EFFECT OF RENAL ARTERY STENTING ON HYPERTENSION AND RENAL FUNCTION

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ABSTRACT

Background: Renovascular hypertension and chronic kidney disease secondary to renal artery stenosis (RAS) can be treated by medical therapy, percutaneous transluminal angioplasty with or without stenting. **Objective:** To determine the effects of renal artery stenting on hypertension and renal function in patients with renal artery stenosis. **Patients and Methods:** This was an observational study in which 216 patients were identified retrospectively from 1st October, 2001 to 31st December 2006, who underwent 232 procedures. Clinical data pertaining to demographics, presence or absence of hypertension, creatinine, number of blood pressure medications and co morbidities was collected pre and post renal artery stenting. Follow up data was available for 144 procedures, with mean follow up period of 14 months. **Results**: In total, 232 procedures were performed on 216 patients. Of these, 95 (40.9%) had bilateral RAS (group 1), 117 (50.4%) had unilateral RAS (group 2), and 20 (8%) had RAS in a solitary functioning kidney (group 3). Complete follow-up data was available on 144 patients. Indications for renal artery stenting were poorly controlled hypertension (56.9%), worsening renal function (8.6%), both (24.6%), and other (8.1%). Procedural success was 100%, with no major in-lab complications. At a mean follow-up of 14.5 months, renal function remained stable with no significant difference in creatinine values but statistically significant drop in systolic blood pressure post stenting for the entire cohort and all the sub-groups. **Conclusion:** Renal artery stenting is a safe procedure with improvement of blood pressure control, stabilization or improvement in renal function in patients with unilateral, bilateral and RAS in solitary functioning kidneys.

Keywords: Renal artery stenting, Hypertension, Renal function

INTRODUCTION

Atherosclerotic renal artery stenosis (ARAS) and its treatment became area of active research since the recognition of association between hypertension and renovascular disease by Goldblatt in 1934.[1] Incidence of the renal artery stenosis (RAS) and occlusion is 1.5% and 0.4% in ESRD patients respectively.[2] Atherosclerosis accounts for 90 percent of cases of renal-artery stenosis and usually involves the ostium and proximal third of the main renal artery and the perirenal aorta.[3] Atherosclerotic renal-artery stenosis is a progressive disease; with the cumulative incidence of ARAS progression of 35% at 3 years and 51% at 5 years. The 3 year progression rate was 49% for renal arteries initially classified as $\geq$ 60% stenosis, with 3% to complete occlusion.[4] Patients with diabetes or systolic hypertension are at higher risk of progression.[4]

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RAS can present as refractory hypertension, unexplained azotemia or azotemia after starting ACEI,[3] pulmonary edema,[5] unstable angina or CHF.[6] One of the important consequences of RAS is cardiovascular morbidity and mortality as its presence was significantly and independently associated with adverse coronary events in a population-based study.[7]

Renovascular hypertension and chronic kidney disease secondary to RAS can be treated by medical therapy, Percutaneous Transluminal Angioplasty (PTA) with or without stenting and surgery.[8] Among the invasive modalities PTA with stenting is preferable because surgery is associated with high complications rate.[9] Renal artery stenting is a commonly performed procedure with almost 40,000 procedures reported annually in USA.[10] The rationale of renal artery stenting is to relieve the stenosis with likely improvement in blood pressure control and attenuation of adverse effects i.e. prolonging the predialysis phase in this relentlessly progressive disease,[11] and regression of left ventricular hypertrophy.[12]

Along with the advancements in the treatment of RAS, there is development of new methods for its diagnosis. These advancements in diagnostic modalities are resulting in early asymptomatic RAS detection and question arises whether or not to treat asymptomatic disease. The recent data indicates that baseline renal insufficiency is strong predictor of all

cause mortality in RAS,[13] and this supports early diagnosis and treatment of RAS. We report the effect of renal artery stenting on hypertension and renal insufficiency in patients with RAS as these are the most common indications for renal artery intervention.

PATIENTS & METHODS

*T*his is an observational study in which 216 patients were identified retrospectively from 1st October 2001 to 31th December 2006, who underwent 232 procedures. Clinical data pertaining to demographics, presence or absence of hypertension, creatinine, number of blood pressure medications and co morbidities was collected before renal artery stenting and at follow up period. Follow up data was available for 144 procedures with mean follow up period of 14 months. Follow up data was collected from hospital, primary care physicians' office records and from direct telephone inquiries with patients.
Creatinine was considered an indicator for renal function and an improvement or deterioration of renal function was defined by 20% decrease or increase in creatinine (Cr) levels respectively. Pre procedure (baseline) systolic and diastolic blood pressure (BP) readings were noted from the same hospital admission (within 24 hours prior to procedure) and follow up readings were noted from the outpatient or inpatient follow ups. Patients' antihypertensive medications prescribed by the primary care physician were noted at baseline and at follow up encounters. Loop diuretics and nitrates were not included as antihypertensive medications. Severe stenosis was taken as 70% and critical as 90% stenosis. Microsoft Excel and SPSS version 15 was used for statistical analysis. Paired t test was used, with P value of less than 5% as significant.

RESULTS

Out of 252 consecutive cases, we had data on 232. Out of these, complete follow up data was available for 144/232 (62%). Baseline characteristics of entire cohort are summarized in Table 1. Baseline characteristics of patients with and without the follow up are summarized in Table II. Complete follow up for 62 % procedures was available with mean follow up 14 months (range 0.5 50 months). There was no significant difference in patients characteristics as shown in table II.

Table I: Baseline characteristics of entire cohort

Patient Characteristics	Entire Cohort (232)
Age (yrs) (mean ± SD)	72 ± 9
Range	35 – 91 yrs
Gender	
a) Male	95 (41%)
b) Female	137 (59%)
Race	
a) Caucasian	199 (86%)
b) African American	25 (11%)
c) Others/ Unknown	8 (3%)
Co morbidities	
HTN	226(97%)
CAD	179 (77%)
CHF	65 (28%)
DM	70 (30%)
HLP	183 (79%)
TOB	101 (43%)
PVD	116 (50%)
Presenting values	
Pre stenting SBP	163 ± 27
Pre stenting DBP	75 ± 13
Pre stenting Baseline Creatinine	1.4 ± 0.72
Pre stenting Number of BP meds	2.05 ± 1.05
Indications for Stenting	
a) Hypertension	132 (57%)
b) Hypertension/Elevated creatinine	57 (25%)
c) Elevated creatinine	20(9%)
d) Incidental	14 (6%)
e) Hypertension/Elevated Creatinine/PE	1 (0.4%)
f) Hypertension/ Flash PE	3 (1.3%)
g) Acute renal failure (ARF)	1 (0.4%)

HTN -Hypertension, CAD - Coronary artery disease, CHF- Congestive heart failure, DM-Diabetes Mellitus, HLP-Hyperlipidemia, Tob-Tobacco use, PVD-Peripheral Vascular Disease.
Changes in creatinine, SBP, DBP and blood pressure medications were calculated in cohort with follow up and in subgroups (BL vs UL vs renal artery stenosis in a solitary kidney)

As shown in table III, in more than 70% of patients, Creatinine didn't worsen. This is also true in subgroup analysis (Table IV).

There was significant improvement in SBP after renal artery stenting in entire cohort with follow up and also in subgroup analysis. There was no significant difference in the DBP, Cr and number of BP medications before and after the stenting. (Table V)

Table II: Baseline characteristics of patients with and without follow up

Patients' characteristics	Cohort with FU (n = 144)	Cohort without FU (n = 88)
Age (yrs) (mean ± SD)	72 ± 8	73 ± 9
Gender a) Male	56 (39%)	39 (44%)
b) Female	88 (61%)	49 (56%)
Race a) Caucasian	122 (85%)	77(87%)
b) African American	16 (11%)	9 (10%)
c) Unknown	6 (4%)	2 (2%)
Indications for stenting		
a) Hypertension	81 (56%)	51 (58%)
b) Elevated Cr	15 (10%)	5 (6%)
c) Hypertension/Elevated Cr	36 (25%)	21 (24%)
d) Incidental finding	7 (5%)	7 (8%)
e) Hypertension/Elevated Creatinine/PE	1 (0.7%)	0
f) Hypertension/ Flash PE	3 (2%)	0
g) Acute renal failure (ARF)	1 (0.7%)	0
Pre- stenting SBP	162 ± 29	164± 25
Pre- stenting DBP	74 ± 14	76 ± 12
Pre- stenting Cr	1.5 ± 0.8	1.35 ± 0.5
Pre- stenting antihypertensive medications	1.99 ± 1	2.15 ± 1.1
Co-morbidities		
a) HTN	140 (97%)	86 (98%)
b) CAD	109 (76%)	70 (79%)
c) CHF	37 (26%)	28 (32%)
d) DM	38 (26%)	32 (36%)
e) HLP	110 (76%)	73 (83%)
f) Tob	64 (44%)	37 (42%)
g) PVD	71 (49%)	45 (51%)
Bilateral disease (Group 1)	58 (40%)	37 (42%)
Unilateral disease (Group 2)	74 (51%)	43 (49%)
Solitary kidney disease (Group 3)	12 (8%)	7 (8%)

Table III: Change in Creatinine (entire cohort with FU):

Change in Creatinine (Cr)	Number of Patients	Percentage
Improvement	17	12%
Worsening	30	21%
No change	88	61%

Table IV: Change in Creatinine in subgroups:

Change in Cr	Entire Cohort	Group 1 (BL)	Group 2(UL)	Group 3(Sol)
Improvement	17 (12%)	7(12%)	7(9%)	3 (25%)
Worsening	30 (21%)	13(22%)	14(19%)	3 (25%)
No change	88 (61%)	34(59%)	49 (66%)	5 (42%)

Table V: Sub group analysis

	Pre-stent	Post-stent	p value
Entire Cohort with FU(n= 144			
a) SBP	162 ±28	141 ± 20	0.001*
b) DBP	74 ±14	70 ± 14	0.002*
c) BP meds	2.02 ± 1.02	1.9 ± 1	0.78
d) Cr	1.5 ± 0.8	1.6 ± 0.9	0.07
Group1(n=58)			
a) SBP	162 ± 32	144 ± 18	0.001*
b) DBP	70 ± 14	66 ± 14	0.03*
c) BP meds	2.3 ± 1.07	2.04 ± 0.9	0.079
d) Cr	1.5 ± 0.7	1.69 ± 0.9	0.07
Group2(n = 74)			
a) SBP	161 ± 23	139± 20	0.001*
b) DBP	76 ± 13	73 ± 13	0.17
c) BP meds	1.82 ± 0.9	1.94 ± 1.04	0.37
d) Cr	1.43 ± 0.8	1.45 ± 0.7	0.77
Group3(n = 12)			
a) SBP	172 ± 39	138 ± 29	0.002*
b) DBP	86 ± 12	73 ± 13	0.014*
c) BP meds	1.92 ± 0.9	2.08 ± 1.2	0.73
d) Cr	1.84 ± 1	2.1 ± 1.8	0.36

Percent stenosis:
76% had 80% stenosis or greater. Mean percent stenosis was 83%.
Residual stenosis:
72.4% had 0% residual stenosis, 2.2% had residual stenosis from 15- 30%, rest had stenosis ≤ 10%.
Complications:
Complications rate was 6% which included descending aortic dissection, groin arterio-venous fistula (AVF) formation, distal embolization, Pseudo-aneurysm (PSA), groin hematoma and ARF.

DISCUSSION

Atherosclerotic renal artery disease is a progressive disease. Renal artery revascularization can halt the progression of kidney disease as demonstrated by the studies that many patients came off the dialysis after restoration of the blood flow to the kidneys.[14] It's important to study the effects of renal artery stenting on two most common indications i.e. hypertension and renal insufficiency for this procedure.

Effects on Blood pressure:
One of the important reasons to consider revascularization has been hypertension especially when it is difficult to control it on medical therapy alone. Our study showed a statistically significant drop in SBP post stenting for the entire cohort and all the sub-groups. Statistical analysis of Framingham study suggested that SBP is more potent contributor to cardiovascular sequel.[15] Thus reduction in SBP can be considered as an important outcome of renal revascularization procedure. Also, our study demonstrated that most of the patients had decrease or no change in number of BP medications which is another indirect indicator of improvement or stabilizations of BP control. Also one need to keep in mind that the some BP medications (beta blockers, Angiotensin converting enzyme inhibitors) are used for purposes other than BP control based on concomitant co morbidities.

Effects on Serum Creatinine:
There was no statistically significant change in serum creatinine. By stratifying the cohort in subgroups according to stabilization, improvement or worsening of Cr then we found that (21%) had worsening of Cr, 12% had improvement in Cr and 62% had no significant change in Cr (data was not available for 9 pts). More than 75% patients had no worsening in Cr. Based on this; we believe that renal artery revascularization helped in stabilization of renal function. These results are consistent with the other similar observational studies.[16-21]
Reviewing the previous data (Table VI) on RAS and

Table VI: Previously published/available data on RAS.

Authors	No. of patients	Decrease in SBP	Decrease in DBP	Decrease in No. of meds	Serum Cr
Rocha-Singh K et al - [22]	208	<.001	<.001	N/A	No change
Bloch MJ et al [20]	89	<.01	Positive trend	Positive trend	
Henry M et al [23]	210	<.001	<.001	<.02	
van de Ven PJ et al [24]	85	Positive	Positive trend	No change	No Change
White CJ et al [25]	100	<.001	<.001	<.001	
Rocha-Singh KJ et al [26]	51	<.001	<.001	<.001	<0.001
Lederman RJ et al [18]	300	<.005	<.005		
Bush RL et al [27]	73	<.001	<.001	<.001	
Raza M et al (our study)	216	<.0001	0.18	NS	0.67

Safety of renal artery stenting:

Renal artery stenting is a safe procedure with high technical success rate and associated with very low mortality and morbidity rate. There were very few complications 6.5 % as mentioned earlier. This rate is comparable to previous studies, although complication rate varies from 4%-24% in previous studies.[21,24,28,29]

CONCLUSION

Data from our study demonstrates that renal artery stenting resulted in improvement in systolic blood pressure, reduction in number of blood pressure medications and stabilization or improvement in renal function in majority of patients. This observation is reflected in unilateral, bilateral and solitary renal artery stenosis categories. We recommend considering renal artery stenting especially in patients with uncontrolled BP despite maximal medical management or in patients with progressive renal function deterioration.

Limitations: This includes deficiencies related to retrospective data, absence of comparison group with medical management only and collection of follow up data at one point of time.

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