Atherosclerotic renal artery stenosis

Atherosclerotic renal artery stenosis is largely a disease of the elderly and is commonly associated with hypertension and renal dysfunction. Blood pressure can be controlled successfully in more than 90 per cent of patients, but careful monitoring of renal function is necessary. In this article, **Dr Ashit Kumar Shetty, GM Morris and VS Aithal** discuss management options.

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Atherosclerotic renovascular disease accounts for more than 90 per cent of renal artery stenosis in the western population, with fibromuscular dysplasia accounting for the remainder[1]. In the Indian subcontinent and the far-east, Takayasu's arteritis is responsible for up to 60 per cent of cases with renal artery stenosis[2]. Atherosclerotic renal artery stenosis (ARAS) is largely a disease of the elderly and is commonly associated with hypertension and renal dysfunction (*Table 1*). However, it is being increasingly diagnosed in the younger age groups because of improvement in the screening for renal failure and also easy access to sensitive noninvasive imaging techniques.

Prevalence

Atherosclerotic renovascular disease is common in the elderly. Incidental renal artery stenosis of more than 50 per cent was found in 40 per cent of patients older than 75 years at post mortem[3]. The prevalence and incidence of atherosclerotic renal artery disease in patients older than 67 years based on Medicare data from the US was 0.5 per cent and 3.7 per 1,000 patient years respectively[4]. The prevalence of ARAS is higher in those with coronary atherosclerosis and peripheral vascular disease. Incidental 50 and 75 per cent stenosis was found in 9.1 per cent and 4.8 per cent respectively in a review of 4,000 patients who underwent abdominal aortography following coronary angiogram[5]. The presence of 75 per cent stenosis was associated with a significant decrease in survival (57 per cent versus 89 per cent adjusted HR 2.0 for mortality). Also 11 to 42 per cent of patients with peripheral vascular disease were noted to have up to 50 per cent narrowing in at least one renal artery in other studies[6]. In addition, atherosclerotic renovascular disease may be responsible for five to 22 per cent of patients with advanced renal failure who are over the age of 50 years[7]. Data from the USRDS database between 1991–1997 shows that renovascular disease related end stage renal disease (ESRD) is increasingly faster than other-cause ESRD with an annual increase of 12.4 per cent per year[8].

Table 1. Types of renal artery stenosis

Fibromuscular dysplasia	Atherosclerotic renal artery stenosis
Affects younger age group	Older age group
Predominantly affects females	Males
Presents as hypertension	Causes refractory hypertension
Rarely causes renal failure	Often causes renal failure

Clinical features

Atherosclerotic renovascular disease is found in two to five per cent of all cases of hypertension and 90 per cent of patients with atherosclerotic renovascular disease are hypertensives. The cooperative study of renovascular hypertension was established in order to define the clinical characteristics differentiating atherosclerotic renovascular disease from essential hypertension[8].

The urinary sediment in renovascular disease is usually bland with a few red cells and mild to moderate proteinuria. Renal impairment occurs due to a combination of the effects of severe hypertension on the intrarenal circulation and the chronic hypo-perfusion that occurs when the systemic blood pressure drops as a result of antihypertensive therapy.

Progression of renal artery lesions

Atherosclerotic lesions progress at varying rates. Studies where serial arteriography or Doppler ultrasonography were performed suggested that progressive stenosis occurs in 11 per cent of arteries with atherosclerotic lesions at 2.6 years[9] and in 30 to 60 per cent within four to seven years[10] despite adequate control of the blood pressure. In a prospective study, serial duplex Doppler ultrasonography was performed on 295 kidneys in 170 patients with ARAS, almost all of whom were on antihypertensive therapy[11].

The cumulative incidence of any progression at three years was 28 per cent among arteries with an initial stenosis that was less than 60 per cent and 49 per cent among arteries with more than 60 per cent stenosis at entry. However, complete occlusion occurred in only nine renal arteries (three per cent), seven of which were initially classified as having >60 per cent stenosis. Thus, significant stenosis carries a higher risk of progression and long-term loss of renal mass and function.

Diagnosis

Atherosclerotic renovascular disease should be suspected in patients presenting with renal dysfunction and hypertension on a background of atheromatous disease elsewhere.

Investigations

Investigations in the workup of ARAS can be divided in to those that demonstrate the presence and degree of stenosis and functional studies that attempt to identify the response to revascularisation.

Treatment of atherosclerotic renovascular disease

The management of ARAS has suffered from the lack of large well-designed trials comparing conservative medical management with interventional procedures. The available data on the natural history of the disease favours conservative management in patients with stable renal failure and well controlled hypertension.

The difficulty in predicting a beneficial result and the concerns that the lesions might progress quicker following an angioplasty+/- stent also makes conservative management a safer option in patients who are stable.

With some suspect vessels, the rate of restenosis after stenting has been as high as 18 per cent per year, a higher rate than observed with untouched suspect vessels. As with coronary artery disease, this phenomenon may be due to thrombosis and/or accelerated neointimal formation resulting from vascular injury.

Table 2. Clinical features suggestive of renovascular disease

Hypertension
1. Abrupt onset of hypertension in patients aged less than 30 years or more than 50 years
2. Absent family history of hypertension
3. Accelerated hypertension or malignant hypertension
4. Resistance to therapy (more than three drugs)

Renal abnormalities
1. Unexplained renal failure in patients aged more than 50 years
2. Elevation of plasma creatinine level after the initiation of ACE inhibitor or ARB therapy
3.Ultrasonography reveals a >1.5cm difference in kidney size

Others
1. Unexplained acute pulmonary oedema
2. Femoral, renal, aortic or carotid bruit
3. History of extra renal vascular disease
4. Hypokalaemia

Medical management

General renal and cardiovascular outcomes with medical therapy alone were best studied in a retrospective report of 68 patients with high-grade (>70 per cent) ARAS who did not undergo revascularisation[12]. From this, 21 patients had bilateral stenosis or stenosis in a single kidney. Among these 21 patients (average age 75 years), the average serum creatinine concentration was 1.6mg/dL (141µmol/L) compared to 1.3mg/dL (115µmol/L) for those with unilateral disease. At three-year follow-up, the mean blood pressure was 160/81mmHg.

An increase of at least 50 per cent in the serum creatinine concentration was observed in four of the 21 patients (19 per cent), two of whom progressed to end-stage disease. The remaining 17 patients had stable renal function. However, the mortality rate was 43 per cent, due most commonly to myocardial infarction or heart failure. The outcomes were better in patients with unilateral disease with 13 per cent showing a decline in their renal function and a mortality rate of 21 per cent.

The corner stones of medical treatment are optimal blood pressure control with agents including ACE inhibitors, risk factor management including cessation of smoking, glycaemic control in diabetics, aspirin and lipid management with statins. The use of ACE inhibition in renal artery stenosis can have a beneficial effect on the unaffected kidney in unilateral disease. In bilateral disease, ACE inhibitors have a predictable deleterious effect on the GFR specially when used in conjunction with diuretics, but this effect is usually reversible. Persistent severe stenosis appears to carry the risk of long-term loss of renal mass and whether this effect is seen more with ACE inhibitors is debatable.

Blood pressure can be controlled successfully in more than 90 per cent of patients with ARAS, but careful monitoring of renal function is necessary particularly in patients with significant bilateral renal artery stenosis and renal artery stenosis affecting the solitary kidney.

Revascularisation

The revascularisation procedure of choice in most centres is percutaneous angioplasty with stent implantation. This recommendation is based upon clinical experience and the success of stenting in coronary lesions. Surgical revascularisation is performed if angioplasty fails or concomitant aortic surgery is required, as for an abdominal aortic aneurysm or aortic occlusive disease.

Angioplasty has been primarily used for nonostial lesions, as these are most amenable to this procedure. Previous published reports suggest a 65 to 70 per cent initial success rate followed by improvement in renal function in 35 to 50 per cent and stabilisation of renal functions in 12 to 50 per cent of patients[13,14]. In one study, a 20 per cent or greater fall in the plasma creatinine concentration

Table 3. Investigations that show the presence and degree of stenosis

1 Duplex ultrasonography has a sensitivity of 92–98 per cent but is very operator dependent
2. Spiral CT angiography has a sensitivity of 83–100 per cent but is associated with the risks of contrast nephropathy
3. Magnetic resonance angiography has a sensitivity of 83–100 per cent and a specificity of 92–97 per cent. Gadolinium enhanced angiography is useful for evaluating the proximal renal vasculature and the aorta.
4. Renal arteriography is the gold standard but is associated with complications related to arterial catheterisation and risks of contrast nephropathy. The diagnostic yield of any of these investigations correlates with the pretest probability of the illness being present. Therefore the yield is higher in high-risk patients.

Table 4. Investigations for identifying the response to revascularisation

1. Colour Doppler ultrasonography with resistive index measurement (1-end diastolic velocity/peak systolic velocity). If the resistive index is more than 80 the response to revascularisation is likely to be poor.
2. Captopril enhanced scintigraphy provides information about total and single kidney glomerular filtration rate and whether renal artery stenosis is functionally significant. However the limitation of this test is that it is not very useful in the presence of renal failure (serum creatinine more than 2.5mgm/dL)
3. Renal biopsy- revascularisation is unlikely to be successful if the renal biopsy shows extensive glomerular sclerosis and interstitial fibrosis.

These investigations are not routinely performed before a decision to revascularise a kidney is made largely because they are cumbersome and show a large inter-operator variability.

was noted in 10 of 27 patients with moderate renal insufficiency (while two were worse after the procedure) and in four of 16 (while four were worse) with more advanced disease (plasma creatinine concentration above 3.4mg/dL or 300µmol/L)[13]. Serious complications (renal artery occlusion or perforation, atheroemboli, or embolic stroke) were noted in 10 per cent of cases. The long-term benefit of angioplasty alone is unclear.

In an attempt to improve the efficacy of angioplasty in ostial lesions and to diminish the incidence of restenosis, balloon-expandable intravascular stents have been placed at the time of angioplasty. Stent placement is associated with a lower restenosis rate than angioplasty alone (17 versus 26 per cent in one review of 14 studies including >600 patients)[15]. With respect to renal function, angioplasty with stent placement can be beneficial as shown in a number of small descriptive non-randomised studies[16,17,18].

However small randomised trials[19,20,21] have so far demonstrated modest improvements in blood pressure control and no improvement in renal function. A randomised trial comparing stenting versus angioplasty[22] showed better arterial patency with stenting without any significant improvement in renal function. Similarly a non-randomised study comparing revascularisation with medical treatment failed to show a significant difference in renal function or mortality between the two groups at five years[23].

Identification of patients who respond to revascularisation is difficult. A high resistive index on duplex Doppler ultrasonography may indicate intrarenal disease and therefore predict poor outcome[24]. Revascularisation appears to work better when there is an acute decline in renal function. Revascularisation in kidneys, which measure less than 8cm, and in patients with advanced chronic renal failure is less likely to result in improvement in renal functions. However it can sometimes delay the need for renal replacement in people with advanced renal failure[25].

With the current available evidence; the indications for revascularisation in clinical practice are:

> Recurrent flash pulmonary oedema with >60 per cent stenosis
> Significant renal artery stenosis with severe hypertension resistant to maximal medical therapy

Key points

- Atherosclerotic renovascular disease accounts for more than 90 per cent of renal artery stenosis in the western population.
- ARAS is largely a disease of the ageing and is commonly associated with hypertension and renal dysfunction.
- It should be suspected in patients presenting with renal dysfunction and hypertension or a background of atheromatous disease elsewhere.
- Blood pressure can be controlled successfully in more than 90 per cent of patients with ARAS, but careful monitoring of renal function is necessary particularly in patients with significant bilateral renal artery stenosis and renal artery stenosis affecting the solitary kidney.
- Revasularisation unfortunately does not lead to predictable improvement in blood pressure or renal function in patients with ARAS.
- Further well designed large scale randomised trials are essential to determine the subgroup of patients who benefit from revascularisation.

> Inability to maintain renal function as systemic blood pressure drops
> Deteriorating renal functions in patients who cannot be taken off ACE inhibitors
> Unexplained progressive renal failure.

Conclusion

Atherosclerotic renovascular disease accounts for the majority of renal artery stenosis cases in the western population. There is little controversy regarding the management of fibromuscular dysplasia, which is treated by percutaneous transluminal renal angioplasty. Revascularisation unfortunately does not lead to predictable improvements in blood pressure or renal function in patients with atherosclerotic renovascular disease. Further well designed large scale randomised trials are essential to determine the subgroup of patients who benefit from revascularisation and compare medical treatment versus revascularisation. Two ongoing European trials (ASTRAL and STAR) and one American trial may be able to throw some light on this issue.

Conflict of interest: none declared

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