The case for renal artery stenting for treatment of atherosclerotic renal artery stenosis

S. Gang
Department of Nephrology, Muljibhai Patel Urological Hospital, Nadiad, Gujarat, India

Introduction

The case favoring renal artery stenting in patients with atherosclerotic renal artery stenosis (ARAS) is supported by its natural history and effects on cardio-renal physiology.[1]

Natural History

Atherosclerosis is a progressive disease. Despite availability of statins, progression of atherosclerotic lesions does occur. Renal artery stenosis (RAS) is associated with loss of the renal size, whereas significant loss of renal size is uncommon without RAS.[2] In patients with greater than 60% RAS, one of the four ipsilateral kidneys demonstrated atrophy of >1 cm in length. Loss of the renal size is a crude but reasonable measure of deteriorating the renal function.[3-5] Though several mechanisms have been proposed for renal dysfunction in patients with RAS, chronic ischemia remains the most important proximate reason for progressive loss of renal mass.

Cardiorenal Effects

RAS leads to endocrine activation with generation of potent vasoconstrictor Angiotensin II and profibrorogenic aldostenone. There is also increased production of vasoactive reactive oxygen species and activation of the sympathetic nervous system. This leads to sustained hypertension and altered cardiovascular physiology. This leads to increased cardiovascular morbidity and mortality.[6]

Limitation of Medical Therapy

Medications inhibiting the renin-angiotensin-aldosterone pathways, statin, and antiplatelets drugs have demonstrated significant benefit in patients with hypertension and cardiovascular diseases. However, these drugs have to be taken life-long. Variable bioavailability and inadequate round the clock blood levels might limit their effectiveness. They are associated with adverse effects and there is a problem of compliance. Revascularization addresses the root cause and has been shown to reset the altered physiology.

Clinical Trials

I agree that prospective randomized control trials provide the best evidence for guiding treatment. However, the three trials published so far have serious limitations.[7]

The DRASTIC trial

The Dutch Renal Artery Stenosis Intervention Cooperative (DRASTIC) study[8] randomly assigned 106 patients to treatment by percutaneous balloon angioplasty renal angioplasty (PTRA) (n=56) or medical therapy (n=50). The sample size was insufficient to detect a significant difference. Renal artery stenosis was defined as greater than 50% stenosis. This allowed a large number of patients with hemodynamically and clinically insignificant lesions to be enrolled in the trial. The design of the trial was such that patient with refractory hypertension were allowed to receive PTRA. Twenty-two of the 50 patients (44%) crossed over to angioplasty group. Moreover, renal artery stent placement is the standard of care today and substantially improves the technical and clinical outcome compared to PTRA. The authors' conclusion that treatment of patients with hypertension and renal artery stenosis, angioplasty has little advantage over antihypertensive drug therapy is based on very feeble evidence.

Address for correspondence:
Dr. Sishir Gang, Department of Nephrology, Muljibhai Patel Urological Hospital, Dr. VV Desai Road, Nadiad, Gujarat-397001, India.
E-mail: sishirgang@hotmail.com

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The STAR trial

In the stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function (STAR) trial,[9] 140 patients with creatinine clearance of less than 80 mL/min/1.73 m^2, renal artery stenosis greater than 50% , and well controlled blood pressure were randomized to either renal artery stenting plus medical therapy (n=64) or medical therapy alone (n=76). The primary end point was a 20% or greater decrease in creatinine clearance. Secondary end points included measures of safety and cardiovascular morbidity and mortality. The authors concluded that stent placement with medical treatment had no clear effect on progression of the impaired renal function but led to a small number of significant procedure related complications. However, there are serious limitations of the study that render the authors conclusion void. More than half of the patients had unilateral disease. In a trial investigating the effect on renal function only patients with bilateral stenosis or stenosis to solitary functioning kidney should be included. It is unlikely that patients with unilateral stenosis to have measurable impact on the renal function. Secondly, 33% of the patients included in this trial had mild renal artery stenosis (50% to 70%). Thirdly, only 46 (72%) of the 64 patients randomized to stenting actually received stents. There were two technical failures and 12 patients had less than 50% stenosis. Yet all 64 patients were analyzed in the stent group. Again, this study was significantly underpowered to answer the question.

The ASTRAL trial

In the angioplasty and stenting for renal artery lesions (ASTRAL) trial,[10] 806 patients with at least one stenotic renal artery considered suitable for balloon angioplasty, stenting or both were randomized to undergo intervention or medical management. The primary outcome was the rate of decline of the renal function over time. Secondary outcome included blood pressure control, renal events, cardiovascular events, and deaths. The authors concluded that patients with atherosclerotic renovascular disease did not derive any worthwhile benefit from revascularization. Despite the adequate size the trial has several flaws in its design. The patients were included in the trial only if the managing physician was uncertain of the appropriate management. Therefore, all patients where the benefit was likely were excluded. This introduced a significant selection bias. Moreover, there were 25% patients had normal renal function at the outset of the trial and 41% patients had stenosis less than 70%. In a trial aiming to assess the decline of the renal function, inclusion of such patients would render the results inconclusive. There was no core laboratory to interpret the severity of lesions. Visual assessment of the degree of stenosis always leads to overestimation.

Hopefully, the cardiovascular outcomes in renal atherosclerotic lesion (CORAL) trial will answer this question.

I agree that all arteries with stenosis do not need stenting, but those with a good clinical indication should not be denied the benefits of revascularization. It seems prudent to adhere to the American College of Cardiology/American Heart Association guidelines on indications for stenting the renal artery.[11]

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