Renovascular disease

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Abstract

In Western populations, fibromuscular disease accounts for around 10% of all cases of renal artery stenosis (RAS), usually presenting as hypertension in young people, most often women, and there is often a successful response to angioplasty.

Atherosclerotic renovascular disease (ARVD) accounts for the remaining 90% of cases of RAS. ARVD is a disease of ageing, frequently associated with hypertension and renal dysfunction. It is commonly accompanied by major atherosclerotic vascular disease in other parts of the body, such as coronary artery disease, peripheral vascular disease, cerebrovascular disease and aortic aneurysms. Clinical presentations include hypertension, chronic or acute kidney disease and heart failure, although many patients with ARVD are identified incidentally when being screened for extra-renal vascular disease. The main treatment options involve general vascular protection (blood pressure control, antiplatelet and statin therapy) and interventional procedures, notably percutaneous renal angioplasty and/or stenting. Two recent large prospective randomized controlled trials (RCTs), ASTRAL and CORAL, have failed to show an overall benefit of intervention over optimal medical therapy in the trial setting. However, there is evidence that revascularization may still play a role in the management of patients with high-risk phenotypes such as flash pulmonary oedema. Future research is needed to help identify those patients who benefit from revascularization, while avoiding this procedure and its attendant risks in others.

Keywords ASTRAL trial; atherosclerotic renovascular disease (ARVD); chronic kidney disease (CKD); fibromuscular disease (FMD); hypertension; renal artery stenosis (RAS); renal revascularization

Renal artery stenosis (RAS) refers to narrowing of the renal arteries. It is a common condition that can cause, or be associated with, serious clinical abnormalities. Atherosclerotic renovascular disease (ARVD) accounts for over 90% of RAS in Western populations, and the remainder are due to fibromuscular disease (FMD). In the Indian subcontinent and the Far East, vasculitis, such as Takayasu's arteritis, may be responsible for up to 60% of cases of RAS.[1] The epidemiology and outcomes of FMD and ARVD differ markedly, and so they are considered separately in this article, with greatest attention being directed to ARVD.

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What's new?

- The latest and largest prospective randomized controlled trial on atherosclerotic renovascular disease to date, the CORAL trial, has shown that patients who undergo revascularization in addition to medical therapy do not have better clinical outcomes than patients given medical therapy alone
- However, these data refer to large groups of trial patients and do not consider the phenotype of individual higher-risk patients, many of whom were not included in the trial
- There is evidence that patients with certain high-risk presentations do have better outcomes with revascularization, but further research is necessary to confirm this

Fibromuscular disease of the renal arteries

FMD accounts for up to 10% of RAS cases. Studies of healthy renal donor populations (pre-transplantation) using catheter or CT angiography have shown a prevalence ranging between 2.6 and 6.6%.[2] It is less common in Africans and Asians. FMD involves the renal arteries in 60–75% of cases, but other major arteries can be involved, such as the carotids (in 15%), vertebral, mesenteric, coeliac axis, and coronary vessels.

Pathology

The aetiology of FMD is unknown. Given the large female preponderance, female hormones may be important, although genetics could also play a role.[3] The commonest pathological form of FMD is medial fibroplasia, which is typically found in women presenting in their fourth decade. Areas of intimal and medial thinning with loss of the elastic lamina occur in the vessel wall and lead to multiple small aneurysm formation. These areas alternate with localized regions of narrowing due to fibrosis, giving a classical appearance at angiography resembling a 'string of beads' (Figure 1). FMD tends to affect the middle and distal part of the renal artery.

Clinical picture

The classical presentation of FMD is with hypertension and well-preserved renal function in young adults, but there are reports of cases presenting in older age. The diagnosis must be considered in young patients (e.g. <35 years old) who present with severe or accelerated-phase hypertension. An abdominal bruit may be detected, whereas neurological features, mesenteric angina or claudication may be manifestations of extra-renal FMD at other sites. Progressive narrowing of the renal arteries occurs in a third of patients, but this rarely progresses to occlusion.

Management

The management of patients with FMD is far clearer than that for atherosclerotic lesions and percutaneous transluminal renal angioplasty (PTRA), usually without stenting, is the intervention of choice. Response rates are good, with 36% of patients cured of hypertension, and many of the remainder having improved blood pressure control and a reduced antihypertensive burden.[4]

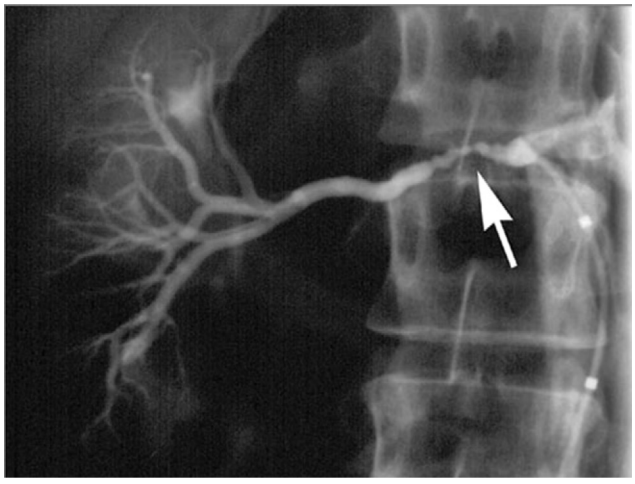

Figure 1 Fibromuscular renal artery stenosis of the right renal artery. A 'string of beads' appearance characterizes the arterial narrowing (arrowed).

Atheromatous renovascular disease

Over 90% of atheromatous RAS lesions are 'ostial', occurring within 1 cm of the origin of the renal artery (Figure 2), and the lesions are bilateral in about 50% of cases.

Epidemiology

ARVD occurs commonly in the setting of generalized atherosclerotic disease such as coronary artery disease (CAD) and peripheral vascular disease (PVD). It is also more prevalent in older patients with associated cardiovascular risk factors such as smoking, diabetes mellitus and hypertension. Given that ARVD is usually asymptomatic, the true prevalence in the general population may be underreported. One American study found that 6.8% of healthy elderly people had incidental RAS (defined as narrowing >60%).[5] Only a few studies have focused on the incidence of ARVD and how this has changed over the years.

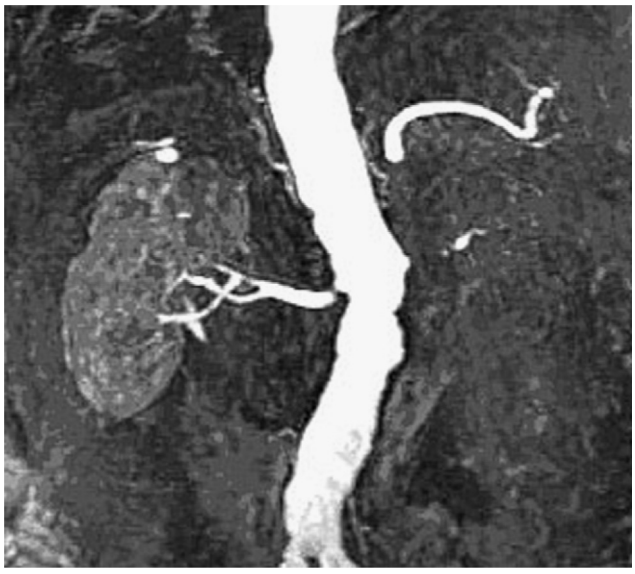

Figure 2 Magnetic resonance renal angiogram showing tight stenosis of the right renal artery and occlusion of the left renal artery.

Two studies of the US Medicare population aged over 65 years have demonstrated that ARVD was diagnosed with an incidence of about four cases per 1000 patient years,[6] and that rates of diagnosis increased almost fourfold between 1992 and 2004.[7] This is thought to reflect improved imaging techniques rather than a truly increased incidence of ARVD.

Clinical features

There is a strong association between ARVD and other atheromatous conditions, and many patients have asymptomatic ARVD that is detected incidentally during investigation for extra-renal vascular disease.[8] Hence, ARVD has been found in about 40% of patients with PVD, 15% of those with CAD, 30% of patients with congestive heart failure (CHF), and in about 30% of those undergoing investigation of aortic aneurysms; the association with cerebrovascular disease is significant if slightly less marked.

ARVD may be found in about 2% of all cases of hypertension, whereas over 95% of patients with ARVD are hypertensive. Causality is uncertain; in many cases it is likely that essential hypertension contributes to the development of ARVD, rather than the latter being important in the pathophysiology of the hypertension. In ARVD, severe systolic hypertension resistant to medical therapy is often found, in keeping with ageing and vascular stiffness.

Acute kidney injury (AKI) can complicate ARVD in patients with very severe bilateral RAS or occlusion, cholesterol atheroembolization (seen in patients with severe aortic atheroma who undergo angiographic procedures or anticoagulation) or damage caused by radio-contrast agents during angiography (contrast-induced nephropathy, CIN). AKI may also result from treatment with either angiotensin-converting enzyme inhibitors (ACE-I) or angiotensin II receptor blockers (ARB), which underpin renin-angiotensin blockade (RAB). Clinical suspicion of underlying RAS should be raised in those with significant functional deterioration (e.g. >30% increase in serum creatinine) after initiation of the agents; renal vascular imaging should be considered, as revascularization of significant RAS may be necessary to facilitate safe re-introduction of these useful drugs. Nevertheless, RAB should be considered the standard of care for the majority of patients with ARVD as the frequent presence of cardiac structural abnormalities, renin-mediated hypertension and proteinuria are indications for treatment, and in practice this therapy is tolerated by most, even those with significant bilateral disease.[9]

The commonest presentation of ARVD is relatively stable CKD with hypertension. In a small sub-group, patients have rapidly deteriorating renal function, usually with severe hypertension. Progression to end-stage kidney disease (ESKD) is recognized, but is uncommon (<2% per year) once the ARVD diagnosis has been made and basic vascular protective treatment initiated. Some reports suggest that around 10% of ESKD patients have ARVD but this is usually an associated finding rather than a contributory cause.[10] In most patients with ESKD, hypertension and intra-renal vascular damage (rather than RAS) are the dominant factors in the pathogenesis of CKD. This has implications for treatment and is reflected in the outcomes after renal revascularization procedures.

The importance of concomitant cardiac disease in ARVD is recognized, with over 90% of patients having structural or

