

Atherosclerotic renal artery stenosis: from diagnosis to treatment

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Summary

Renovascular hypertension represents a form of correctable hypertension and preventable renal failure. Such patients need to be identified early so that specific therapy can be instigated. Patient identification requires a high index of suspicion in patients with certain clinical features. Subsequent non-invasive imaging may result in angiography which is required for diagnostic purposes and for planning intervention. Correctable therapy takes one of two forms, namely percutaneous transluminal renal angioplasty, with or without stenting, or surgical revascularisation, together with modification of underlying risk factors.

Keywords: atherosclerosis; renal artery stenosis; hypertension

Atherosclerotic renal artery stenosis (ARAS) is a recognised cause of renal impairment (12–14% of all patients entering dialysis programmes^{1,2}) and secondary hypertension (1–5% of all hypertensives^{3–5}). Awareness of this condition is important as its prevalence is increasing and it represents a potentially reversible form of hypertension and renal impairment. ARAS is a progressive condition which, if untreated, has serious sequelae. Due to associated comorbidity in these patients their prognosis is poor. Therefore, an important challenge to clinicians is early identification and treatment.

Definition

The important consequences of ARAS include hypertension and renal impairment. Renovascular hypertension (RVH) may be defined as hypertension that results from renal ischaemia. A requisite is that reperfusion of the kidney must either improve or cure the elevated blood pressure. Ischaemic nephropathy may be defined as a reduction in glomerular filtration rate (GFR) in patients with haemodynamically significant renovascular occlusive disease supplying the total functioning renal parenchyma.

Prevalence

The mean age of patients with renovascular hypertension is over 50 years. Two thirds are male. Those presenting with ischaemic nephropathy tend to be older.^{6,7} A precise estimate of the prevalence of ARAS is not available, although autopsy and angiographic studies in patients with renovascular hypertension provide an indication. RVH accounts for approximately 1–5% of all causes of hypertension, however, autopsy data indicate a greater prevalence of renal artery stenosis.^{8–11} These data are summarised in table 1. Note the increased prevalence of renal artery stenosis in individuals with hypertension and diabetes mellitus. Other factors that affect prevalence include the presence of vascular disease elsewhere. Thus, the prevalence of ARAS (>50% stenosis) has been reported to range from 11% in patients with coronary artery disease¹² to 42% in patients with aorto-iliac disease.¹³

Anatomical correlation

ARAS most often involves the renal ostium and/or the proximal third of the vessel. Non-ostial lesions comprise only 15–20% of all ARAS with less than 5% involving the second or distal third of the renal artery.¹⁴ ARAS may be bilateral in approximately 50% of cases.¹⁵ The lesions may be eccentric and can often be complicated by post-stenotic dilatation.

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Accepted 28 April 1999

Table 1 Assessment of RAS prevalence in the general population

Reference	Association	% RAS (total number)
8	Postmortem	24 (154)
9	Postmortem	
	All	53 (295)
	Normotensive	49 (256)
	Hypertensive	77 (39)
10	Postmortem	
	All	4.3 (5194)
	Diabetes mellitus	8.3

Pathophysiology of renovascular hypertension and ischaemic nephropathy

An understanding of the underlying pathophysiology of ARAS dates from 1934 when Goldblatt and co-workers, in their seminal studies, demonstrated that partial occlusion of one renal artery resulted in a significant increase in blood pressure.¹⁶ The implication of this work was not appreciated until many years later. The important concept demonstrated by such experiments was that a reduction in renal perfusion pressure was sufficient to induce sustained hypertension. The importance of the renin-angiotensin system in the initiation of this state has been subsequently demonstrated and other factors, such as nitric oxide and prostaglandins, play an important role in its maintenance.¹⁷ Renal hypoperfusion results in reduced preglomerular pressure and flow. Renin secretion with production of angiotensin II occurs consequent to reduced shear stress on the afferent arteriole. This results in vasoconstriction of the efferent arteriole and decreased production of prostacyclin and nitric oxide. The efferent arteriole is rich in angiotensin II receptors. Progressive constriction of this vessel is essential to preserve the jeopardised GFR in this setting.¹⁸

ISCHAEMIC NEPHROPATHY

The pathophysiology of this condition varies from acute ischaemic changes secondary to total occlusion of the renal vascular supply, to those changes that develop insidiously over a prolonged period of time as a result of a partially compromised vascular supply. In the acute setting marked features secondary to ischaemia are evident at the level of the glomerulus with 'collapse' of the glomeruli and reduplication of the basement membrane. In the subacute setting the glomerulus is relatively spared with interstitial changes predominating.^{19, 20} These include loss of tubular integrity, thickening of tubular basement membrane, tubular cell necrosis, interstitial fibrosis and localised areas of chronic inflammation. Evidence of athero-embolic lesions may also be found.²¹ Chronic hypoperfusion is usually accompanied by renal atrophy. The post-stenotic kidney demonstrates a mixture of vascular sclerosis, tubular atrophy, interstitial fibrosis, cholesterol crystals, inflammatory cells and focal or global glomerulosclerosis.²² Angiotensin II is thought to play a central role in contributing to renal fibrogenesis through induction of transforming growth factor β , platelet-derived growth factor B, and SPARC (secreted protein acidic and rich in cysteine) by glomerular and interstitial cells.²³ In this context, interstitial myofibroblasts defined by expression of α -smooth muscle actin have been demonstrated. Such cells are associated with increased production of collagens which promote fibrosis. Others have suggested that renal tubular ischaemia triggers an autoimmune interstitial nephritis.²⁴ Another hypothesis is that the stenotic kidney is deprived of a putative growth factor referred to as 'renotropin', which is thought to be responsible for compensatory renal growth.²⁵

NATURAL HISTORY

ARAS is a progressive disease. One of the first prospective studies undertaken was that by Dean and associates in the early 1980s.²⁶ Forty-one patients with known renovascular hypertension between the ages of 40 and 65 years were randomised to medical treatment. Criteria used to assess deterioration in renal status included:

- a decrease in renal length by 1.5 cm
- a 25% increase in serum creatinine, and
- a decrease in isotopically determined GFR.

During a mean follow-up period of 36 months, 40% developed a decrease in renal function and 37% a reduction in renal size. No correlation with progression was demonstrated for either hyperlipidaemia or blood pressure. Retrospective studies

Table 2 Progression of atherosclerotic renal artery disease in 126 diseased renal arteries (excluding five with 100% initial occlusion, 25 persistently normal, and 13 with *de novo* stenosis (10<50%, 3>50%).²⁷ Figures are given as the number of diseased renal arteries in each category with percentage values in parentheses

% Stenosis on initial angiogram	% Stenosis on sequential angiogram			
	50	50-74	75-99	100
<50 (n=78)	54 (69)	12 (15)	8 (10)	4 (5)
Mean angiographic interval (months)	41±0.58	36±1.8	51±3	59±5.4
50-74 (n=30)		16 (53)	11 (37)	3 (10)
Mean angiographic interval (months)		29±1.2	34±1.7	23±7.1
75-99 (n=18)			1 (5)	7 (39)
Mean angiographic interval (months)			21±1.5	13±0.8

Table 3 Important clinical parameters that may contribute to the diagnosis of ARAS

<i>History</i>	<i>Clinical examination</i>
Smoker	Abdominal/femoral bruit
Recent onset of hypertension (within 2 years)	Evidence of peripheral vascular disease
Difficult to control hypertension (three or more medications)	Grade III/IV hypertensive retinopathy
Accelerated hypertension	
Age (>70 years)	
Antihypertensive medication-induced renal impairment especially by ACE inhibitors	
Ischaemic heart disease	
Peripheral vascular disease	
Episodes of unexplained pulmonary oedema (flash pulmonary oedema)	
Renal impairment with any of the above	

have demonstrated a similar outcome (table 2).^{27, 28} The rate of progression to occlusion correlates with the initial degree of stenosis. Thus, for significant stenoses (>75%), approximately 39% of patients progressed over a 12-month period to total occlusion and for moderate stenoses (50–75%) 47% progressed, with 10% experiencing complete occlusion.²⁷ The time interval for progression of moderate stenoses was longer at 34 and 23 months for progression and occlusion, respectively. In a prospective study using colour Doppler ultrasonography, patients were categorised as having either <60% stenosis (Group 1) or >60% stenosis (Group 2).²⁹ Progression to total occlusion for Group 2 was 5% at 1 year and 11% at 2 years and for progression from Group 1 to Group 2, 23% at 1 year and 42% at 2 years. Studies such as these highlight the progressive nature of ARAS.³⁰

CLINICAL FEATURES

There is no clinical sign or symptom that is specific for renovascular disease. Nevertheless, certain collective clinical features have been demonstrated to be suggestive of this diagnosis. Therefore, the initial step in detecting ARAS is to identify the at-risk population. Clinical history can aid this process. The important features are listed in table 3. The Cooperative Study of Renovascular Hypertension was a large multicentre study designed to clarify the clinical differences between essential and renovascular hypertension. Based on the assessment of 2442 patients, 175 were identified as having renovascular hypertension, defined by surgical cure. When these patients were compared against 339 patients with essential hypertension, significant differences were observed for: loss of blood pressure control, accelerated hypertension, presence of vascular disease, abdominal/flank bruit and grade III/IV hypertensive retinopathy.^{31, 32} These parameters have been subsequently assessed in a small prospective study which highlighted the importance of an abdominal/flank bruit and refractory hypertension (defined as failure to obtain control with three medications) as predictive factors for ARAS.³³ Flash pulmonary oedema is a well-described entity, though the incidence remains unknown. In a retrospective analysis of 191 patients undergoing renal revascularisation, 17 patients (8.9%) were found to have recurrent pulmonary oedema and hypertension.³⁴ Flash pulmonary oedema was cured by revascularisation.

Investigative techniques

For a screening test it is important to consider the sensitivity, specificity, and predictive values of the investigation, as well as prevalence of the target disease in the population to be screened. Ideally, the test should be safe, accurate and reproducible. In a non-selected hypertensive population, the prevalence of RVH is low (1–5%).^{3–5} For an investigation with a sensitivity and specificity of 90%, such a low prevalence results in the investigation having only a 20% positive predictive value.^{35, 36} Therefore it is important to select patients clinically prior to investigation (as described). Investigative tests include the captopril test,^{37, 38} colour duplex ultrasonography,^{39, 40} captopril renography,^{41, 42} magnetic resonance arteriography (MRA),^{43, 44} and spiral computed tomography (CT).^{45, 46} The standard against which all tests are compared is selective renal arteriography.⁴⁷ The degree of stenosis that is regarded as significant remains controversial. Experimental studies in rats have indicated that >50% stenosis in large peripheral vessels is associated with pressure and flow reduction, however, in the renal vasculature this may not occur until >75% stenosis,⁴⁸ indeed a figure as high as 80–85% has been quoted.⁴⁹ The value of >75% stenosis is operationally used by most clinicians to indicate a significant stenosis. It is important to appreciate that relying on the degree of stenosis to make a management decision should be

treated with caution as other factors contribute to pressure reduction, such as length of stenosis, contour and distal vascular resistance. Limitations in the usage of degree of stenosis are highlighted by the fact that not every patient with ARAS has RVH.

CAPTOPRIL TEST

Measurement of peripheral or renal vein renin has been shown to be inadequate for the diagnosis of RVH. Although peripheral renin activity is usually elevated in patients with renovascular hypertension, approximately 20% of patients with RVH have a normal peripheral renin activity whilst up to 16% of patients with essential hypertension may have an elevated peripheral renin activity.^{41 42} The use of angiotensin-converting enzyme (ACE) inhibition improves the discrimination of peripheral renin activity for renovascular hypertension by approximately two-fold.³⁵

COLOUR DUPLEX ULTRASONOGRAPHY

This refers to the use of ultrasonographic imaging combined with Doppler techniques to measure blood flow velocity. A number of different approaches may be utilised to confirm the presence of renal artery stenosis such as assessment of morphology, haemodynamic changes and spectral findings.^{39 40} Doppler measurements can assess a range of parameters such as peak systolic velocity, renal:aortic ratio, end-diastolic velocity, resistive index, acceleration time and acceleration index. Comparison of the peak systolic velocity with that in the adjacent aorta is referred to as the renal:aortic ratio. A peak systolic velocity in the renal artery of >180 cm/s or a renal:aortic ratio of >3.5, individually or together, indicate a stenotic lesion of >60%.³⁹ Advantages for this technique include non-invasiveness and cost, whilst disadvantages include operator-dependency, and the fact that it is time-consuming, not universally applicable and offers poor assessment of distal or branch vessels.

MRA

This is a non-invasive technique that requires neither ionising radiation nor nephrotoxic contrast. Results are best for proximal lesions, however, and more distal lesions (beyond the first half) and accessory renal arteries are frequently missed. MRA has been advocated as a screening test in high-risk individuals with impaired renal function.⁴⁴

SPIRAL CT

Spiral CT provides good visualisation of the renal blood supply and is minimally invasive.^{45 46} The main drawback is that the contrast injection has to be maintained over a 20–30-s period, resulting in large contrast volumes of 130–150 ml. The risk of nephrotoxicity in high-risk patients is substantial.

CAPTOPRIL RENOGRAPHY

Renal scanning with technetium [99m]Tc-diethylenetriaminepentacetic acid (DTPA)⁵⁶ or [99m]Tc-mercaptoacetyl triglycerine (MAG₃)⁵⁷ are both non-invasive and safe even in patients with renal insufficiency. DTPA is filtered by the kidney and not reabsorbed and therefore may serve as a marker for glomerular filtration rate, whilst MAG₃ is both filtered and secreted into the tubules and may serve as a marker for renal plasma flow. The rationale of performing scans after ACE inhibition derives from the fact that reduction of angiotensin II in the stenotic kidney reduces the GFR by reducing efferent arteriolar vasoconstriction, resulting in delayed isotope excretion. The accuracy of this test decreases in patients with increasing serum creatinine values, particularly in excess of 180 µmol/l.⁵⁸

RENAL ARTERIOGRAPHY

Renal arteriography remains the gold standard for the identification and confirmation of renovascular disease.⁴⁷ Side-effects of this procedure, such as invasiveness, contrast-induced nephrotoxicity, and athero-embolic disease, have resulted in alternative investigative techniques being sought for screening purposes. Complications of arteriography predominantly fall into two groups, namely, contrast-induced nephropathy and athero-embolic disease. In contrast-induced nephropathy, the serum creatinine begins to rise 24–48 hours following contrast administration, peaks within 3–5 days and then returns to baseline levels within 7–10 days.^{59 60} In patients with severe nephrotoxicity, the serum creatinine may continue to rise for 5–10 days or until dialysis is required. The incidence of contrast-induced nephropathy in non-high-risk patients has been quoted at 0–7%,^{60 61} with an average of 3%.^{62 63} High-risk patient groups include diabetes mellitus, multiple myeloma and pre-existing impaired renal function.^{59 64–67} Sev-

Table 4 Potential findings in patients with athero-embolic disease/cholesterol emboli syndrome

<i>Clinical</i> ^{50 51}	<i>Biochemical</i> ^{50 52 53}	<i>Histological</i> ^{50 51 54}
Livedo reticularis	Eosinophilia	Glomerular tuft ischaemia
Digital infarcts	Hypocomplementaemia	Basement membrane wrinkling
Trash feet	Polyclonal Ig response	Atrophic wedge-shaped segments
GI bleeding	Acute phase response	Cholesterol clefts
Ischaemic bowel		
Pancreatitis		
Hepatitis		
Cardiac events		
Neurological events		

eral prophylactic strategies have been developed to reduce the incidence of contrast-induced nephropathy, including saline hydration with or without frusemide, mannitol, aminophylline and calcium channel blockers.⁶⁸⁻⁷¹ None of these reagents have been demonstrated as having a clear benefit over saline hydration, however.

Athero-embolic disease is a recognised complication of angiography.⁷²⁻⁷⁴ This syndrome has a protean presentation with variable severity ranging from an innocuous rash to death. The clinical and biochemical features of this are listed in table 4. It has been attributed to occlusion of small (150–200 µm) arteries by athero-embolic material from eroded atherosclerotic plaques in diseased aortas. Renal involvement ranges from fulminant oliguric renal failure to an insidious non-oliguric state with progressive development of uraemia. It is often associated with a poor outcome, although exceptions have been reported.^{75 76} Up to 30% of autopsies on patients with significant atherosclerosis or abdominal aortic aneurysm have demonstrated evidence of athero-embolic disease.⁷⁷ An inciting stimulus can usually be detected, such as traumatic manipulation,⁷⁸ systemic anticoagulation, or thrombolytic therapy.^{75 76 78-81} A number of studies assessing the incidence of athero-embolic disease complicating renal artery angioplasty have quoted a prevalence ranging from 0.6% to 6%.⁸²⁻⁸⁴

Sensitivity and specificity for the investigative tests discussed above are listed in table 5.

Patient assessment

This starts with history and examination. For those patients with features that suggest further investigation to be appropriate (table 3), then renal function and cardiovascular risk factors need to be assessed. A renal ultrasound scan should be undertaken for renal size, a differential in renal size of >1 cm may heighten one's suspicion of underlying ARAS. Where the expertise exists, a colour duplex ultrasound should be undertaken at this point and, if positive, one would then proceed to selective renal angiography. In the absence of colour duplex ultrasound, a captopril renogram should be performed. It is important to appreciate that both colour duplex ultrasonography and captopril renography can result in false positive results even in optimally selected patients. Values quoted vary from 5–16% and 7–10%, respectively, with potentially higher values in routine clinical practice. Therefore, if one's clinical suspicions are sufficiently high, one may proceed to angiography despite a negative scan. The sensitivity and specificity of captopril renography is further reduced in the setting of renal impairment.

Treatment

Indications for intervention in atherosclerotic renovascular disease include treatment of hypertension, preservation of renal function or a combination of both. There still exists much debate as to what constitutes appropriate manage-

Table 5 Screening tests for renal artery stenosis

<i>Test</i>	<i>Sensitivity (%)</i>	<i>Specificity (%)</i>
Captopril stimulated plasma renin activity	73–100	72–95
Tests for lateralisation:		
Renal vein renin	64	87
Captopril renography	90–93	93–98
Intravenous urography	59	89
Duplex & doppler sonography	84–95	81–98

Table 6 Renal outcome of surgical revascularisation in ischaemic renal disease

Reference	Year	Patient number	Mean/median follow-up (months)	Renal function result (%)			
				Improved	Stable	Worse	Mortality
86	1984	23	24*	65	0	35	17
87	1987	161	37*	58	31	11	11
88	1987	91	24*	22	53	25	7.1
89	1992	70	24	49	36	15	2.5
90	1992	40	24	55	25	20	<3
91	1992	91	33	49	35	16	6

*Estimated from data in paper

ment, ie, medical, angioplasty, or surgical. Factors that require consideration in determining the choice of therapy include the general medical condition of the patient, natural history of renal arterial disease, renal function, and the expertise available to perform either surgical revascularisation or percutaneous transluminal renal angioplasty (PTRA), with or without stenting. The underlying pathophysiology of chronic ischaemic nephropathy remains poorly elucidated and no marker exists to indicate reliably which patients might benefit from intervention. In patient assessment it is important to balance the risks of revascularisation with the risk of progression of the renal artery stenosis.

CONSERVATIVE MEDICAL TREATMENT

Such treatment should be restricted to patients with absolute contraindications to PTRA/surgery or to those with a sufficiently reduced life expectancy due to comorbid illnesses. Medical management should address optimal blood pressure control, stabilisation of renal function, prevention of lesion progression, modification of cardiovascular risk factors, and treatment of any concomitant cardiovascular and cerebrovascular disease to improve survival. Unfortunately, control of hypertension does not alter the primary disease process and the vascular lesion progresses.

SURGICAL TREATMENT

Surgical renal revascularisation is well established as an effective treatment for patients with severe hypertension, renal insufficiency, or both (table 6).⁸⁶⁻⁹¹ Mortality has decreased in the more recently reported studies despite a demographic shift to an older population with greater comorbidity.⁹⁰ This reflects better preliminary screening with correction of existing coronary and cerebrovascular occlusive disease together with the development of more effective revascularisation techniques that avoid operating on badly diseased aortas. In the past, control of hypertension was the main surgical indication; this has been replaced by the need to preserve renal function. Preservation of renal function has been successfully achieved for the majority of patients with immediate as well as longer term benefit demonstrated.⁹³⁻⁹⁶ Depending on the nature of the lesion a range of different approaches may be used including; endarterectomy, aortorenal and extra-anatomic bypass procedures.^{95-97 99-101} Extra-anatomic approaches have been developed to reduce the mortality and morbidity associated with simultaneous aortic replacement and renal revascularisation.^{102 103} These approaches include hepatorenal artery bypass, gastroduodenal-renal artery bypass, spleno-renal bypass, iliorenal bypass, and bypasses stemming from the superior mesenteric artery. Mortality from these procedures is low, quoted at <1-6% in various series.^{98 103} Successful preservation or restoration of renal function varies from 60-100%, whilst improvement of hypertension in 65-90% with a cure rate at 7-15%. The incidence of late bypass graft stenosis is approximately 10% over 5-10 years.⁹⁸ Pooled data suggests that, for preservation of renal function, the best outcome was found in patients with serum creatinine <250 $\mu\text{mol/l}$ and in those who have experienced a rapid decline in renal function in the preceding 6 months.⁹⁹ Exceptions to these general statements exist, with several groups reporting patients presenting with dialysis-dependent renal failure who have had salvageable renal function.^{97 98 104} In a large retrospective study (222 patients) for the period 1974 to 1987 with a mean follow-up of 7.4 years, operative mortality was reported at 2.2%, improvement in hypertension at 72.4%, and preservation of renal function at 71.3%. Five-year survival was comparable with an age-matched control population whereas the 10-year survival was less (53% *vs* 77%). The latter observation correlated with underlying cardiovascular disease.¹⁰⁵ Thus, surgical intervention sets the standards against which the other treatment modalities should be compared. Other groups have confirmed the efficacy of surgical revascularisation as well as its long-term benefit.¹⁰⁶ Surgical patients are,

however, a selected group, as not everyone is suitable for such intervention. There is a tendency to use angioplasty with or without stenting in a wider range of patients. There have been few studies making a direct comparison of surgical revascularisation with PTRA. One such study clearly demonstrated benefit of the former over the latter.¹⁰⁷ No direct comparison between surgical revascularisation and PTRA plus stenting has been undertaken. Despite the perception that surgical revascularisation is a high-risk option, the quoted mortality and morbidity figures are comparable with those of PTRA with or without stenting.

Adverse prognostic features for surgical intervention include failure to respond to surgical intervention (increased mortality), impaired renal function (creatinine >250 µmol/l), and extensive vascular disease.^{89–99} Although comparable data are not available for PTRA, similar factors might be expected to apply. For salvageable renal function, size of the kidney is one of the most important parameters with kidneys <8 cm in length tending to derive little benefit from intervention.⁸⁵

PERCUTANEOUS TRANSLUMINAL RENAL ANGIOPLASTY

Gruntzig and colleagues in 1978 were the first to describe the application of this technique to the renal artery.¹⁰⁸ This procedure has many advantages over surgical intervention, such as shorter hospital stay, avoidance of general anaesthesia and ease of repetition. The principle involved is mechanical dilatation of the stenotic artery with an inflatable balloon catheter placed across the stenotic lesion and then inflated usually to 5 atmospheres. Dilatation occurs by rupturing the plaque, producing fissures in the intima and media and by over-distending the adventitia. The atherosclerotic material is therefore displaced and remodelled.

In experienced centres, technical success rates for PTRA range from 79% to 96% of renal arteries depending on the series, with lower patency rates affected by type of lesion. For non-ostial lesions the re-stenosis rates are low (10–30%),^{109–113} whereas for ostial lesions this figure is greater with rates of 25–50% reported at 6 months.^{114–115} Such high re-stenosis rates have prompted the use of stents which have resulted in better initial haemodynamic results (primary patency) with reduced re-stenosis rates of 11–25%.^{116–117} A retrospective study of PTRA plus stenting for ostial lesions in 68 hypertensive patients with a 27-month follow-up period, demonstrated a re-stenosis rate of only 11%.¹¹⁸ In this study hypertension was cured in 16% and improved in 62% of patients whilst renal function remained unchanged for the study group as a whole as well as those with mild (17) (134–169 µmol/l) and severe (three) renal impairment (>177 µmol/l). A prospective randomised trial comparing PTRA with PTRA plus stenting for ostial lesions demonstrated the benefit of the latter with respect to both primary patency (90% *vs* 63%) and re-stenosis rates at 6 months (14% *vs* 48%) with no increased morbidity.¹¹⁹ There is evidence from the cardiovascular literature to suggest that the incidence of re-stenosis declines with the passage of time.¹²⁰ Improvement or stabilisation of renal function has been variable, with different groups reporting response values of 50–70%.^{121–124} A prospective study of PTRA plus stenting, although demonstrating improvement or stabilisation of renal function in 69% of patients, also reported a one-year mortality rate of 40%.¹²⁵ Observations such as this reinforce the need for careful patient selection.

Although blood pressure improvement has been reported for PTRA with or without stenting this is usually modest and for the majority takes the form of drug sparing; improvement has been reported to range from 40% to 80% of hypertensives.^{121–124} Most of these quoted figures are not based on intention-to-treat analysis. One of the few direct comparisons of medical therapy with PTRA for hypertension control failed to demonstrate a difference in level of control between the two groups. Relative drug sparing was documented for 60% of the PTRA-treated group, however, this was associated with increased morbidity ranging from mild (groin haematoma) to severe (renal artery dissection) complications.¹²⁶

Surgical revascularisation in experienced centres has clearly demonstrated short term benefit over PTRA with or without stenting and long-term benefit over PTRA. Insufficient data exist to make the long-term comparison between surgery and PTRA plus stenting. However, due to associated comorbidity, there will be a proportion of patients who are not suitable for surgery and for these PTRA, with or without stenting, may be an option. An important factor that will determine preference of surgical intervention over PTRA, or *vice versa*, will be that of local expertise.

Indications for intervention

This remains a source of ongoing debate. There exists a need to identify patients with progressive disease. Intervention (surgery or PTRAs) at too early a stage may unnecessarily expose the patient to undue risk. Targeting the correct patient group is therefore paramount. Patients with progressive disease are more likely to exhibit impairment of renal function and a reduction in renal size. A reliable marker for progression does not exist. Based on the natural history of the disease process it would be appropriate to intervene in those patients with ostial or main vessel stenoses of >75%, regardless of hypertension. Intervention for ostial lesions (within 1 cm of the origin) should be by PTRAs plus stenting or a surgical revascularisation procedure. For non-ostial lesions, angioplasty is sufficient except where there is an indication to stent, namely, excess elastic recoil, inadequate dilatation, or partial dissection. Patients need to be assessed individually, those least likely to benefit from intervention include patients with reduced kidney size (<8 cm), impaired renal function (creatinine >250 mmol/l) and extensive vascular disease. The natural history of those patients with a stenosis in the range of 50–75% would suggest that regular monitoring and treatment of risk factors is probably the most appropriate policy as up to 53% of such patients may fail to progress over a 2 to 3 year period.²⁷

The above arbitrary classification of degree of stenosis and correlation with treatment modality will undoubtedly be modified as more data become available with respect to the natural history of this disease process and more importantly data on the longer term efficacy of PTRAs plus stenting, so that the risk:benefit ratio of intervention can be properly assessed.

Follow-up

The purpose of monitoring is to detect a change within a time frame that minimises the chances of irreversible damage. Pre-procedure assessment includes renal size, GFR and blood pressure. The GFR and blood pressure need to be re-assessed 1 month post-procedure and thereafter 6 monthly in conjunction with a renal ultrasound scan. Arbitrary cut-off points that should prompt further assessment in the form of a repeat renal angiogram include a decrease in renal size of >1 cm, a decrease in GFR of >20% or an increase in mean arterial blood pressure >10 mmHg. These are not fixed criteria and are given for guidance only. As stated above, a similar type of assessment needs to be made for patients with 50–75% stenosis, to enable intervention to be targeted only at those patients that progress.

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