Atherosclerotic Renal Artery Stenosis (ARAS) Manifestations and Management

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Atherosclerotic renal artery stenosis can cause complications like ischaemic nephropathy and athero-embolic renal failure superimposed on renovascular hypertension. It is a progressive disease, involves the ostium and early part of renal artery and is often bilateral.

Introduction

Atherosclerosis involving renal arteries is not uncommon among patients having evidence of generalized atherosclerosis, hypertension and renal insufficiency. ARAS has received much less attention from clinicians as well as interventionists; unlike the involvement of coronary arteries. Atherosclerosis of the renal artery may present as:

a) renovascular hypertension,
b) ischaemic nephropathy,
c) athero-embolic renal failure,
d) asymptomatic incidental finding on abdominal arteriography or

e) combination of the above.

Renovascular hypertension is said to be present when on treatment of the anatomical lesion hypertension is cured and hypertension recurs on restenosis. Ischaemic nephropathy is defined as clinically important reduction in glomerular filtration rate or loss of renal parenchyma caused by haemodynamically significant renal artery stenosis. Atheroembolic renal disease usually presents as acute or chronic renal failure usually following angiography/plasty for coronary artery disease or following surgery on aorta; however, it may occur spontaneously.

Atherosclerosis involves the ostium and early part of the renal artery and is often bilateral. Like in other arterial beds, it is a progressive disease.

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Incidence

It is difficult to know the exact incidence of renovascular hypertension. Various series have reported the prevalence to vary between 0.2% and 32% [Olin J.W. 1978]. It is carefully selected group of hypertensives with a strong clinical suspicion the prevalence may be in the range of 30 to 40%.

In our study of 148 patients of suspected renovascular hypertension, 60 patients [40.54%] were proven by angiography to have significant renovascular disease. Out of these, 60 patients 29 [48.33%] were atherosclerotic in origin. [Rajapakar M.M. Abstract: West Zone - Urological Society of India, 1995, Goa].

Uza et al. 1997, in a 12 years autopsy study, reported on the prevalence and predictors of renal artery stenosis. Out of 297 patients with evidence of myocardial infarction, ARAS was found in 35 [12%] and 10 had bilateral disease. In patients with hypertension, proteinuria and renal insufficiency, renal artery stenosis was seen in 19%, 39% and 39% respectively. These were identified as independent predictors of risk of renal artery stenosis by multiple regression analysis; the risk increased by 3.4, 13.5 and 4.8 fold in patients with myocardial infarction.

In a recent study of 395 consecutive patients with peripheral vascular disease who had no clinical clues to suspect renovascular disease; 38% with abdominal aortic aneurysm, 35% with aorto-iliac disease and 39% with lower extremity occlusive disease had renal artery stenosis [Olin J.W. 1998] in another series, 22 out of 76 [29%] patients had more than 50% renal artery stenosis [Ventrovac 1989]. Similarly, [Harding et al, 1992] reported 164 [20%] out of 817 had significant renal artery stenosis when screened during coronary angiography.
Atherosclerotic renal artery stenosis is probably a frequent cause of ESRD amongst the elderly patients on dialysis. Reported incident varies from 3.2 percent to 25 percent in different age groups of elderly.

In a prospective study which included 149 patients; severe ARAS, carotid artery disease and peripheral arterial disease was seen in 44%, 19% and 21% respectively and severity of the renal artery disease was more with increasing degree of other arterial disease. Prevalence of severe carotid artery disease increased from 7% in mild renal artery disease group to 28% in the severe renal artery disease group [Beach, et al 1998]4.

Thus, patients having atherosclerosis elsewhere specially those having coronary artery disease, abdominal aortic aneurysm, peripheral vascular disease or carotid artery disease have high prevalence of significant renal artery disease; even in the absence of usual clinical clues to suspect renal artery stenosis. Diabetics have been shown to have prevalence similar to nondiabetics [Olin J.W. 1990]3.

Clinical clues for diagnosis

As stated above, patients with evidence of generalized atherosclerosis and hypertension; specially if associated with renal insufficiency, are candidates for having significant associated renal artery disease.

In a retrospective study at our institution we found patients having:
a) worsening of hypertension after age of 55,
b) hypertensive retinopathy grade iii and iv without evidence of renal parenchymal disease,
c) unilateral small kidney,
d) presence of renal bruit and
e) rise of creatinine following use of ACE inhibitors, to be at significantly high risk for high grade (>60%) renal artery stenosis (Table 1).

Repeated episodes of pulmonary oedema and congestive heart failure have been reported as associated commonly with bilateral renal artery stenosis or stenosis of the renal artery to single functioning kidney. The pulmonary oedema can be successfully prevented by revascularisation. Bloch et al 1999 reported that 23 out of 56 [41%] subjects with bilateral renal artery stenosis had history of pulmonary oedema before revascularisation. 17 out of the 23 [77%] subjects had no further pulmonary oedema after stent placement in both renal arteries.

The patients with ARAS like those having coronary artery disease have similar risk factors viz. smoking, tobacco chewing, hyperlipidaemia, family history etc.

Natural history

Like lesions of atherosclerosis elsewhere the ARAS is a progressive disease. This leads to progressive narrowing and ultimately to occlusion. Clinically this manifests as progressive worsening of hypertension, renal atrophy and loss of GFR. It is not possible to predict clinically which lesions will progress. Progression may also be clinically silent.

Zierler et al 1996 in a prospective study reported on the fate of 132 renal arteries assessed by Duplex scanning. The mean age of this study group was 67 years and mean follow up was 32 months. The cumulative incidence of progression from <60% stenosis to >60% stenosis was 30% at one year, 44% at 2 years and 48% at 3 years. Four renal arteries progressed to occlusion and all of them had >60% stenosis at initial assessment.

Strandness 1994 reported that kidneys having >60% renal artery stenosis had a decrease in renal length by more than 1 cm in 26% of cases, over average follow up period of 14.4 months. The estimated risk of loss of more than 1 cm in length was 19% at 1 year.

Atherosclerotic renovascular disease is probably a frequent cause of ESRD among elderly patients on dialysis. Coen et al, in a prospective study of 133 hypertensive CRF patients above the age of 50 years, found haemodynamically significant stenosis in 3.2% in the 50 to 59 years' age group, 20% in 60 to 69 years' age group and 25% in more than 70 years age group.

Diagnosis

No clinical algorithm has been developed that has significant accuracy to provide a reliable diagnosis of renovascular hypertension from clinical features alone. Wilcox C.S. 1995.

High index of suspicion is needed in a given clinical setting. The confirmatory test to make diagnosis of anatomical
HYPERTENSION SERIES

**Table 1. Relative risk of clinical causes for suspected RVHT: Study of 140 patients of renal artery disease at MPUH, Nadiad**

<table>
<thead>
<tr>
<th>Causes</th>
<th>R.R</th>
<th>Spe. %</th>
<th>Sen. %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newly diagnosed HT after age 55 yrs.</td>
<td>0.001</td>
<td>100</td>
<td>2</td>
<td>100</td>
<td>82</td>
</tr>
<tr>
<td>Worsening HT after age 55 yrs.</td>
<td>13.35</td>
<td>85</td>
<td>27</td>
<td>56</td>
<td>66</td>
</tr>
<tr>
<td>HT Retinopathy, grade III and IV</td>
<td>0.491</td>
<td>90</td>
<td>20</td>
<td>55</td>
<td>64</td>
</tr>
<tr>
<td>Without reno-parenchymal disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral small kidney</td>
<td>0.491</td>
<td>52</td>
<td>73</td>
<td>49</td>
<td>75</td>
</tr>
<tr>
<td>Evidence of peripheral vascular disease</td>
<td>0.001</td>
<td>92</td>
<td>24</td>
<td>65</td>
<td>75</td>
</tr>
<tr>
<td>Hypokalemic metabolic alkalosis</td>
<td>0.003</td>
<td>95</td>
<td>11</td>
<td>75</td>
<td>64</td>
</tr>
<tr>
<td>Presence of renal brut</td>
<td>0.491</td>
<td>88</td>
<td>20</td>
<td>50</td>
<td>64</td>
</tr>
<tr>
<td>Rise in serum creatinine after ACEI</td>
<td>0.491</td>
<td>100</td>
<td>20</td>
<td>55</td>
<td>62</td>
</tr>
<tr>
<td>Recurrent Pulmonary Oedema</td>
<td>0.003</td>
<td>95</td>
<td>7</td>
<td>50</td>
<td>62</td>
</tr>
</tbody>
</table>

R.R.: Relative Risk [Rajapkar, 1995 WZUSL, Goa];
Spe.: Specificity;
Sen.: Sensitivity;
PPV: Positive Predictive Value;
NPV: Negative Predictive Value.

Stenosis is angiography. Angiography however is an invasive investigation having significant procedure related risks. Therefore, a battery of noninvasive tests could be employed; when clinically suspected, prior to advising angiography. It is not practice to advice angiography only if the patient is willing and suitable for subsequent revascularisation procedure; either percutaneous or surgical. If any significant anatomic lesion is found.

Commonly employed preliminary noninvasive tests are duplex or colour Doppler scanning, Captopril test, radionuclide scanning with or without Captopril. These are done in addition to clinical examination, renal function tests, urinalysis, serum electrolytes and bicarbonate estimation. Most of these tests are observer and equipment dependent involving a learning curve. Their sensitivity, specificity, positive and negative predictive values have been therefore reported over a wide range in literature. Each institution should therefore evolve a system of assessing clinically suspected renal artery disease based on availability of experienced personnel and quality of equipment before subjecting patient to angiography.

Physiological predictors of outcome and for lateralising following tests are most useful:

a) Differential renal vein renin estimation,
b) Captopril test and
c) Captopril renogram.

Alternatives to conventional angiography are:

a) Intra arterial digital subtraction angiography

b) Magnetic resonance angiography

c) High resolution spiral CT angiography.

These alternatives are much less invasive, however the initial equipment cost makes them much more expensive.

Management

There is enough evidence to suggest that renal revascularisation, either surgically or percutaneously, leads to:

a) Better blood pressure control.
b) Improvement of renal function.
c) Preservation of renal function.
d) Slower decline of GFR.
e) Reduction of need for antihypertensive medication and a few dialysis dependant patients.
f) Avoids need for dialysis.

Following revascularisation procedures are available:

a) Percutaneous transluminal renal angioplasty with or without endovascular stenting of the stenotic lesion and

b) Surgical revascularisation.

Both procedures have significant procedure related
HYPERTENSION SERIES

morbidity and mortality. Widely varying results reported in literature probably reflect the initial selection of patients, comorbid conditions at the time of revascularisation and the centre's experience.

Klow et al 199812 reported 92% initial angiographic success in 295 patients with ARAS. 8% hypertensives were cured and 58% improved. Two deaths and 4.7% clinically significant complications were seen in this series.

Von Knoering et al 199611 in a 4 years follow up of 38 ARAS reported 92% primary success rate. Four patients developed restenosis, 12 of these patients had bilateral disease, 83% patients had long term benefit, 11% were cured, 74% improved and 15% were failures. 75% with bilateral occlusive disease had long term benefits. Two patients died of acute myocardial infarction.

Fiola et al. 199813 reported 95% immediate technical success rate in 21 patients with bilateral atherosclerotic renal artery ostial lesions. The mean arterial blood pressure improved [p=0.002] and serum creatinine decreased significantly [p=0.07] over a mean follow up of 2 years. Renal angioplasty with primary stenting was done. The cumulative restenosis rate was 18% at 2 years. Six major complications occurred in 4 patients, no mortality was seen.

In our study of 53 patients having ARAS who underwent angioplasty, review. Thirty-three patients had unilateral involvement and 20 had bilateral renovascular disease. There were 11 ostial lesions included. Seventy-nine PTIA procedures were carried out on 73 vessels. Six patients had ostial lesions. The study included 42 males and 11 females. The average age was 49 years. Nineteen diabetics were included and the mean follow up was 14 months. The patients were classified in 4 groups according to their serum creatinine.

    The patients were analyzed for improvement in blood pressure control, reduction in anti-hypertensive drug requirement, reduction in serum creatinine and becoming dialysis independent. The results are shown in Table 2.

In summary, 66% patients with ARAS achieved satisfactory blood pressure control and reduction in the need of antihypertensive drugs. No deterioration in serum creatinine was seen in patients having serum creatinine less than 1.7 mg/dl. 40.5% patients showed definite improvement in their serum creatinine whose initial serum creatinine was above 1.7 mg/dl. Primary technical success rate in our hands was 94%. Clinically significant restenosis occurred in 6 cases within 1 year.

In a recently conducted study by Plurin et al.1998, blood pressure outcome of angioplasty for atherosclerotic renal artery stenosis were compared with drug treatment alone in prospective multicentric randomized manner - Essai Multicentrique Medicaents vs Angioplastic (EMMA) study group. The conclusion was that in unilateral atherosclerotic renal artery stenosis, angioplasty is a drug sparing procedure that involves some morbidity. It was also concluded that previous uncontrolled and unblinded assessments of angioplasty overestimated its potential for blood pressure lowering.

Surgery

Successful revascularisation of renal artery can be undertaken by a variety of surgical techniques such as:

a) aortorenal bypass using variety of conduits.

b) with or without simultaneous surgery for aorta and revascularisation of other arterial beds.

Table 2: Showing results of angioplasty for atherosclerotic renal artery disease at MPUH, Nadia-1998

<table>
<thead>
<tr>
<th></th>
<th>A (n=16)</th>
<th>B (n=9)</th>
<th>C (n=18)</th>
<th>D (n=10)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BP control</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Achieved</td>
<td>14 [88%]</td>
<td>4 [45%]</td>
<td>7 [39%]</td>
<td>9 [90%]</td>
<td>35/55</td>
</tr>
<tr>
<td><strong>BP Before</strong></td>
<td>188/112</td>
<td>207/111</td>
<td>178/105</td>
<td>192</td>
<td></td>
</tr>
<tr>
<td>After</td>
<td>146/87</td>
<td>153/89</td>
<td>153/89</td>
<td>148/89</td>
<td></td>
</tr>
<tr>
<td><strong>Anti-HT Before</strong></td>
<td>2.6</td>
<td>2.9</td>
<td>2.8</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>After</td>
<td>1.1</td>
<td>1.5</td>
<td>1.7</td>
<td>1.8</td>
<td></td>
</tr>
<tr>
<td><strong>Reduction in</strong></td>
<td>No</td>
<td>4 [45%]</td>
<td>7 [39%]</td>
<td>4 [40%]</td>
<td>15/37</td>
</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td>[&gt;0.5]</td>
<td>[&gt;1]</td>
<td>Off dialysis</td>
<td>[40.54%]</td>
</tr>
</tbody>
</table>

Primary technical failure 5 out of 73 vessels [6.84%] [Rajapurkar, 1999]14

12

c) autotransplantation and

d) nephrectomy.

In this usually high risk population, surgery carries a higher risk compared to percutaneous procedures but have better long term patency rates after successful operation.

Erdoes et al 1996\textsuperscript{14} compared PTRA and operation for renal revascularisation and concluded that morbidity and mortality rates associated with PTRA were 33\% and 4.8\% respectively, while for surgery the morbidity rate was 7\% and mortality was 5.3\% [P value not significant]. Functional improvement was 74\% in all surgically treated versus 22\% in PTRA group [p<0.01]. Actual renal artery primary patency at 4 years was 81\% in surgical group and 17\% in PTA group [p<0.01].

Definite indications for surgery over PTRA are:

a) Failed PTRA

b) Associated aneurysm and

c) Aortic or other arterial disease needing surgical repair.

Cambria et al, 1996\textsuperscript{10} have reported on 13 year experience of renal artery reconstruction surgery for preservation and restoration of renal function in patients with atherosclerotic disease. 139 patients underwent renal artery primary patency having clinical characteristics of advanced cardiac [history of myocardial infarct, CCF] and renal [serum creatinine >2mg/dl] disease. Operative management consisted of aorta-renal bypass in 47\%, extra anatomic bypass in 45\% and endarterectomy in 8\%. 45\% needed combined aortic surgery. Operative mortality was 8\% and significant perioperative renal dysfunction occurred in 10\%. 54\% patients had more than 20\% reduction in creatinine after surgery, 87\% patients had follow up data at a mean duration for 4 years. Actuarial survival at 5 years was 52\%±5\%. Continued deterioration of GFR occurred in 24\% and 15\% eventually needed maintenance dialysis. Deterioration of renal function was associated with increasing levels of preoperative creatinine [RR=1.6, p=0.001 for each 1.0mg/dl increase in creatinine] and was inversely related to early postoperative improvement of creatinine [RR=0.41 p=0.04]. The authors recommended early aggressive approach to achieve improved long term results for renal artery reconstruction.

Aggressive approach is also necessary for salvage of function in patients with single functioning ischaemic kidney. Mccready et al, 1987\textsuperscript{20} reported their results of surgical revascularisation in 19 patients having ischaemic single kidney over 20 years period from 1965 to 1985. Mean preoperative serum creatinine was 3.7mg/dl and reduced to 2.2mg/dl postoperatively. Diastolic blood pressure also reduced significantly [p<0.001]. Three patients had died perioperatively, 14 had improvement, one was cured and one did not benefit. None of their patients had their hypertension worsened.

Weibull et al 1993\textsuperscript{31}, in a prospective randomized study to compare PTRA and operation as initial therapy for atherosclerotic renal artery lesions concluded that PTRA is recommended as first choice therapy for atherosclerotic renal artery stenosis causing renovascular hypertension if combined with intensive follow up and aggressive reintervention.

Medical management

Any interventional approach to ARAS must always be complimentary to use of antihypertensive medication for appropriate control of blood pressure; both before and after the intervention. Medical management of the atherosclerotic process is absolutely essential for control of risk factors for atherosclerosis.

In case of a high risk patient for surgery and/or failure of PTRA, medical management to control blood pressure with antihypertensive medication is indicated. This may be the only choice in patients not willing to undergo surgery or PTRA. The drug regimen should include ACE inhibitors while carefully monitoring for rise of serum creatinine and potassium. In a series of 41 such patients there was evident loss of kidney size over 3 years follow up period of medical therapy alone; however, there was rarity of significant loss of renal function; only 8 out of 41 experienced doubling of serum creatinine [Dean et al,1981]\textsuperscript{32}.

Conclusion

1. ARAS is a common occurrence in patients having generalized atherosclerosis of other vascular beds.

2. ARAS significantly contributes to hypertension and renal insufficiency.

3. High index of suspicion is needed for diagnosis of ARAS.

4. ARAS is a progressive disease leading to increasing hypertension and loss of renal function.

5. Renal revascularisation by PTRA with or without stent or surgery leads to better blood pressure control with less medications and may improve renal function and prevent further deterioration.

References


