Renal Stenting for Kidney Salvage in the Management of Renal Artery Atherosclerotic Stenosis

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Abstract
We studied the usefulness of preoperative resistance index to select patients who will benefit most from renal stenting. Sixty-two patients underwent renal stenting. All had chronic renal insufficiency with serum creatinine values ranging from 1.5 to 2.5 mg/dL and blood urea nitrogen between 80 and 107 mg/dL. All treated renal artery stenosis were >70%. Reduction in blood pressure in the early stages was observed in 39 (62.9%) patients; 31 (79.4%) patients returned to preoperative values within 12 months. A progressive reduction in creatinine values and blood urea nitrogen was reached in 43 (69.4%) patients, 12 (19.4%) patients remained unchanged, and the remaining 7 (11.2%) patients worsened. The best improvement in renal function was obtained in patients with a resistance index of \( \leq 0.75 \) A preoperative resistance index up to 0.75 could be used as an indicator to predict which candidates will have improved renal function after stenting.

Keywords
renal stenting, hypertension, renal salvage

Introduction
The pressure gradient across a renal arterial stenosis (RAS) is one component of renovascular disease that also involves extension of atherosclerosis to the branches of the renal artery, arteriolar thickening, tubular and glomerular atrophy, and glomerulosclerosis.1 The management of RAS-related hypertension remains controversial due to the low number of patients enrolled in each study and the poor reproducibility of data in the literature.2

For a long-time aortorenal bypass or renal artery reimplantation has been the conventional surgical approach for RAS.3 However, the poor patency rate and the invasiveness of this procedure led to a search for other treatment options.4 The advent of percutaneous transluminal angioplasty (PTA) or stenting has modified the approach to atherosclerotic RAS and currently it is an option due to its relatively low mortality and morbidity.5

Up to now, 3 randomized controlled trials (RCTs)6-8 and several subsequent studies failed to demonstrate the advantages of stenting over surgery.1 Moreover, new available drugs are able to maintain adequate blood pressure (BP) control in patients with untreated RAS.9

On the basis of these data, the current indication for renal stenting should be salvaging renal function rather than treating hypertension. The aim of our study was to determine the effectiveness of renal stenting in improving renal function. We also assessed the usefulness of preoperative resistance index (RI) to select patients who will benefit most from this procedure. At our center, this sonographic index is measured using the following traditional formula: RI = (peak systolic velocity (PSV) – end diastolic velocity)/PSV, with normal values ranging from 0.5 to 0.7.10,11

Materials and Methods
From January 2008 to January 2013, 62 patients (48 males), mean age 69 years, underwent renal artery stenting for obstructive atherosclerotic lesions with a total of 65 stents (3 bilateral). All patients had a mild to moderate chronic renal insufficiency with serum creatinine (sCr) values ranging from 1.5 mg/dL (132 \( \mu \)mol/L) to 2.5 mg/dL (220 \( \mu \)mol/L), while blood urea

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narrowing (BUN) was between 80 and 107 mg/dL. All had hypertension (mean BP 150/95 mm Hg) despite pharmacological therapy with >2 drugs (except for angiotensin-converting enzyme inhibitors). Type 2 diabetes was present in 15 cases and 18 had a history of myocardial infarction (MI). Screening test was performed by color duplex scanning (CDS). Computed tomography angiography with 3-dimensional reconstructions or magnetic resonance angiography was performed to confirm the ultrasound findings. The RI was measured in the segmental arteries of both kidneys.

Individuals with unilateral or bilateral hydronephrosis, renal cysts, tumors, or stones were excluded from the study. All patients were stratified for unilateral or bilateral renal artery stenosis and RI as detected by CDS. A systolic peak velocity ≥200 cm/s and a renal aortic ratio >3.5 were considered hemodynamically significant (>70% diameter stenosis) as assessed by CDS.

Patients were stratified on the basis of their intrarenal RI < 0.76 or > 0.70. Indication for stenting was renal artery stenosis >70%, as detected both on CDS and on angio-computerized tomography (CT)/magnetic resonance imaging (MRI). Both CDS and CT/RM findings correlated closely with an intraoperative angiographic diameter reduction of at least 70%.

Color duplex scanning showed an RAS ranging from 70% to 85% in 45 unilateral cases and 3 bilateral cases. A unilateral RAS >85% was found in 14 cases. The mean RI ranged from 0.76 to 0.89 in 14 patients and from 0.58 to 0.75 in the remaining cases.

In 3 cases, stenting was bilateral, and an iliac stenting was associated to correct a critical stenosis in 4 cases. The endovascular procedure consisted of a previous selective renal angiography and subsequent primary renal stenting through a guiding catheter (Boston Scientific Corporation, Natick, Massachusetts; 6F) without distal protection in all patients. This guiding catheter (Boston Scientific Corporation, Natick, Massachusetts; 6F) allowed us to administer very low dosage of contrast material (10-50 mL) for the entire procedure. Nitrogen (BUN) was between 80 and 107 mg/dL. All had hypertension (mean BP 150/95 mm Hg) despite pharmacological therapy with >2 drugs (except for angiotensin-converting enzyme inhibitors). Type 2 diabetes was present in 15 cases and 18 had a history of myocardial infarction (MI). Screening test was performed by color duplex scanning (CDS). Computed tomography angiography with 3-dimensional reconstructions or magnetic resonance angiography was performed to confirm the ultrasound findings. The RI was measured in the segmental arteries of both kidneys.

A clinical interview with an analysis of the trends of the systemic BP and the number/doses of antihypertensive medication was recorded in all cases every 6 months. Serum creatinine level and creatinine clearance were measured before discharge, at 3, 6, and 12 months, and yearly thereafter. A 20% increase in these levels at each follow-up control indicated declining renal function.

Statistical Methods

The effects of renal stenting on renal function were analyzed using the Kolmogorov-Smirnov, the Lilliefors, and the Friedman analysis of variance (ANOVA) tests. Descriptive statistics of renal function, RI, central tendency (mean, median, and mode), and variability (variance, standard deviation, error standard, and quartiles) were also used.

The relationship between the RI, age of patients, and the parameters of renal function as indicators of the possible improvement in renal function after stenting was assessed by the principal components analysis and Spearman correlation.

Results

All renal artery stenting procedures were technically successful. Stenting-related mortality was nil. No major procedure-related events (acute thrombosis, dissection, hemorrhage, or acute renal function decline) occurred. In 1 case, a femoral pseudoaneurysm was treated surgically.

During follow-up (mean 29 months), 4 patients died for MI and 1 for unknown reasons with an 8% mortality incidence rate. Ten patients with an RAS >80% developed a critical intrastent restenosis and needed a further PTA. Therefore, the cumulative primary patency rate was 83.8%, and the secondary patency rate was 93.5% at 5 years. Concerning hypertension, in 24 (38.7%) patients, renal stenting led to a permanent improvement in hypertension, while in 7 (11.3%) patients, its benefits decreased slowly over the next 5 years of follow-up.

In the remaining 31 (50%) patients, RAS was followed by a dramatic BP reduction in the first 3 to 6 months; nevertheless, these results were limited in time so that BP returned to the preoperative values and again drugs were restarted despite a patent renal artery stent.

Renal function improved progressively over time in 43 (69.4%) patients, including the 3 with bilateral stenting. Renal function remained unchanged in 12 (19.3%) patients, and in the remaining 7 (11.3%) patients a worsening occurred so that 3 needed dialysis.

Using the Friedman ANOVA test, the median values of sCr and BUN measured in the preoperative phase were higher than those measured postoperatively and the latter was higher than those recorded 24 months after renal stenting. These data are statistically significant for both parameters as shown in Figures 1 to 3 and Tables 1 and 2. It must be underlined that in this study, of 14 patients with an RI >0.75 (71.4%), 10 experienced no improvement or even a decline in renal function, despite a successful procedure.
All cases with an RI >0.80 preoperatively tended to have an overall deterioration in renal function 24 months after stenting. Conversely, all patients with preoperative RI values <0.75 showed an improvement in renal function. These data are statistically significant as showed by the logarithmic relation between pre- and postoperative sCr and BUN levels and the preoperative RI (Figure 4A and B).

Discussion

Significant RAS is observed in almost 5% of the patients with hypertension; this incidence rate increases up to 12% and 40% in patients with coexisting coronary artery disease or peripheral artery disease, respectively. Although renal artery stenting can be performed successfully with low complication rates, currently, hypertension due to RAS can be controlled with best medical therapy, making indications for endovascular treatment a matter of ongoing debate.

Several RCTs and systematic reviews compared the effects of angioplasty and medical treatment for patients having hypertension with RAS. However, up to now, these data fail to support a broad application of renal revascularization since just small groups of patients experience long-term clinical benefits after endovascular treatment of RAS and some may be exposed to significant complications, including renal atheroembolism.

The 2 most recent trials, the Angioplasty and Stenting for Renal Artery Lesions (ASTRAL) and the Cardiovascular
Outcomes in Renal Atherosclerotic Lesions (CORAL) trials, suggested that renal artery stenting did not confer a significant benefit in patients with atherosclerotic RAS and hypertension or chronic kidney disease when compared to multifactorial medical therapy. Both of these trials raised many concerns. In our experience, many patients subjected to renal artery stenting only had limited benefits regarding BP response, irrespective of unilateral or bilateral disease. Our results are consistent with Arthur experience showing only a transient reduction in BP values that returned to preprocedural values within 6 months after stenting and, therefore, it was necessary.

### Table 1. The Friedman ANOVA Test Shows That the Difference Between the Median Values of Creatinine and BUN, Collected in the 3 Periods, Are Statistically Significant.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Average Rank</th>
<th>Sum of Ranks</th>
<th>Mean</th>
<th>Std Dev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative creatinine</td>
<td>2.47</td>
<td>153.5</td>
<td>1.98</td>
<td>0.30</td>
</tr>
<tr>
<td>Postoperative creatinine</td>
<td>2.09</td>
<td>130</td>
<td>1.92</td>
<td>0.73</td>
</tr>
<tr>
<td>24 Months creatinine</td>
<td>1.42</td>
<td>88.5</td>
<td>1.99</td>
<td>1.81</td>
</tr>
<tr>
<td>Preoperative BUN</td>
<td>2.40</td>
<td>149</td>
<td>88.09</td>
<td>7.49</td>
</tr>
<tr>
<td>Postoperative BUN</td>
<td>2.07</td>
<td>128.5</td>
<td>83.79</td>
<td>27.84</td>
</tr>
<tr>
<td>24 Months BUN</td>
<td>1.52</td>
<td>94.5</td>
<td>86.77</td>
<td>74.25</td>
</tr>
</tbody>
</table>

### Table 2. The Friedman ANOVA Test Shows That the Difference Between the Median Values of RI, Collected in the 3 Periods, Are not Statistically Significant.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Average Rank</th>
<th>Sum of Ranks</th>
<th>Mean</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative RI</td>
<td>1.94</td>
<td>120.5</td>
<td>72.6</td>
<td>7.69</td>
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<tr>
<td>Postoperative RI</td>
<td>2.02</td>
<td>125.5</td>
<td>72.8</td>
<td>8.53</td>
</tr>
<tr>
<td>24 Months RI</td>
<td>2.03</td>
<td>126</td>
<td>72.04</td>
<td>12.76</td>
</tr>
</tbody>
</table>

Abbreviations: ANOVA, analysis of variance; Coeff, coefficient; Chi Sqr, chi-square; Aver, average; Std Dev, standard deviation; BUN, blood urea nitrogen; RI, resistance index.
to resume antihypertensive agents. The temporary improvement after renal stenting demonstrates that renovascular occlusive disease is involved in hypertension, but further investigations are needed to determine why this response is lost over time, despite a 90% to 100% patency rate of renal artery stents.

Regardless of being a cause of hypertension, critical RAS may result in renal failure within 5 years after diagnosis. Several studies have suggested that renal artery stenting is aimed to slow the renal function decline and delay the requirement for hemodialysis.

In the present study, no patient experienced immediate worsening of renal function due to the contrast media used during endovascular procedure. In the follow-up, most of our patients subjected to renal artery stenting showed a stable reduction in the sCr values below 1.4 mg/dL or a stabilization of their renal function. In our evaluation, renal artery stenting may delay hemodialysis also in those cases who experienced a decline in their renal function categorized as failures although the stent was patent. If we consider preservation or improvement of renal function as the main indication for selective renal stenting, it becomes necessary to identify those patients who may benefit from this procedure.

In our opinion, in those patients with severe RAS, sCr and BUN levels must not be considered as indications for stenting. An RI as a measure of the underlying chronic parenchymal disease is still questionable. Several investigators have indicated a wide interval of threshold values for renal impairment and/or of poor renal outcome at >0.70; this contributes to questions about the clinical utility of this measurement.

Rocha-Singh et al demonstrated an improvement or stabilization in renal function after renal artery stenting irrespective of renal RI. Conversely, as also documented by Radermacher et al, we observed a significant correlation between postoperative high sCr and BUN levels and preoperative pathological RI. In our series, the baseline RI threshold value of poor renal outcome range was >0.75.

**Conclusion**

Our experience confirms that renal artery stenting can be performed with negligible periprocedural complication rate, and >93% patency can be obtained. Permanent improvement in hypertension was achieved in a minority of patients undergoing renal endoluminal revascularization while the benefit is only transient in most of cases.

Our results allow the following conclusions: stenting has produced an overall improvement in renal function in most of patients. Serum creatinine and BUN are reliable indicators of this improvement and they are essentially equivalent from the statistical point of view.

A preoperative RI up to 0.75 could be used as an indicator to predict which candidates will have a consistent improvement in renal function within 24 months after stenting. If we assume that the current indication for renal stenting is the prevention or improvement of chronic renal failure rather than the treatment of systemic arterial hypertension, the use of IR <0.75 as an indicator of potential improvement of renal function should limit even further the indication for this procedure.

This study is limited by a small cohort size and a retrospective analysis. Randomized controlled trials will be needed to determine the impact of renal stenting to prevent or arrest the progression to hemodialysis.

**Authors’ Note**

Each author warrants that they participated sufficiently in the intellectual content, the analysis and interpretation of data, and the writing of...
the work to take public responsibility for it. Each has reviewed the final version of the work, believes it represents valid work, and approves it for publication.

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