Effect of Renal Artery Stenting on Renal Function in Patients With Ischemic Nephropathy

Erdoğan İLKAY,1 MD, A. İhsan GÜNAL,2 MD, Mustafa YAVUZKIR,1 MD, Necati DAĞLI,1 MD, Ilgın KARACA,1 MD, Huseyin CELIKER,2 MD, Ayhan DOĞUKAN,2 MD, and Nadi ARSLAN,1 MD

SUMMARY

The aim of this study was to evaluate the effects of stenting on blood pressure and renal functions in azotemic patients with proximal/ostial atherosclerotic renal artery stenosis.

Thirteen azotemic patients (5 females, 8 males, average age, 62.7 ± 8.3 years) who had renal artery stenosis were included in the study. Their blood pressure, estimated glomerular filtration rate (EGFR), and creatinine levels were measured at baseline and during follow-up.

Stents were implanted successfully in all of the cases. The average stent diameter and stent length were 7.2 ± 0.5 mm and 17.2 ± 3.4 mm, respectively. Antihypertensive drug was abandoned in 1 (7.6%) patient, reduced in 10 patients (76.9%), and not changed in 2 (15.3%) patients. Significant improvement was observed in the mean serum creatinine level at the 12th month when compared with baseline (2.56 ± 0.88; 1.83 ± 0.62, P < 0.001). EGFR was 18.38 ± 4.64 before the procedure and 22.67 ± 3.81 during follow-up (P < 0.0001). According to the EGFR criteria, renal function was determined to be worse in 1 (7.6%) patient, stabilized in 2 (15.3%), and improved in 10 (76.9%) patients. One patient died during the follow-up period. Angiographic restenosis was observed in 2 (15.3%) patients. Follow-up major events were observed in 3 (23%) patients.

Stenting azotemic patients with renal artery stenosis is a reliable and effective procedure for achieving an improvement in renal function. (Jpn Heart J 2004; 45: 637-645)

Key words: Renal artery stenosis, Azotemia, Hypertension, Stent

ATHEROSCLEROSIS is the most frequent cause of ischemic renal disease.1) The true incidence of atherosclerotic renal artery stenosis (RAS) as a cause of end-stage renal disease remains unknown. Retrospective data, however, suggest that 10-20% of dialysis patients have RAS and ischemic nephropathy as a result of their end-stage renal disease.2) There are over 80,000 new dialysis patients per year in the United States (US Renal Data System 1999 Annual Data Report), and

From the 1Department of Cardiology and 3Department of Nephrology, Flrat University, Elazığ, Turkey.
Address for correspondence: Erdoğan İlkay, MD, Department of Cardiology, Flrat University, Zübeyde Hanım Cad. 116/6 Elazığ, Turkey.
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presumably 20% of those patients progress to dialysis due to ischemic nephropathy. The US RDS, however, attributes only 6696 new dialysis cases annually to RAS.\(^3\) Clearly the vast majority of patients with ischemic nephropathy are under-diagnosed. Early diagnosis and timely revascularization for this group is imperative. Surgical renal revascularization can delay or prevent progression to end-stage renal disease and may reverse progressive renal failure in selected patients.\(^4\)-\(^6\) However, surgical intervention is associated with high mortality and morbidity rates.\(^7\),\(^8\)

It has been reported that blood pressure is more easily controlled and attacks of angina and pulmonary edema are reduced and renal function is protected by renal angioplasty in patients with RAS.\(^9\)-\(^14\) In addition, complications associated with the procedure have been reported to be low in these reports. However, the results of renal artery angioplasty are still debatable and less clear in patients with ischemic nephropathy.

We report here the medium-term results of renal angioplasty performed in our patients with renal azotemia and proximal/ostial RAS.

**METHODS**

**Selection of patients:** This study included a total of 13 patients (5 females and 8 males) with a diagnosis of azotemia and proximal/ostial atherosclerotic renal artery stenosis exceeding 70%. The average age of the patients was 62.7 ± 8.3 years. Azotemia was defined as a serum creatinine level > 1.5 mg/dL at the time of intervention.

Measurement of renal outcomes included the change in estimated glomerular filtration rate (EGFR) using the Cockcroft and Gault formula adjusted for body surface area.\(^15\) The procedural effect on EGFR was defined as improved (an increase > 20%), worse (a decrease more > 20%), or stabilized (a change < 20%).\(^16\)

**Stenting:** All patients received aspirin and ticlopidine or clopidogrel before the procedure. They also received a heparin bolus or infusion in order to achieve an activated clotting time ≥ 300 seconds.

Right femoral artery access in 11 cases (85%) and left femoral artery access in 2 cases (15%) were performed. The guidewires used included a 0.018 inch (Boston Scientific/Schneider) in 4 cases (31%) and a 0.014 inch (ACS-Flopy-extrasupport) guidewire in 9 cases (69%).

The stent was implanted without predilatation in 1 case (8%) and after performing predilatation in 12 cases (92%). Predilatation was performed by a single inflation at the nominal pressure with a small balloon having a diameter smaller than the reference vessel (Figure 1A-C).
Figure 1. Ostial stenosis in renal artery (A), stent implantation 1-2 mm out of ostium (B) and postoperation appearance (C).
**Stent type:** AVE renal bridge (Medtronics AVE USA), Corinthian (Johnson and Johnson, USA).

**Major in-hospital events:** Major in-hospital events were defined as an emergency renal artery bypass, nephrectomy, acute or subacute thrombus, stroke, death, and myocardial infarction (MI). Procedural success was defined as no major in-hospital events plus restenosis less than 20% after the procedure. A major event during follow-up was defined as more medication for blood pressure control, an increase in EGFR exceeding 20%, mortality, and restenosis.

**Statistical analysis:** Data are presented as the mean ± standard deviation. The Wilcoxon signed rank test was used in the evaluation of changes in creatinine level and EGFR and blood pressure. A \( P < 0.05 \) was accepted as significant.

**RESULTS**

Unilateral renal artery stenosis in 4 cases and bilateral renal artery stenosis in 9 cases were ascertained. The main characteristics of the cases are presented in Table I. All of the cases were treated by a single stent. In all cases, bilateral renal artery lesions were treated at the same setting. The mean stent diameter was 7.2 ± 0.5 mm, mean stent length was 17.2 ± 3.4 mm, and the inflation pressure was 10.3 ± 1.8 atm.

**Effect on blood pressure:** The blood pressure values 12 months after stent implantation were significantly lower than the preoperational values. Systolic blood pressure was 196.15 ± 22.56 mmHg before the procedure and decreased to 131.92 ± 11.46 mmHg after stent implantation (\( P = 0.001 \)). Diastolic blood pressure was 108.07 ± 9.90 mmHg before the procedure and decreased to 81.15 ± 5.06 mmHg after stent implantation (\( P < 0.001 \)). Mean blood pressure was 137.00 ± 11.19 mmHg before the procedure and decreased to 99.76 ± 7.15 mmHg after stent implantation (\( P < 0.002 \)) (Table II).

<table>
<thead>
<tr>
<th>N: 13</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>62.7 ± 8.3</td>
</tr>
<tr>
<td>Female</td>
<td>5  38</td>
</tr>
<tr>
<td>Male</td>
<td>8  62</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5  38</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>10  77</td>
</tr>
<tr>
<td>Smoking</td>
<td>11  85</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>8  62</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>5  38</td>
</tr>
<tr>
<td>Bilateral RAS</td>
<td>9  70</td>
</tr>
<tr>
<td>Unilateral RAS</td>
<td>4  30</td>
</tr>
</tbody>
</table>
Antihypertensive drug usage: All medications were abandoned in 1 case (8%) while the dosages were reduced in 10 (77%). The dosages were not altered in the remaining 2 (15%).

Effect on creatinine values: The mean serum creatinine value was 2.56 ± 0.88 mg/dL (range, 1.7-4.4 mg/dL) before the procedure. At the 12th month, the mean creatinine value was significantly decreased compared to baseline (2.56 ± 0.88; 1.83 ± 0.62, \( P < 0.001 \)) (Figure 2). EGFR was 18.38 ± 4.64 before the procedure and 22.67 ± 3.81 (\( P < 0.0001 \)) during follow-up (Figure 3). Renal function was judged to be impaired according to EGFR criteria in 1 case (8%) (the patient died), stabilized in 2 cases (15%), and improved in 10 cases (77%).

Complication Transient hemodialysis in 2 cases and blood transfusion for iatrogenic anemia in 1 patient were necessary. No major in-hospital events were observed in any cases. The procedural success rate was 100%. All 13 patients were successfully discharged after stent deployment.

One patient (8%) who had bilateral stenosis, diabetes mellitus, and a baseline creatinine value of 4.4 mg/dL died during follow-up. The cause of death was myocardial infarction. A reincrease in blood pressure was observed in 2 cases. Creatinine level increased in one while it did not in the other in which a bilateral renal stent was implanted. Restenosis was observed in their control angiography and balloon angioplasty was reperformed in these cases. Restenosis was not observed by renal Doppler ultrasound in 10 cases with clinical and laboratory improvements. Major events during follow-up were observed in 3 cases (23%). Survey of 12 months was by 92% (Table III).

Table II. Effect of Renal Artery Stenting on Blood Pressure

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>12 months</th>
<th>( P ) value</th>
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</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>196.15 ± 22.56</td>
<td>131.92 ± 11.46</td>
<td>( P &lt; 0.001 )</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>108.07 ± 9.90</td>
<td>81.15 ± 5.06</td>
<td>( P &lt; 0.001 )</td>
</tr>
<tr>
<td>MBP (mmHg)</td>
<td>137.00 ± 11.19</td>
<td>99.76 ± 7.15</td>
<td>( P &lt; 0.002 )</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; DBP = diastolic blood pressure; MBP = mean blood pressure.
Figure 2. Effect of renal artery stenting on serum creatinine (SC) level.

Figure 3. Effect of renal artery stenting on estimated glomerular filtration rate (EGFR).

Table III. Acute Procedural and Late Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>22</td>
</tr>
<tr>
<td>Procedural success, n/n (%)</td>
<td>22/22 (100%)</td>
</tr>
<tr>
<td>Follow-up revascularization, n (%) (Repeat angioplasty)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (8%)</td>
</tr>
<tr>
<td>Major follow-up events</td>
<td>3 (23%)</td>
</tr>
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</table>
EFFECT OF RENAL ARTERY STENTING ON RENAL FUNCTION

DISCUSSION

We observed that renal stent revascularization improves renal functions in patients with azotemia due to ischemic nephropathy.

The short and long-term results of balloon angioplasty alone have been reported to be poor for stent application in proximal/ostial RAS. Therefore, we performed stent implantation in all of our cases. The clinical merits and cost-efficacy of this strategy are supported by Van De Ven, et al.

Renal intervention has been reported to be effective in blood pressure control. In the present study, medication was abandoned or reduced in 85% of the cases. The effectiveness of renal intervention has been previously reported to be 42-91%. In contrast, van Jaarsveld, et al randomized 106 cases into a drug or angioplasty group and observed no difference between the groups. However, in their study, in 44% of the cases, renal angioplasty had been performed for uncontrolled hypertension despite a combination of three medications.

Renal stent implantation has been reported to be preventive in renal ischemic nephropathy. Dean, et al reported that surgical renal revascularization in azotemic patients with bilateral renal lesions improved immediate postoperative renal function and slowed the rate of renal function deterioration in 88% of the patients during a one year follow-up period. However, the authors reported a 9% mortality rate, indicating a relatively high surgical risk in this population. Other investigators have reported a mortality risk of 2.1% to 6.1% depending on the type of operation. Rocha-Singh, et al have reported the mortality related to the intervention as being 0%. In our study, we observed no procedure-related deaths in a similar population.

Previous authors have reported that stent revascularization has minimal or no effect on renal functions. The main reasons for this were the different patient populations and eligibility criteria. We excluded patients who would not benefit from renal revascularization (ie, patients with significant renal atrophy and azotemia with unilateral renovascular disease and bilateral functioning kidneys). Rocha-Singh, et al, who had similar criteria as ours, observed similar results. Rodriguez, et al observed the stent had no effect on renal function, in their hypertensive patient population that had normal renal function.

One of our patients died during follow-up. He had bilateral renal stenosis, diabetes mellitus, and a creatinine value of 4.4 mg/dL. Mortality has been reported to be higher in such cases. Restenosis was observed in two cases (15%). Blood pressure reincreased in both but the creatinine level increased in only one case (restenosis was observed in only one renal artery in the case with bilateral renal stenosis and we concluded that the invariable creatinine level in this patient was due to the nonstenotic renal artery). Target vessel diameter was 5
mm in both of these cases. Higher restenosis was reported in such cases in a previous study. The data available are insufficient for determining a correlation with blood parameters. In fact, Zeller did not observe a correlation between blood parameters and restenosis. The 12 month of survey was 92% and the major event rate was 23%.

As a result, stent revascularization protects renal function in azotemic patients. This effect is related to both facilitating blood pressure and decreasing renal ischemia. Therefore, it seems to be an acceptable alternative method for surgery.

**Limits of the study:** The most important limitation was the use of an indirect method. Using serum creatinine values to estimate glomerular filtration rate is controversial, though widely accepted in clinical practice. A previous study compared iothalamate-determined GFR against EGFR values and reported an acceptable correlation of 0.93.

**REFERENCES**