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LECTURE PRESENTATION

Renal Artery Stenosis: Significance and Treatment

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In the early 1960s, selected patients with hypertension were referred for aortography in the hope of demonstrating that renal artery stenosis was the cause of the hypertension. This could then be surgically treated. The indications for, and importance of, aortography for patients with hypertension were described by McMichael in 1961.[1] This author recommended the investigation of patients who had the following features:

- presented with hypertension before the age of 40 years with no obvious cause
- presented with sudden onset severe hypertension when the blood pressure had previously been normal
- were noted at abdominal X-ray or intravenous urography to have 1 kidney that was significantly smaller than its fellow
- had a vascular bruit in the renal area.

The aortograms were performed either by high translumbar puncture or by the per-femoral approach using relatively large catheters and straight guidewires. In 1964, DeBakey et al[2] and Poutasse[3] reported a high prevalence of renovascular hypertension that could be cured by surgery. Most clinicians were not impressed by these claims since their own clinical results did not match those reported by these authors. In 1965, Chamberlain and Gleeson reported significant morbidity in hypertensive patients who submitted to aortography.[4] They also reported that, although the blood pressure was lower or normal following surgery, most patients' blood pressure returned to its preoperative level within a few months. They stated that there was no reliable test that could distinguish renovascular hypertension from essential hypertension with an incidental renal artery stenosis.[4] Medical management of hypertension was generally effective and the risks of aortography and surgery were therefore unjustified. Consequently surgery for renovascular hypertension was generally discontinued in most centres.

In 1978, Gruntzig et al reported treatment of renovascular hypertension by percutaneous dilatation of a renal artery stenosis.[5] Following this report, despite the fact that there was still no test to differentiate between essential hypertension and renovascular hypertension, the technique became widely, if not wisely, used for the treatment of renal artery stenosis in patients with hypertension. The exact role of percutaneous transluminal renal angioplasty (PTRA) in hypertension remains arguable but, during the past decade, attention has focused on deteriorating renal function in the presence of renal artery stenosis. Renal angioplasty and renal stent placement can be technically difficult and deaths from renal artery rupture have been reported. It is therefore important to have a clear understanding of the indications for intervention, the benefits that might accrue, and the risks of the procedure.

PATHOLOGY, PRESENTATION AND NATURAL HISTORY OF RENAL ARTERY STENOSIS

The commonest cause of renal artery stenosis is atherosclerosis and this accounts for at least 90% of patients. Fibromuscular dysplasia is the cause for less than 10% of patients and conditions such as Takayasu's arteritis and neurofibromatosis are occasionally encountered. Fibromuscular dysplasia is essentially a group of conditions that involves the intima, the media, and the adventitia, and is generally encountered in females between the ages of 15 and 50 and is bilateral for 60% of patients. This condition has a tendency to involve the mid and distal renal arteries (Figure 1), which are often seen at angiography to have a beaded appearance that is classically referred to as a 'string of beads'. The stenoses are progressive for 30% of patients but they

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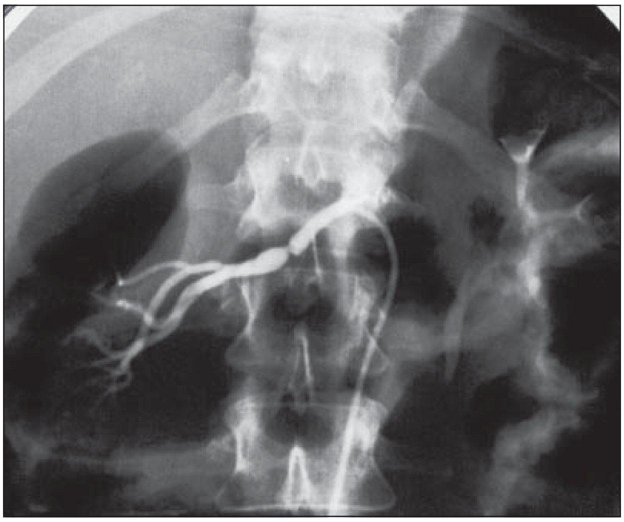

Figure 1. A 35-year-old female with renal artery stenosis due to fibromuscular dysplasia. The stenoses are frequently multiple, giving the appearance of a 'string of beads'.

rarely result in renal artery occlusion. However, renal atrophy occurs, as shown by loss of renal length.[6]

Atherosclerosis is the cause of at least 90% of renal artery stenoses, generally involving the proximal renal artery, the ostium of the renal artery, and the adjacent aortic wall (Figure 2). Atherosclerosis may present clinically as hypertension, chronic renal failure, acute renal failure, particularly after the use of angiotensin converting enzyme (ACE) inhibitors, 'flash' pulmonary oedema, or even congestive cardiac failure.[7-11] Atherosclerotic renal artery stenoses may also be discovered as an incidental finding during aortography. The incidence of unsuspected renal artery stenoses ≥50% revealed by angiography in patients older than 60 years is reported to be 28% (range, 22% to 42%).[12-15]

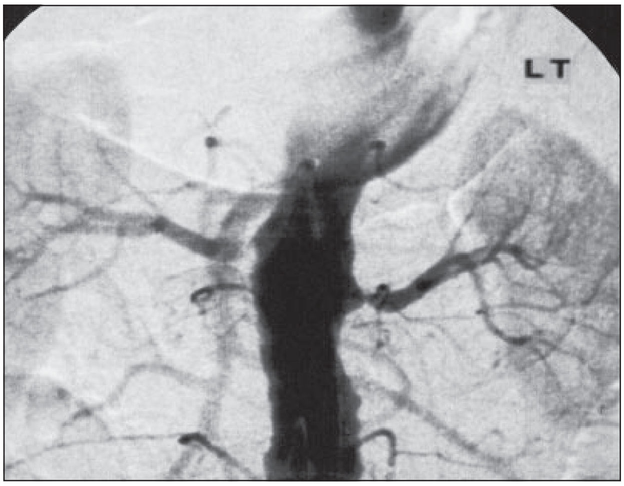

Figure 2. Typical bilateral atherosclerotic renal artery stenoses involving the proximal renal artery, the ostium of the renal artery, and the adjacent wall of the aorta.

Atherosclerotic renal artery stenosis is frequently progressive and recent studies with Doppler ultrasound have shown progression in 51% of arteries over a 5-year period.[16] This study has also demonstrated that a 60% stenosis has a 5% chance of occlusion at 1 year and a 10% chance of occlusion at 2 years.[16] In 19% of patients with a stenosis >60%, the kidney will atrophy and lose 1 cm or more in length by 1 year.[17] Renal atrophy, however, is not simply secondary to the renal artery stenosis, since 25% of patients with a non-progressive renal artery stenosis also develop renal atrophy.[6] Thus, another pathological process, such as athero-embolism or the replacement of glomeruli and tubules with fibrous tissue, must be involved.

Progressive atherosclerotic renovascular disease is increasingly recognised as a cause of end-stage renal failure. Scoble et al reported that 14% of patients older than 50 years who presented with renal failure for dialysis had atherosclerotic renovascular disease as the cause.[8] Since some patients with end-stage renal failure will not even be considered for dialysis because of their other comorbidities the incidence is probably even higher. The prognosis for patients receiving dialysis because of atherosclerotic renal artery stenosis is poor with 50% dying within 2 years.[18] Patients with atherosclerotic renal artery stenosis usually have generalised atherosclerosis and it has been reported that the incidence of mortality following surgery for peripheral vascular disease is 32% compared with nil mortality following operation for patients without renal artery stenosis.[19] For patients with coronary artery disease and atherosclerotic renal artery stenosis, the survival rate at 4 years is 65% compared with 86% for patients with no renal artery stenosis.[20] Atherosclerotic renal artery stenosis thus has a much wider clinical impact than simply the normal presenting manifestations.

Investigation of Renal Artery Stenosis

A number of methods, both non-invasive and invasive, are available for the investigation of renal artery stenosis, but all have relative disadvantages.

Duplex Doppler Ultrasound

Duplex Doppler ultrasound is the least invasive and least expensive method but it is heavily operator-dependent and may fail for up to 20% of patients due to body type or to interposition of bowel gas. It is also time-consuming with reports of examinations taking more than 1 hour to successfully demonstrate the main renal artery in its entirety. This technique nevertheless remains the initial method of choice at some centres with experienced operators.

Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) is increasingly favoured since it is relatively accurate for the proximal 1 cm to 2 cm of the renal artery but it is not capable of demonstrating renal artery branch stenoses. The technique is particularly favoured for the investigation of suspected atherosclerotic renal artery stenosis, as this predominantly involves the proximal renal artery. For patients with impaired renal function, MRA has the added advantage that gadolinium is not nephrotoxic.

Computed Tomography Angiography

CT angiography, like MRA, is most accurate for the proximal renal artery and is not able to demonstrate branch stenoses. In addition, however, the high dose of intravenous contrast medium that is required makes the technique unsuitable for patients with impaired renal function.

Intra-arterial Digital Subtraction Angiography

Intra-arterial digital subtraction angiography (IADSA) remains the gold standard. However, this technique is still usually only undertaken if the decision has been made to proceed to percutaneous transluminal renal angioplasty if a significant renal artery stenosis is demonstrated. The procedure is invasive and uses intra-arterial non-ionic contrast medium that is nephrotoxic. In addition, since many patients have widespread severe atheroma, there are the added risks of athero-embolism and cholesterol embolisation. Most centres now combine IADSA with measurement of pressure gradients across a renal artery stenosis — a gradient of 20 mm Hg is regarded as significant. To avoid the risk of nephrotoxicity some centres perform IADSA using either carbon dioxide or gadolinium as the contrast medium.

INDICATIONS AND RESULTS FOR PERCUTANEOUS TRANSLUMINAL RENAL ANGIOPLASTY AND STENT PLACEMENT

Renovascular Hypertension

The results of percutaneous transluminal renal angioplasty (PTRA) for the treatment of renovascular hypertension are dependent on the underlying cause of the stenosis. Patients with a renal artery stenosis due to fibromuscular dysplasia generally have a good outcome following PTRA. The procedure is technically successful for more than 90% of patients. For those in whom it is successful, 50% (range, 25% to 85%) are cured of their hypertension and for 42% (range, 13% to 63%) their hypertension is improved.[21] Cure is defined as a long-term reduction in diastolic blood pressure to 90 mm Hg or less and improvement is defined as a 15% reduction in diastolic blood pressure, which remains between 95 and 110 mm Hg. There is now general agreement that patients with hypertension and a renal artery stenosis should be treated by PTRA.

The situation is much more complex for patients with atherosclerotic renal artery stenosis. Renal artery stenoses are common, as is essential hypertension, but there is still no definitive test which indicates that a patient's hypertension is caused by the renal artery stenosis. The results for PTRA for hypertension and atherosclerotic renal artery stenoses are poor. The procedure is technically successful for 88% of patients (range, 76% to 97%) and, of those for whom it is successful, 19% (range, 9% to 29%) are cured of their hypertension, 52% (range, 13% to 63%) have an improvement, and for 30% there is no change. The degree to which an improvement is meaningful is also open to question since patients taking medical treatment may also show an improvement over a period of time.[22] For these reasons, renal angiography with a view to PTRA in the presence of a significant renal artery stenosis is generally only undertaken when 1 of the following criteria applies:

- progressive hypertension
- hypertension poorly controlled by medical therapy
- hypertension with impaired renal function
- hypertension in a patient younger than 30 years
- hypertension with deteriorating renal function after treatment with ACE inhibitors.

These results, however, were in series performed before the introduction of renal artery stents. It has always been recognised that PTRA is not effective in treating atherosclerotic renal artery stenoses that involved the ostium of the renal artery since the stenosis is caused by aortic plaque and there is elastic recoil following balloon inflation. The use of renal artery stents prevents this elastic recoil so that there is a considerable increase in the technical success rate of the procedure. However, Blum et al reported a series of 75 patients with hypertension and ostial atherosclerotic renal artery stenoses treated by PTRA and stent placement.[23] Despite renal artery stent placement, only 16% of patients were cured of hypertension and 62% showed an improvement. There was also a stent

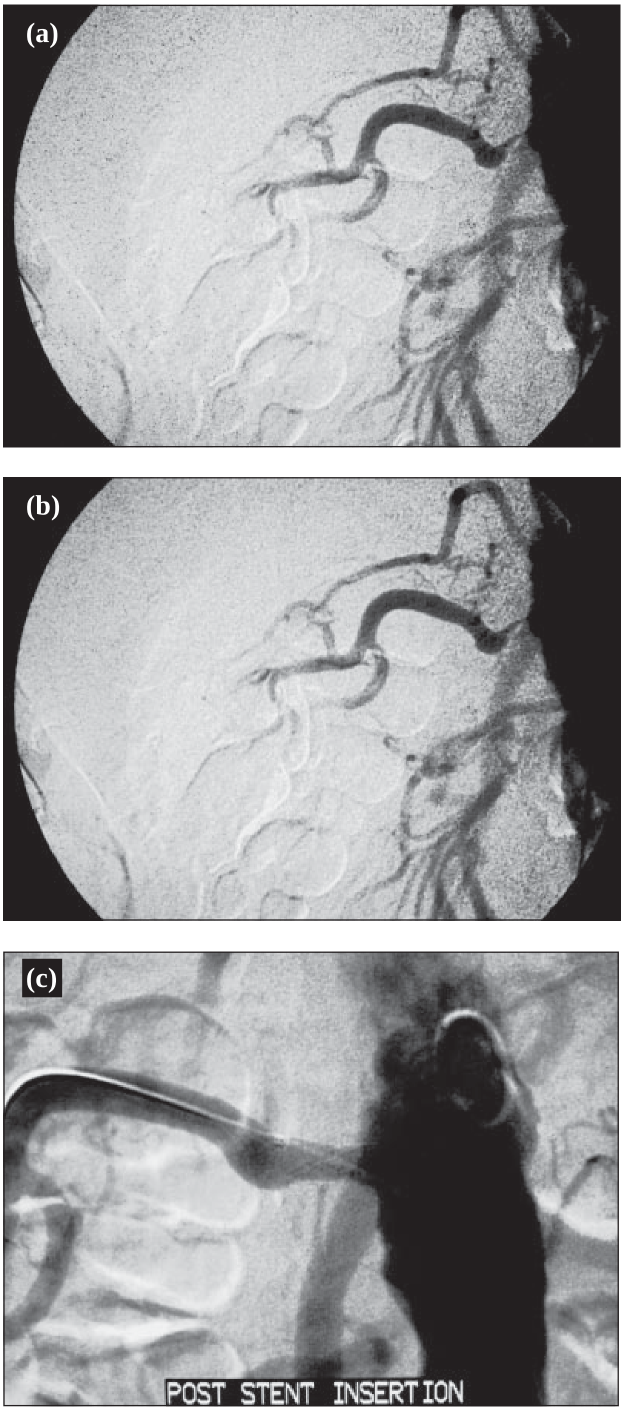

Figure 3. Patient with deteriorating renal function and recurrent pulmonary oedema. (a) Angiography demonstrated a tight ostial atherosclerotic renal artery stenosis; (b) following balloon angioplasty, the stenosis remained unchanged; and (c) following insertion of a 6 mm diameter stent, the artery is widely patent.

restenosis rate of 10%, but this can generally be managed by balloon angioplasty. Thus, improved patency did not improve the outcome for the group of patients who received renal artery stents. It is now generally accepted that renal artery stents should be placed when PTRA fails and there is a residual pressure gradient >20 mm Hg (Figure 3), when there is a flow limiting dissection following PTRA (Figure 4), or when a renal artery stenosis, which was previously treated by PTRA, recurs.

Atheroslerotic Renovascular Disease and Renal Failure

There are a number of reports in the literature of the results of PTRA for the treatment of renal failure due to atherosclerotic renal artery stenosis.[24,25] In general, the patients most likely to benefit are those with bilateral renal artery stenoses, those with a renal artery stenosis in a single functioning kidney, and those in whom the serum creatinine is less than 350 mmol/L at the time of the procedure. Harden et al reported the results of PTRA and stent placement in the treatment of renal artery stenosis and renal failure.[26] In their series, 34% of patients had an improvement in renal function following the procedure, for 34% the renal function was stabilised, and for 28% there was a deterioration in function. One patient died of a haemorrhage following the procedure. An improvement in renal function is defined as a >20% fall in serum creatinine at the latest follow-up measurement. The reasons for deterioration of function following the procedure are not clear but they may well be related to athero-embolism or cholesterol embolisation of the renal artery during the procedure. Research is underway to assess the value of filters of the type developed to collect emboli during carotid artery angioplasty and stenting. Unfortunately, there is as yet no reported randomised trial comparing medical treatment of renal failure with revascularisation by angioplasty with or without stent placement. However, 2 trials are currently recruiting — the Astral trial in the UK and the STAR trial in Europe. It is to be hoped that these resolve the dilemma as to whether PTRA is really indicated in the management of renal artery stenosis and renal failure.

Hypertension in Patients with Chronic Renal Failure and 'Flash' Pulmonary Oedema

Patients who present with hypertension, mild renal impairment, and a history of repeated attacks of pulmonary oedema should be investigated for the presence of either bilateral renal artery stenoses or a single functioning kidney with a renal artery stenosis.[10] The treatment of this type of pulmonary oedema is accepted as the only absolute indication for PTRA. There are also some reports that certain patients with impaired renal failure and congestive cardiac failure may also benefit from PTRA.[11]

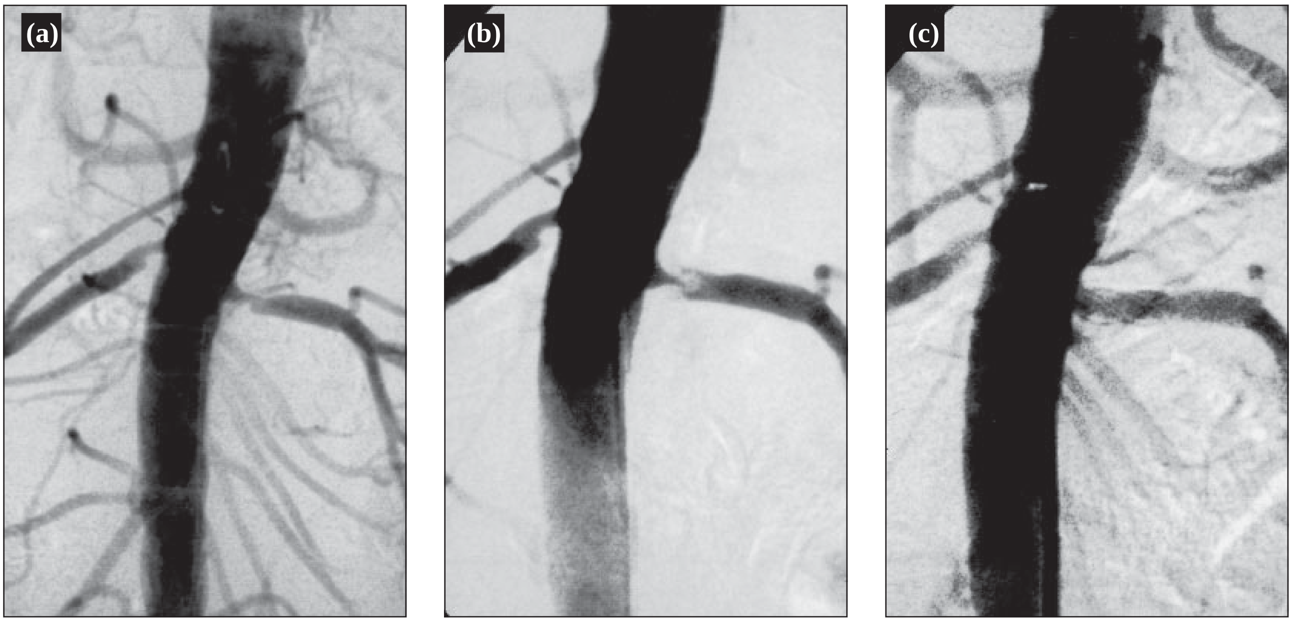

Figure 4. Patient with hypertension and deteriorating renal function. (a) Renal angiogram demonstrated bilateral atherosclerotic renal artery stenoses; (b) following balloon angioplasty a dissection has resulted in near occlusion of the renal artery; and (c) insertion of a 6 mm renal artery stent restored good flow.

Complications of Percutaneous Transluminal Renal Angioplasty

The complications of PTRA are frequently considerably more serious than those of peripheral angioplasty. Renal artery occlusion with loss of the kidney and death from renal artery rupture have both been reported. Complication rates between 9.00% and 30.70% have been reported and the reported mortality rate is 0.43%.[21,27,28] The complications are usually divided into complications at the angioplasty site, complications at the puncture site, and systemic complications. Those at the angioplasty site are renal artery dissection and occlusion, renal artery thrombosis, and renal artery rupture. Those at the puncture site include haematoma requiring transfusion or surgery, puncture site thrombosis, and pseudoaneurysm formation, while systemic complications are renal failure due to contrast media, thromboembolism, and cholesterol embolisation.

Conclusions

Percutaneous transluminal angioplasty is technically demanding and has a significant complication rate and a well-documented mortality rate. Thus it must only be undertaken with very clear clinical indications. Renovascular hypertension due to renal artery stenosis and fibromuscular dysplasia merits PTRA, but there is still no reliable way of distinguishing between essential hypertension and incidental atherosclerotic renal artery stenosis and renovascular hypertension secondary to atherosclerotic renal artery stenosis. PTRA may have a role in the management of renal failure secondary to renovascular disease but its efficacy compared with medical management needs defining. It is probable that this technique could have a role if it was possible to intervene earlier, but methods for predicting the likely progression and outcome of a renal artery stenosis are not yet available. It would seem that our knowledge of renovascular disease has progressed little during the past 40 years.

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