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Four years' experience of renal artery stenosis in a DGH

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In October 1998 we established a multidisciplinary renal artery stenosis (RAS) service to provide consistent investigation, treatment and follow-up of these patients with multiple severe vascular pathology. Patients were identified clinically by progressive or ACEI/ARB induced renal impairment, flash pulmonary oedema, unequal kidneys (>1.5 cm) on ultrasound scan, severe hypertension or coincidentally during imaging.

Initial investigation was by ultrasound with Doppler studies to confirm RAS, exclude aortic aneurysm and to measure bipolar renal lengths. Prior to 2001, the definitive investigation was day case (4F) renal angiography, since then we have used CT renal angiography. A full clinical assessment was performed by the nephrologist. The serum creatinine, creatinine clearance (Cockcroft & Gault formula) and divided renal function (by DMSA scanning) were measured before angioplasty and at 3-monthly and subsequently at yearly intervals. Blood pressure was treated to a target of <140/85 mmHg, cholesterol to <5 mmol and all patients received low-dose aspirin.

29 patients (18 men and 11 women) with a mean age of 60 years (range 41–78 years) have undergone renal angioplasty. 28 patients had atherosclerotic RAS (4 ostial and 24 proximal) and 1 had fibro-muscular hyperplasia. Primary angioplasty was successful in 17 patients and stents were inserted in 7 patients. In 5 patients angioplasty failed but 2 underwent successful surgical revascularisation, in 1 it was not possible to cannulate the artery and 2 patients suffered renal artery occlusion.

There were no statistically significant differences in the mean serum creatinine, creatinine clearance and divided renal function before angioplasty and at 1, 2 and 3 years after treatment (Table 1). Three patients had severe renal impairment at baseline and continued to deteriorate. However, for the majority of patients who had mild–moderate renal impairment, the renal function remained stable and there was a trend towards improvement after treatment (Table 2). There were no significant differences in the BP and anti-hypertensive drug requirements of the patients' before and at the latest follow-up. During the follow-up period 1 patient died as a possible complication of angioplasty, 3 patients died from unrelated conditions, 2 developed ESRF and 3 recurrent RAS.

These results are likely to reflect DGH practice, with a failure, renal artery occlusion, re-stenosis and death rate. Although not statistically significant, patients with mild–moderate renal impairment show a trend towards improvement. Patients with severe renal impairment did badly in this series. We await the results of the ASTRAL trial, but whatever the outcome, these difficult patients need a multidisciplinary approach with consistent investigations, treatments and follow-up.

Table 1

	Before R_x	After angioplasty		
		1 Year	2 Years	3 Years
Sr creatinine $\mu\text{m/l}$ (S.D.)	163 (± 87)	202 (± 203)	120 (± 60)	109 (± 49)
Creatinine cl. ml/min (S.D.)	49 (± 20)	51 (± 25)	58 (± 19)	62 (± 22)

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Table 2

	Before R_x	After angioplasty		
		1 Year	2 Years	3 Years
Sr creatinine $\mu\text{m}/\text{l}$ (All patients with mild-mod renal impairment)	136 (± 43)	122 (± 40)	120 (± 60)	109 (± 49)
Creatinine cl. ml/min (All patients with mild-mod renal impairment)	53 (± 18)	58 (± 20)	58 (± 19)	62 (± 22)

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Long term follow-up of hypertensive patients with atheromatous renal artery stenosis

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There is a paucity of long term major outcomes data in patients with renal artery stenosis. We undertook a retrospective review of the records of 68 patients with atheromatous renal artery stenosis originally identified between 1985 and 1992 during recruitment in Aberdeen for the Scottish and Newcastle Renal Artery Stenosis Trial^[1]. Vital status at June 2002 was ascertained in all patients and causes of death determined from inspection of Death Certificates and hospital case records. Over a ten-year period, mortality was 50% (34/68). The recorded causes of death were predominantly cardiovascular (6), cerebrovascular (8) and renal (6).

Full details satisfying our predetermined dataset were unavailable in 22 patients who had died—the result of a local hospital policy of destroying case records five years after death. However, a more detailed data set was obtained in 46 patients. In this group, overall mortality was 12/46 (26%), with a mean time from diagnosis to death of 7.8 years. End stage renal failure had developed in 9/46 (20%)—of whom 4 are on haemodialysis, 2 have received a renal transplant and 3 were being managed medically at the time of review. Mean blood pressure (BP) at diagnosis was 200/114 mmHg in those who died and 202/110 in those who survived (ns). Mean BP prior to death was 179/92 and at most recent follow up in the survivors was 152/82 ($P < 0.01$). 36% of those who died and 38% of those still alive have had some form of renal revascularisation procedure attempted.

This review confirms the high mortality in patients with atheromatous renal artery stenosis. Intervention does not appear to have been conspicuously successful on long term outcome. BP control appears to be better in those who survive than in those who died. It is not clear if the better survival is a direct result better BP control, although the high frequency of cardiovascular mortal events and the known inverse relationship between achieved blood pressure and favourable outcomes in other settings would strongly support this interpretation.

A number of case series have described major outcomes in atheromatous renal artery stenosis, but all of these (including our own data presented here) are subject to conscious and unconscious confounding factors which make interpretation of the influence of interventions very difficult. None of the three randomised trials comparing endovascular intervention with medical therapy for atheromatous renal artery stenosis (EMMA [49 randomised], Scottish & Newcastle [55 randomised], DRASTIC [106 randomised]) have been large enough to address the question of whether such intervention influences mortality or major morbidity. Surrogate endpoints such as BP control or change in renal function have been difficult enough to measure reliably. The ASTRAL trial will accumulate significantly larger numbers of such patients than all other randomised trials in renal artery stenosis put together. Although it has not been designed primarily as a major outcomes study it has the potential to provide a significant amount of such data if patients are followed for long enough and if major morbid and fatal events are carefully recorded, including sources other than Death Certificate data. It is unlikely that a similar opportunity will be available again.

Reference

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Renal stenting from the radial artery

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Purpose: To describe the technique and feasibility of renal artery angioplasty and stenting from the radial artery.

Methods: Renal artery intervention has been performed in 40 patients from a transradial approach. Procedures are performed using carbon dioxide gas (CO₂) as the preferred angiographic contrast agent. Intervention is performed through a 4 or 5 french radial artery sheath using low profile balloons and balloon expandable stents.

Results: On an intention to treat basis stenting from the radial route was successful in 39 patients. In one patient the descending aorta could not be catheterised. There have been 2 complications directly related to radial access. One patient experienced a cerebrovascular event during intervention. In the second patient, loss of balloon catheter position due to a tortuous aortic arch resulted in non-target vessel stent deployment.

Conclusion: Transradial renal artery intervention is technically feasible using low profile angioplasty balloons and stents. This route offers advantages in renal arteries with a caudal angulation and in patients with diseased or tortuous iliac arteries.

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Discovering renal impairment in peripheral vascular disease using creatinine clearance in patients with normal serum creatinine

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Objective: The incidence of peripheral vascular disease (PVD) and angiography/angioplasty is rising annually. The UK Small Aneurysm Trial and other trials have shown renal function is a predictor of increased mortality^[1] and failed infrainguinal bypass despite patent vessels^[2]. Renal function is classically assessed by serum creatinine (SC). However, SC can be normal despite significant renal impairment. A more sensitive test is creatinine clearance (CC) as determined by 24 h urine collection in combination with SC. We studied the incidence of renal impairment, as defined by CC, in PVD patients with normal SC.

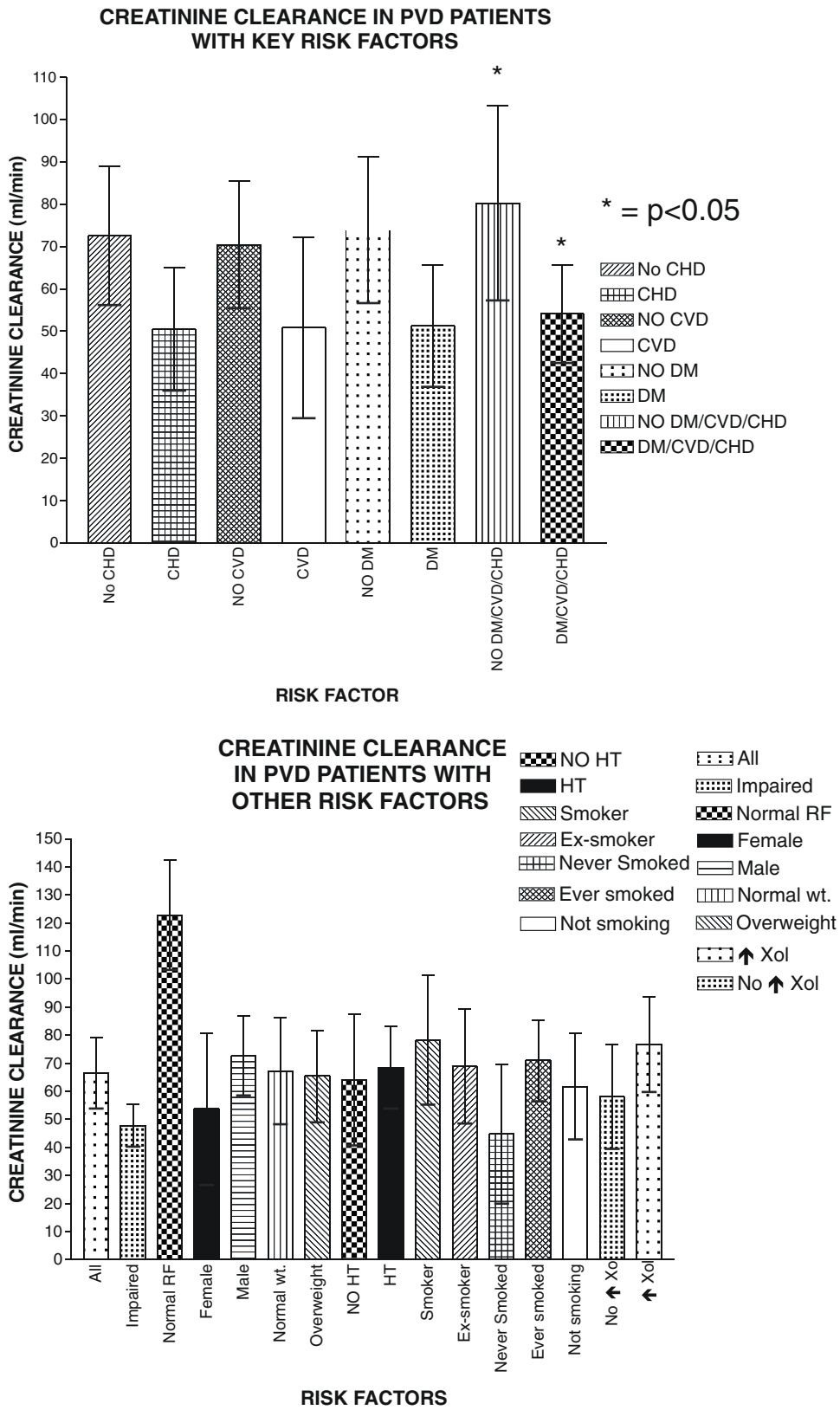


Figure 1

Methodology: All patients with PVD sufficient to necessitate angiography and normal SC ($<120 \mu\text{mol/l}$ —men; $<97 \mu\text{mol/l}$ —women) had their CC assessed, prior to angiography. Various blood tests, a detailed history and examination were performed.

Results: 30 of 40 patients (75%) with normal SC had a CC below normal ($<100 \text{ ml/min}$). The mean CC was 66.9 for all patients and 47.7 for those with subnormal CC.

Possession of either diabetes, coronary heart or cerebrovascular disease was associated with a significant decrease in CC: 42.5 vs. 80.2 for those without any of these risk factors ($P < 0.05$). Sex, hypertension, obesity, hypercholesterolaemia and smoking did not significantly affect CC (see graphs).

Conclusion: Most PVD patients with normal serum creatinine have occult, significantly impaired renal function as defined by creatinine clearance. Vascular surgeons should include creatinine clearance in pre-operative assessment of renal function especially in patients with a history of diabetes, coronary heart disease or stroke. This would allow appropriate early referral to a nephrologist for further investigation and management. Furthermore, patients undergoing angiography could have their management altered by specifically looking for renal artery stenosis^[3] or the use of N-Acetylcysteine^[4]. Further work is now needed on the relative contributions of intrarenal disease, renal artery stenosis and atheroembolism to the decline in renal function in PVD patients.

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Renal arterial intervention to permit sustained use of ACEI/ARB in ARAS is a safe and effective treatment for ARAS-hypertension

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In ARAS 'difficult' hypertension is a common finding, and is one of several cardiovascular risk factors that are responsible for the high cardiovascular mortality seen in ARAS patients. Renal arterial intervention *per se* generally has a modest impact on BP control, which often remains suboptimal. In this population there is little potential or enthusiasm for sustained use of ACEI/ARB despite their cardioprotective and antihypertensive properties—there is evidence of improved survival in ARAS patients given ACEI.

We report an intention-to-treat analysis of 18 patients from Guy's Hospital between 1998 and 2002 in whom renal artery angioplasty and/or stenting was followed by the deliberate use of ACEI/ARB. Statins and aspirin were also used. We followed clinic BP, plasma creatinine and single kidney GFR results.

Mean age was 72 (range 55–81) years at presentation. 16/18 had shown a significant rise in creatinine, or ARF, with ACEI/ARB pre-intervention. 17/18 were longstanding hypertensives ($>140/90$ for >2 years) on multiple drug therapy (excluding ACEI/ARB) pre-intervention; one patient had severe LVF. Mean BP was 181 (range 134–230)/91 (43–130) mmHg. All 18 had at least one RAS $>70\%$ —15 had bilateral ARAS. Pre-intervention mean creatinine was

196 $\mu\text{mol/l}$ (96–380) and mean cGFR was 37.3 ml/min (25–64). 22 angioplasties (21 successful) were performed and 17 RA stents were placed; there were 2 renal artery bypass procedures.

One month post-intervention BP was 171 (130–250)/84 (55–112) mmHg on 2.4 (2–5) drugs/patient (no ACEI/ARB). At mean 11 (range 1–100) months post-renal artery intervention ACEI/ARB were introduced. At a mean follow up of 22 months (range 3–48) post use of ACEI/ARB BP was 141 (122–168)/75 (70–90) mmHg—now only 8/18 patients were hypertensive ($>140/90$) on a mean of 2.2 (1–4) drugs/patient ($P < 0.001$ cf. pre-intervention BP). Mean creatinine was 225 $\mu\text{mol/l}$ (94–847; 2 patients had reached dialysis), mean cGFR was 19.5 ml/min. Four patients did not stay on ACEI/ARB long-term. There was no ARF and no deaths. There was one case of hyperkalaemia necessitating temporary ACEI/ARB cessation.

These preliminary clinical observations suggest that with careful monitoring the use of ACEI/ARB-based antihypertensive therapy can significantly and safely reduce BP in ‘difficult’ ARAS hypertension. A systematic BP/survival trial would be of interest.

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The epidemic of cardiac dysfunction in patients with atherosclerotic renovascular disease

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Atherosclerotic renovascular disease (ARVD) is commonly associated with coronary artery disease and cardiac failure, as well as other vascular pathologies. Although the cardiovascular mortality of patients with ARVD is high, surprisingly, there have been few systematic studies of cardiac structure and function in this high risk group. In this cross-sectional study we investigated 79 consecutive patients with angiographically-proven ARVD presenting to one Renal Centre with non-dialysis requiring renal impairment and/or hypertension. They underwent 24 hour ambulatory blood pressure monitoring and a detailed echocardiographic protocol which assessed both left ventricular (LV) systolic and diastolic function, LV mass index (LVMI) and wall motion abnormalities indicative of ischaemic damage. Blood pressure and echocardiographic results were compared to demographic and clinical parameters to investigate associations between cardiac function, blood pressure, renovascular anatomy, renal function and vascular co-morbidity.

The mean \pm SD age of the group was 70.7 ± 7.5 years with 46 males and 33 females. Mean CrCl was 36.2 ± 19.2 ml/min (range 10.7–93.5 ml/min) and 24 h mean blood pressure $140.5 \pm 19.1/73.7 \pm 12.7$ mmHg with MAP 97.6 ± 13.7 mmHg. LVH was prevalent in 75.9% of patients. Symptomatic IHD was reported in 32.9% of patients but 59.5% of patients actually had left ventricular wall motion abnormalities. Mean LV ejection fraction was $52.8 \pm 11.8\%$ (range 23.1–76.8%); 64.6% had evidence of systolic dysfunction. LV diastolic dysfunction (abnormal transmitral E:A ratio, E velocity wave deceleration time or isovolumetric relaxation time) was present in 74.7%. Both systolic and diastolic LV dysfunction were present in 46.8% of patients but only 5.2% of patients had no evidence of any cardiac abnormality. Multivariate analysis revealed that decreased CrCl, bilateral ARVD, increased systolic and mean arterial blood pressures were predictors of LVH ($P < 0.05$). When grouped according to baseline renal function (preserved function, moderate or severe renal failure—CrCl >50 , 25–50 or <25 ml/min, respectively), no significant differences in blood pressure or renovascular anatomy were apparent. Analysis by renovascular anatomy (residual renal artery patency 1–1.5 [mild], 0.5–1.0 [moderate] or <0.5 [severe]) revealed no significant differences in clinical parameters, blood pressure or echocardiographic data between these groups. Patients with bilateral disease (51 [64.6%]) had a higher prevalence of symptomatic congestive cardiac failure ($P < 0.01$), greater LVMI ($P < 0.04$) and more left ventricular wall motion abnormalities ($P < 0.04$) than those with unilateral ARVD (28 [35.4%]).

There is a higher prevalence of LVH in patients with ARVD than in the general chronic renal failure population (34–49%); a high proportion of ARVD patients exhibit left ventricular systolic and diastolic dysfunction. There is

also a high prevalence of silent ischaemic damage to the left ventricle in patients with ARVD. These findings help to explain the high incidence of cardiac morbidity and mortality suffered by this patient population.

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Where next for lipid lowering in progressive renal disease?

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Premature cardiovascular disease is the leading cause of death in all patients with progressive renal disease (PRD). CV risk is increased from the earliest stages of PRD, is approximately 20-fold higher in dialysis patients than matched and improves following successful transplantation. Although patients with PRD have many 'conventional' cardiovascular risk factors, the relationship with CV outcome is incompletely understood. As a result the use of interventions, proven in other populations, such as statin therapy have not become established in the management of patients with renal disease. Subgroup analyses of larger studies—most recently the HPS—have shown survival benefits from statin usage in patients with early PRD. Smaller studies have identified surrogate benefits—on progression, proteinuria and lipid levels—in advanced and end-stage renal disease. Retrospective registry studies suggest improved survival of dialysis and transplant patients who received statins and this spring sees the report of ALERT, the first large scale interventional study of Fluvastatin vs. placebo in 2100 renal transplant recipients followed for 5 years. At least 3 other studies are planned or in progress—4D, AURORA and SHARP. The question is at what level of evidence do we accept that statins are beneficial and move on to other CV risk factors or lipid targets?