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'EVIDENCE DRIVEN' CLINICAL SCENARIO

Symptomatic Renal Artery Stenosis and Infra-renal AAA

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CLINICAL VIGNETTE

I have a 75-year-old male patient with a history of hypertension and mild renal impairment awaiting EVAR for treatment of a 6 cm infrarenal AAA. However, his CT angiogram shows that he has severe bilateral renal artery stenoses. Is there any evidence that I should angioplasty or stent these prior to the EVAR?

Objectives: To identify evidence to guide the vascular surgeon as to the relevance of renal artery stenting in a patient with symptomatic renal artery stenosis undergoing elective endovascular aortic aneurysm repair (EVAR).
Methods: A comprehensive literature search of MEDLINE was performed without time limits. The following terms were used in the first instance: renal artery stenting and renal artery stenosis, and any other analogous terms identified during the search. Selection criteria were set to randomised control trials.
Results: Despite several large, randomised controlled trials investigating renal artery stenting against medical treatment alone in symptomatic renal artery stenosis, there has been no significant benefit identified in terms of improvement in renal function, control of blood pressure, or need for dialysis. The stented populations were also more likely to suffer from complications caused by the procedure such as bleeding, cholesterol embolisation and flash pulmonary oedema.
Conclusion: There is no evidence for the use of renal artery stenting over optimal medical management in the treatment of patients with symptomatic atherosclerotic renal artery stenosis, irrelevant of the degree of stenosis. In the setting of EVAR, prevention of deterioration of renal function should be with involvement of the renal physicians, adequate hydration, and use of minimal contrast agent. Repair should be undertaken in centres with access to 24-hour haemofiltration services.

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BACKGROUND

Patients with abdominal aortic aneurysms (AAAs) and occlusive arterial disease often have concomitant atherosclerotic renal artery stenosis (RAS; Fig. 1).[1] RAS can be associated with hypertension, progressive ischaemic nephropathy, renal failure, and eventually lead to renal replacement therapy.[2] Following endovascular AAA repair (EVAR), a 10% decrease in creatinine clearance in the first year has been observed, independent of the type of graft or the use of suprarenal fixation.[3] There are likely to be several factors influencing this decline, including progressive atherosclerotic disease, pre-existing impairment and the effects of contrast induced nephropathy (CIN).[4]

Baseline renal dysfunction prior to EVAR is associated with peri-operative mortality rates as high as 27%.[4] Consequently, for a patient with bilateral atherosclerotic RAS, hypertension, and mild renal impairment, preventative measures should be considered to prevent worsening dysfunction and therefore improve peri-operative outcome.

Single case reports have demonstrated the usefulness of successful renal artery stenting in specific scenarios. One such report described a patient awaiting repair of a thoraco abdominal aneurysm with uncontrolled hypertension, worsening heart failure, and progressive renal insufficiency (serum creatinine: 3.8 mg/dL), caused by a high-degree (80%) atherosclerotic RAS in a solitary functioning kidney. Treatment led to normalisation of serum creatinine and blood pressure prior to successful surgical treatment of the aneurysm.[5]

EVIDENCE FOR RENAL ARTERY STENTING IN RAS

For patients without such clear manifestations of RAS, there is little evidence that treatment with renal artery stenting

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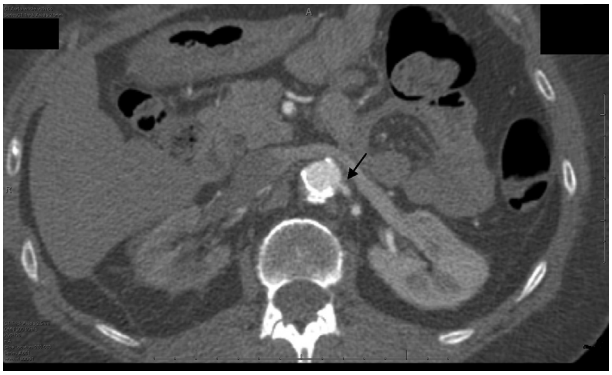

Figure 1. Case study: CT angiogram of a 72-year-old woman presenting with 5.6 cm infra-renal AAA and a background of chronic renal disease (eGFR 27). Imaging demonstrated a right renal artery occlusion, and left RAS. Management included pre-operative optimisation, sodium chloride intravenous hydration 24 hours pre-EVAR, and post-operative monitoring in a level-2 setting. Post-operatively, eGFR improved to 33. The patient was discharged without any complications.

confers additional benefits over medical treatment alone. Meta-analysis of three small randomised controlled trials of renal artery stenting compared with medical therapy alone failed to demonstrate significant improvements in serum creatinine or blood pressure in a combined total of 210 patients followed up to 6 months.[6–9] Since then, several larger multicentre randomised trials have looked into the effects of stenting in this group of patients.

The STAR trial recruited 140 patients with a creatinine clearance of less than 80 mL/min/1.73 m^2 and stenosis of 50% or greater, and randomised them to renal artery stenting plus medical therapy versus medical therapy alone (Table 1).[10] The primary endpoint was a >20% decrease in creatinine clearance in the absence of arterial restenosis. There was no significant difference between the two groups: 16% of patients (10/64) in the stent placement group reached primary endpoint compared with 22% (16/76) in the medication group. Stenting was associated with several complications, including three deaths (two following renal artery perforation, one septic haematoma). Morbidity was caused by false aneurysms of the femoral artery (two), and deteriorating renal function and dialysis following cholesterol embolisation. In conclusion, stenting did not demonstrate benefit in impaired renal function compared with medical therapy alone and led to a number of significant procedure-related complications. Of 140 patients, 33% had only mild (50–70%) atherosclerotic RAS on invasive imaging. Furthermore, 12/64 patients in the stenting arm with stenosis <50% did not receive a stent but were still analysed in the intention-to-treat analysis. Six patients also did not receive a stent (one angioplasty only, one mortality pre-placement, two declined, two technical failures) despite inclusion in analysis for the intention-to-treat cohort.

The larger and more robust Angioplasty and STenting for Renal Artery Lesions (ASTRAL) trial was a multicentre randomised unblinded clinical trial, recruiting 806 patients with atherosclerotic renovascular disease.[11] Patients were randomised to undergo angioplasty and stenting plus medical therapy or medical therapy alone (as per the local centre protocols — management of hypertension, statin, and anti-platelet). Primary outcome was creatinine clearance out to 5 years. Secondary outcomes included blood pressure, time to first renal or major cardiovascular event, and mortality. As with studies before it, there were no significant differences in primary outcome between any cohort ($p = .06$), although there appeared to be a trend towards favourable results in the stenting group. This lack of benefit persisted even after subgroup analysis for varying degrees of renal artery stenosis ($p = .23$). Over the course of the study, 31 serious complications of revascularisation occurred in 23 (9%) patients (Table 2). There was no apparent overall clinical benefit from revascularisation compared with medical therapy alone in those with any degree of atherosclerotic renovascular disease. Of note, patients were only enrolled if their referring physician felt there was equipoise between stenting and medical treatment. In addition, individuals requiring revascularisation within 6 months were excluded. Only 83% of the patients randomised to stenting underwent the procedure. This may be because one-quarter of the patients had normal renal function at baseline, and 41% had less than 70% atherosclerotic renal artery stenosis on invasive imaging.

Table 1. Approach to Medical optimization of the patient with atherosclerotic RAS and impaired renal function.[10]

1. Management of hypertension:
   - Target blood pressure <140/90 mmHg
2. 10 mg of atorvastatin, titrated to 20 mg as tolerated (irrelevant of lipid levels)
3. Aspirin 75—100 mg o.d.
4. Smoking cessation counselling

The most recent, multicentre open-label randomised controlled trial was the Cardiovascular Outcomes in Renal Atherosclerotic Lesions (CORAL) study. It also compared medical therapy alone versus medical therapy plus stenting in 947 patients with RAS and chronic kidney disease, hypertension, or both.[12] Patients were categorised by degree of arterial stenosis (60—80%, 80—99%). Hypertension was classed as a systolic pressure of >155 mmHg despite two anti-hypertensive agents, and chronic kidney disease an eGFR <60 mL/min/1.73 m^2. The protocol for medical therapy required use of the angiotensin II type-1 receptor blocker candesartan (with or without hydrochlorothiazide) and the combination agent amlodipine—atorvastatin. The dose was adjusted to achieve targets of <140/90 mmHg in patients without comorbidities, and less than 130/80 mm Hg in patients with diabetes or chronic kidney disease.

Endpoints were progressive renal insufficiency and need for renal replacement therapy out to 2 years. They found no significant difference between the two groups in terms of decline in renal function (stenting: 68/459 [14.8%], medical therapy alone: 77/472 patients [16.3%], $p = .58$), or decrease in systolic blood pressure ($p = .03$). The CORAL investigators concluded that renal artery stenting did not