Screening, Diagnosis, and Treatment of Renal Artery Stenosis by Percutaneous Transluminal Renal Angioplasty with Stenting

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**ABSTRACT:** Background: Renal artery stenosis is one of the most frequent causes of secondary hypertension. Appropriate methods for screening, diagnosis and therapy are currently under debate.

Objectives: To evaluate and recommend methods for screening and diagnosing renal artery stenosis, and to assess the clinical outcomes of renal artery stenting.

Methods: A total of 450 patients undergoing non-emergent coronary angiography fulfilled the selection criteria for selective renal arteriography; those with severe (luminal narrowing ≥ 70%) renal artery stenosis underwent percutaneous transluminal renal angioplasty with renal artery stenting.

Results: Of 166 patients (36.9%) with renal artery stenosis, 41 (9.1%) had severe stenosis that required renal artery stenting, and 83% had ostial renal stenosis. The primary success rate was 100% and there were no complications. During the follow-up period, two patients required a second PTRA. After stent deployment, significant reductions were observed in systolic and diastolic pressures (P < 0.001 and P = 0.01, respectively) and in the number of antihypertensive drugs used by the patients (P < 0.001). These reductions were sustained during follow-up. Hypertension was cured (systolic blood pressure < 130 mmHg) in 9 patients (21.4%) and improved in 27 (64.3%). Plasma creatinine did not change significantly.

Conclusions: Selective renal angiography is an effective diagnostic tool for identifying symptomatic cases of renal artery stenosis in patients undergoing coronary angiography. Our finding of a high success rate and low complication rate supports the use of primary renal artery stenting in symptomatic patients with renal artery stenosis.

**KEY WORDS:** renal artery stenosis, selective renal angiography, hypertension, renal artery stenting, renal angioplasty

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Renal artery stenosis is one of the most common causes of hypertension [1,2] and end-stage renal disease [3]. It is currently estimated that RAS accounts for 10–40% of ESRD cases in elderly, hypertensive patients without primary renal disease [4]. Apart from ESRD, renal artery stenosis may manifest as malignant hypertension, ischemic nephropathy, “apparent” congestive heart failure, or any combination of these [5,6]. In patients with bilateral disease, RAS was a strong predictor of all causes of mortality and was associated with up to 52% of 4 year mortality rates [7,8].

The diagnosis of renal artery stenosis is often referred to as a “fortuitous diagnosis,” mainly because it is frequently an incidental finding in cardiac and non-cardiac patients [9-11]. Angiography is the gold standard for diagnosing RAS; however, there is no clear method for determining which patients should undergo renal angiography. In this study, several criteria are suggested for the screening and selection of these patients.

There is no consensus regarding the appropriate treatment for patients with RAS. Stenting of the renal artery is considered a promising approach, but data-based evidence is lacking. The CORAL trial (Cardiovascular Outcomes in Renal Atherosclerotic Lesions) is expected to yield clinical evidence for the efficacy and safety of renal artery stenting. However, the CORAL trial will not be completed until 2010. This trial aims to extend the currently published findings regarding clinical outcomes for renal artery stenting.

**PATIENTS AND METHODS**

**SCREENING AND PATIENT SELECTION**

Between 2001 and 2007 all patients undergoing non-emergent diagnostic cardiac catheterization at the Bnai-Zion Medical Center were screened and evaluated for study inclusion according to predefined criteria.

All patients gave written informed consent. Before cardiac catheterization, we recorded the demographic data, cardiac
history, indications for cardiac catheterization, atherosclerotic risk factors, history, features of non-coronary vascular disease, current use of antihypertensive medications, and participation in cardiac therapy. Patients undergoing coronary angiography were selected for renal angiography if they also had at least one of the following predetermined criteria:

- Multiple atherosclerotic diseases – at least two of the following:
  - Coronary artery disease
  - Peripheral vascular disease
  - Carotid diseases
- Hypertension resistant to medical therapy or controlled by multiple (≥ 3) drugs
- Chronic renal failure (serum creatinine levels > 1.5 mg/dl)
- Flash pulmonary edema

**DIAGNOSIS**

Bilateral selective renal angiography was performed in patients selected as described above. The procedure was performed with 10–15 ml of contrast media. The severity of renal artery stenosis was defined as absent, non-significant (luminal narrowing < 70%), or significant (luminal narrowing ≥ 70%). Patients with significant renal artery stenosis were referred for renal artery stenting.

**TECHNIQUE**

A guiding catheter technique was used in all cases with a femoral access 7 Foley catheter. In 20 cases (46%) direct stenting was performed. In 23 cases (54%) predilatation was done before stent placement. Quantitative Coronary Analysis of the lesion was performed pre- and post-intervention in all patients.

**PATIENT PREPARATION AND FOLLOW-UP**

Prior to intervention and before discharge, the following baseline examinations were mandatory: blood pressure, serum creatinine, and evaluation of drug history. For renal protection, the patients received acetylcysteine 600 mg twice a day and 0.9% normal saline 2 L/day for 2 days before the procedure. Patients were invited for follow-up visits 1 month and 2 years after the procedure. At these visits the following examinations were conducted: ambulatory 24 hour blood pressure monitoring, serum creatinine level testing, and evaluation of antihypertensive treatment. A patient was cured of hypertension if he or she maintained a systolic blood pressure < 130 mmHg.

**STATISTICAL ANALYSIS**

Demographic and procedural data are expressed as counts, percentages, or means ± SD. Chi-square test was used for baseline characteristics. Two-tailed paired Student t-tests were used to assess comparisons of systolic blood pressure (mmHg), renal function (measured by serum creatinine values in mg/dl), the number of antihypertensive drugs (counts), and the percent of luminal narrowing before and after renal artery stenting.

**RESULTS**

We screened 7500 patients who underwent diagnostic coronary angiography. A total of 450 qualified with at least one of the predefined criteria and were enrolled for selective renal artery angiography. The baseline characteristics of these patients are shown in Table I. Renal artery stenosis was found in 166 patients (36.9%); 41 (9.1%) of them were diagnosed with significant renal artery stenosis and 125 (27.8%) with non-significant renal artery stenosis.

Renal artery stenting was performed in 41 patients. Only two patients experienced restenosis and required a second catheterization. Restenosis was diagnosed by Doppler ultrasound that was performed due to blood pressure increase in those patients. Left renal artery stenosis was found in 24 patients (58%), right renal artery stenosis in 9 (22%), and bilateral renal artery stenosis in 8 (20%). Ostial renal artery stenosis was found in 34 patients (83%).

Patients with significant RAS underwent renal artery stenting; unexpectedly, the majority were female (64%, P = NS), 8 (19%) were smokers, and, in addition to the co-morbidities shown in Table I, 28% had peripheral vascular disease and 22% had carotid artery disease.

The primary success rate was 100%, and there were no procedural or peri-procedural complications. Vessel diameters were narrowed by a mean of 88 ± 8% before the procedure and 12.9 ± 7% after the procedure (P < 0.001). Restenosis was observed in 2 patients (4.9%), and a second PTRA was performed.

Systolic blood pressure was significantly reduced after the procedure, and reductions were maintained at the follow-up assessments [Figure 1]. Diastolic blood pressure was also significantly reduced from 82 ± 13 to 73 ± 10 mmHg (P = 0.01), but this rose at the follow-up assessment to 77 ± 11 mmHg (P = NS).

**Table 1.** Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Significant RAS</th>
<th>Non-significant RAS</th>
<th>Normal renal arteries</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>41</td>
<td>166</td>
<td>243</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>70 ± 9</td>
<td>66 ± 9.5</td>
<td>61 ± 11</td>
<td></td>
</tr>
<tr>
<td>Females (%)</td>
<td>64</td>
<td>35</td>
<td>31</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertensive (%)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>NS</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
<td>72</td>
<td>73</td>
<td>73</td>
<td>NS</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>66</td>
<td>49</td>
<td>45</td>
<td>0.05</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>44</td>
<td>40</td>
<td>38</td>
<td>NS</td>
</tr>
<tr>
<td>Renal failure (%)</td>
<td>22</td>
<td>13</td>
<td>8</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*P value was calculated for the difference between ‘Significant RAS’ group and the other groups. No significant difference was found between the non-significant RAS group and the normal artery group.
The creatinine levels did not change significantly, decreasing from 1.1 ± 0.24 before to 0.98 ± 0.2 mg/dl after the stenting procedure \((P = \text{NS})\).

Nine patients (21%) had renal failure [Table I] with serum creatinine levels of 1.8 ± 0.3 mg/dl. In this group, after renal artery stenting, creatinine levels decreased to 1.55 ± 0.16 mg/dl \((P = \text{NS})\). Before renal artery stenosis, systolic blood pressure was 169 ± 26 mmHg and patients used 3.2 ± 1.5 antihypertensive drugs. Post-intervention, both systolic blood pressure and the use of antihypertensive drugs decreased to 145 ± 5 and 2.5 ± 0.83 mmHg, respectively \((P = 0.05, P < 0.1\) respectively). At follow-up, systolic blood pressure was 153 ± 10 mmHg and patients used 2.6 ± 1.1 antihypertensive drugs \((P = \text{NS}, P < 0.1\) respectively). Two patients (22%) in this group showed no improvement in blood pressure.

**DISCUSSION**

Compared to fibromuscular dysplasia-induced RAS, atherosclerotic RAS is more common in symptomatic patients and has a worse outcome. The disease is usually found among older men who are at risk for cardiac disease (with hypertension, smoking, and hyperlipidemia) and display atherosclerotic co-morbidities [11-13]. The natural history of untreated ARAS includes progressive decline in kidney size and function and may lead to renal artery occlusion, ischemic nephropathy, and ESRD [1,5,14,15]. The prevalence of renal artery stenosis was 7–15% in different populations for patients undergoing coronary angiography [16-18].

We screened 7500 patients in order to select patients with high risk of renal artery stenosis and included 450 in this selective renal angiography study. Significant renal artery stenosis (defined as luminal narrowing ≥ 70%) was found in 9.1% and non-significant stenosis in 27.8% of the patients. These results are similar to those found in another study that used similar methods for selecting patients for renal angiography; they found significant (≥ 70% luminal narrowing) RAS in 7.3% of patients [19].

We found a higher prevalence of renal artery stenosis among males. Surprisingly, significant disease was more common among females (statistically non-significant). Different studies found males to be more prone to have renal artery stenosis [11,12], and further research is needed to evaluate the prevalence of RAS among both genders in Israel.

The wide variety of symptoms associated with renal artery stenosis makes it difficult to find sensitive and specific screening methods. In this study we found that screening patients who were undergoing cardiac angiography facilitated the selection of patients for selective renal angiography.

\(\text{ARAS} = \text{atherosclerotic RAS}\)
The first percutaneous transluminal renal angioplasty was performed by Felix Mahler and Andreas Gruntzig in 1978 [20]. Since then, the role of PTRA in the treatment of RAS has been controversial. Balloon angioplasty is the gold standard of treatment for resistant hypertension in patients with fibromuscular dysplasia-induced RAS [21]; however, the method was found less effective in patients with atherosclerosis-induced RAS. In patients with ARAS, conventional balloon angioplasty showed little advantage over medical therapy in blood pressure control and was associated with high rates of complications (23%) and restenosis (26%) [2,12,22].

Recently, stenting of renal arteries has been described as an “attractive alternative” to conventional balloon angioplasty. Several studies have shown that this technique had better clinical outcomes (blood pressure control, renal function), preserved kidney size, and lower rates of complications and restenosis compared to conventional balloon angioplasty [2,5,22,23].

Our finding of a 100% primary success rate with PTRA is consistent with the high primary success rates found by other researchers; a meta-analysis across 644 patients reported a consistent with the high primary success rates found by other researchers [22-25]. We used selective renal angiography to minimize the exposure of the kidneys to contrast media and found no deterioration of renal function either in patients with chronic renal failure or in the overall group.

The positive effects of renal artery stenting on blood pressure are quiet commonly reported. Several works showed post-procedure improvements in blood pressure and reductions in the use of antihypertensive drugs. We found blood pressure improvements in 85% of the patients, consistent with the high primary success rates found by other researchers [2,12,22].

In studies of patients with or without renal failure, renal function was preserved following stenting of the renal artery [22-25]. We used selective renal angiography to minimize the exposure of the kidneys to contrast media and found no deterioration of renal function either in patients with chronic renal failure or in the overall group.

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