the renin-angiotensin-aldosterone axis, causing hypertension. Renovascular disease is an important cause of secondary hypertension and chronic kidney disease.

Renal vein thrombosis may cause a similar pattern of disease and is discussed in the separate Renal Vein Thrombosis article.

Pathogenesis

- In the developed world, atherosclerosis is by far the most common cause of renovascular disease. This normally develops at the renal artery ostium on the luminal surface of the aorta/proximal renal artery. The atheroma obstructs renal blood flow and leads to chronic renal ischaemia. Atheroma may account for >90% of cases in white vascular high-risk populations. Renal artery atheroma is commonly associated with more generalised atheroma and cerebral, cardiac and/or peripheral arterial disease.
- In the Indian sub-continent and the Far East, Takayasu's arteritis is responsible for about 60% of cases.[1]
- The remainder of renovascular disease is largely due to fibromuscular dysplasia of the renal artery which tends to affect the more distal portions of the renal artery. Fibromuscular dysplasia is an angiopathy of uncertain aetiology that may affect the carotid and vertebral circulation, visceral arteries and peripheral arteries. Some series estimate that fibromuscular dysplasia accounts for up to 10% of cases of renovascular hypertension.[2]

Possible causes of renal hypoperfusion

- Renal artery atheroma/arteriosclerosis.
- Fibromuscular dysplasia of the renal artery.
- Prolonged hypotension or severe dehydration (usually transient but may cause permanent damage).
- Embolic renal disease.
- Renal artery or aortic dissection.
- Neurofibromatosis.
- Renal arteriovenous malformation.
- Takayasu's arteritis.
- Other arteritides - eg, polyarteritis nodosa.
- Post-transplant renal artery stenosis.
- Post-radiotherapy renal artery disease.

Epidemiology[3]

- The prevalence of atherosclerotic renal artery stenosis is high - about 7% in individuals older than 65 years and about 50% in patients with diffuse arterial disease, and it is increasingly frequent in an ageing population.
- About 10-15% of atherosclerotic renal artery stenosis cases lead to the development of resistant hypertension and/or ischaemic nephropathy.
- In a study of people in the UK with type 2 diabetes with hypertension (a high-risk group for renovascular disease) and normal serum creatinine levels, using magnetic resonance angiography to detect the disease, a prevalence of 17% was found. 95% of these patients had unilateral disease.[4]

Risk factors

- Hypertension (but up to 35% of patients with renovascular disease may be normotensive).
- Advanced age (much more common in those aged 60-70 years, with prevalence increasing in those aged >70 years; one unselected post-mortem series showed a prevalence of 42% in those aged over 75 years).
- Evidence of renal impairment.
- Evidence of peripheral arterial or cerebrovascular/cardiovascular disease.
- Diabetes mellitus.
- Smoking.
- Family history of cardiovascular disease or renovascular disease.
- Hyperlipidaemia.
- White racial background (approximately twice the prevalence in those with a white racial background compared with African Americans in a group of patients with severe hypertension).

Presentation

The condition may present in a variety of ways and is usually asymptomatic. The following clinical scenarios are relatively common modes of presentation:
• Hypertension:
  • Abrupt onset of hypertension in middle-aged or older patients.
  • Severe hypertension.
  • Hypertension resistant to standard medical therapy.
  • Hypertension developing in a patient with known peripheral-vascular/cerebrovascular/cardiovascular disease.
  • Hypertension developing in a patient with no family history of hypertension.
  • Hypertension with hypokalaemia (due to hyperaldosteronism) with no provoking medications or other identifiable cause (may be associated with metabolic acidosis).
  • Biochemical or clinical evidence of renal impairment occurring during treatment with angiotensin-converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists.
  • De novo renal impairment developing in a hypertensive or normotensive patient with vascular disease/risk factors.
  • Decompensation of congestive cardiac failure in a hypertensive patient (may present with recurrent episodes of acute pulmonary oedema with no obvious precipitant - so-called ‘flash pulmonary oedema’).

Examination

• Look for evidence of vascular risk factors such as corneal arcus in younger patients, xanthomata, xanthelasmata, elevated blood pressure, etc.
• Look at general appearance: note whether there is any evidence of other causes of secondary hypertension, such as Cushing's syndrome.
• Check for radiofemoral delay and also check blood pressure in both arms to look for aortic coarctation/dissection.
• Palpate peripheral and carotid pulses and auscultate for bruits to look for evidence of generalised vascular disease (the presence of which greatly increases the likelihood that hypertension is due to renovascular disease).
• An abdominal bruit, also heard over the flank, is a relatively common finding in patients with renovascular hypertension, being found in up to 50% of patients with the disease. However, up to 10% of patients with essential primary hypertension may have an abdominal bruit and innocent abdominal bruits are present in a minority of healthy younger patients, so it is not a pathognomonic sign.
• The presence of a systolic-diastolic bruit in a hypertensive patient is highly suggestive of renovascular disease.
• The cardiovascular system should be examined to detect any evidence of cardiac failure or to identify other causes of secondary hypertension.
• Perform ophthalmoscopy to look for evidence of hypertensive retinopathy, indicating long-standing hypertension, or to reveal evidence of occult diabetes.
• Dipstick urine for glucose and protein (mild-to-moderate proteinuria is sometimes a feature).

Differential diagnosis

• Essential primary hypertension.
• Any other cause of renal impairment, particularly glomerulonephritis.
• Iatrogenic renal impairment.
• Other causes of secondary hypertension.
• Malignant primary or secondary hypertension.
• Acute interstitial nephritis caused by medication, autoimmunity or hypersensitivity phenomenon following infection.
• Nephrosclerosis.
• Other causes of hypertension and albuminuria.
• Collagen vascular diseases.
• Arteritides (may cause renovascular disease or present similarly without affecting renal blood flow).

When to refer to secondary care

See the separate Hypertension and Chronic Kidney Disease articles for further discussion, including indications for referral to secondary care.

Investigations

Urine and blood tests

• Blood for renal function tests (including eGFR) and electrolytes.
• Blood glucose.
• 24-hour urinary protein excretion and tests for microalbuminuria may aid in the decision-making process.
• Urinalysis to exclude the presence of red blood cells/red blood cell casts which can be found in glomerulonephritis.
• Serology to exclude systemic lupus erythematosus or vasculitis if suspected (eg, antinuclear antibodies, complement, etc).
• Lipid profile, as renovascular disease is likely to be part of more extensive atherosclerotic disease.

Other investigations[5]

The choice of the best test for diagnosis of stenosis of the visceral arteries, whatever the aetiology, is controversial.

• Renal ultrasound is often performed in those with renal impairment but it is not diagnostic for renovascular disease. The diagnosis is suggested if there is a significant difference in kidney size (>1.5 cm).
• Duplex renal ultrasound combines ultrasound and Doppler techniques and can be a good diagnostic test. However, it is labour-intensive and technician-dependent.
If there is a high clinical index of suspicion of renovascular disease that may be amenable to intervention, conventional angiography should be considered to make the diagnosis. However, there is a risk of complications such as arterial puncture and catheter-induced atheroembolism. It has the advantage that endovascular therapy can be carried out at the same time. CT angiography uses intravenous injection of contrast material to allow images of the renal arteries. There is a risk of contrast-associated nephropathy. Magnetic resonance angiography allows direct visualisation of renal artery lesions and can be used to assess blood flow rate, GFR and renal perfusion rate. However, it has only been validated for disease in the proximal renal arteries. Radionuclide scanning following a dose of captopril can be helpful if fibromuscular disease is suspected in patients with normal renal function. Selective renal vein renin measurements, plasma renin activity and the captopril test (measuring plasma renin activity after administration of captopril) were used in the past but are no longer thought to be useful screening tests.

Fibromuscular dysplasia is a pathological diagnosis. However, there are characteristic changes that can be seen on angiography in one form of fibromuscular dysplasia: medial fibroplasia. This is known as the 'string-of-beads appearance', caused by areas of relative stenoses or webs alternating with small fusiform or saccular aneurysms of the artery.

Associated diseases
- Neurofibromatosis.
- Arteritides, particularly Takayasu’s arteritis and polyarteritis nodosa.
- Diabetes mellitus.
- Fibromuscular dysplasia of the renal artery is possibly associated with alpha-1-antitrypsin deficiency.

Management

Renal artery stenosis
General advice includes:
- Optimise vascular risk profile through smoking cessation, diabetes control, statins and adequate antihypertensive therapy.
- Avoid, or be very cautious in the use of, ACE inhibitors and angiotensin-II receptor antagonists.
- Avoid other potentially nephrotoxic medications where possible, or adjust the dose as advised by formulary - eg, non-steroidal anti-inflammatory drugs (NSAIDs) and renally excreted drugs.
- Seek expert advice if blood pressure cannot be controlled or vascular intervention is considered.

The management of renal artery stenosis can include:
- Medical management with drugs and vascular risk profile optimisation as above.
- Vascular intervention techniques, including angioplasty ± stenting.

Angioplasty with stenting is generally used as the first line in vascular intervention. Open/endovascular surgery to reconstruct the stenosed artery and bypass procedures are also used. The current chronic kidney disease guidelines state that, with regards to angioplasty, it is generally accepted that:
- It is indicated in flash pulmonary oedema.
- It should be considered in refractory/severe hypertension.

Recent studies have shown that medication without angioplasty is preferable for most patients with clinically stable atherosclerotic renal artery stenosis.

Fibromuscular dysplasia
- For patients with fibromuscular disease, the results of percutaneous vascular intervention are generally superior to those of drug therapy alone. Blood pressure outcome after angioplasty is generally better in patients with fibromuscular renal artery disease (who usually do not have chronic kidney disease) than for those with atherosclerotic renal artery stenosis.
- Percutaneous transluminal angioplasty with balloon dilatation ± stenting is the treatment of choice for fibromuscular disease.
- Vascular surgical reconstruction may also be used.

The evidence for best management
A systematic review of 55 relevant studies found that there were no studies directly comparing modern drug treatments for renal artery stenosis with modern angioplasty techniques, including stenting. The review concluded that there was insufficient evidence to support one treatment approach clearly over another for renal artery stenosis.

A large multicentre trial, testing treatment strategies for renal artery stenosis, is currently underway in the USA, comparing optimum medical therapy alone to stenting with optimum medical therapy.

A Cochrane review looked at balloon angioplasty versus medical treatment for renal artery stenosis. It found that balloon angioplasty is superior to medical therapy in lowering blood pressure of people with renal artery stenosis and pharmacologically controlled blood pressure. However, where hypertension is refractory to medical therapy, there was weak evidence that balloon angioplasty lowers blood pressure more effectively than medical therapy. It concluded that randomised controlled trials are needed to compare the effect of balloon angioplasty and medical therapy on the preservation of renal function in the long term.
Complications

- End-organ damage from uncontrolled hypertension.
- Progressive chronic kidney disease.
- Acute kidney injury in rapidly advancing cases, or if there is intercurrent illness or other cause of renal insult.
- Deterioration in renal function in patients taking ACE inhibitors and angiotensin-II receptor antagonists.
- Refractory heart failure or episodic recurrent pulmonary oedema.
- Refractory angina.

Screening

- Atherosclerotic renal artery stenosis is often present in people with atherosclerosis elsewhere and is independently associated with an increased cardiovascular morbidity and mortality.
- The American Heart Association Committee on Diagnostic and Interventional Cardiac Catheterisation, Council on Clinical Cardiology, and the Councils on Cardiovascular Radiology and Intervention and on Kidney in Cardiovascular Disease suggest screening for renal artery stenosis in those who are candidates for coronary revascularisation.\(^\text{[12]}\)

Prognosis

The prognosis is variable depending upon the severity of lesions, whether unilateral or bilateral, comorbidities and co-existing atherosclerotic disease, age and response to medical or surgical therapy.

Prevention

- For atheromatous vascular disease, see the separate Primary Prevention of Cardiovascular Disease and Cardiovascular Risk Assessment articles.

Further reading & references

- Angioplasty and Stent for Renal Artery Lesions trial (ASTRA)

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