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Original Article

Renal Artery Stenting in Atherosclerotic Stenosis: Long-Term Follow up of Results in Blood Pressure and Renal Function

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Abstract

Background. Atherosclerotic renal artery stenosis (RAS) is a known cause of hypertension and renal impairment. The role of revascularisation in the treatment of RAS has been debated. Our aim was to identify those patients with atheromatous RAS more likely to have improvement in blood pressure and/or renal function following renal PTA with stent placement in a long-term follow-up.
Methods. The long-term effects of percutaneous transluminal angioplasty (PTA) with stent placement were assessed in 30 hypertensive patients in 33 renal arteries (18 male, 12 female). All patients had atheromatous renal artery disease (17 unilateral artery stenosis 8 bilateral and 5 in a solitary kidney). Twenty five (83.3%) patients had renal impairment with serum creatinine > 124 μmol/L and in 16 there was ostial lesion. Blood pressure and serum creatinine were estimated before PTA and at the end of follow up.
Results. During 47.5±35.4 months follow-up (4 years) there was a significant reduction in systolic and diastolic BP (20.6/8.3 mm Hg, $p<0.001$, $p<0.003$ respectively). Furthermore, the renal function improved in 34.4% of patients, was unchanged in 27.5% of patients, and worsened in 37.9%. The reduction of medication was significant ($p<0.03$). The best results, however, were seen in hypertensive patients with stenosis to a single functioning where 20% were cured of hypertension and 60% improved. The serum creatinine also, was improved in 80% of these patients.
Conclusion. Our results demonstrate that revascularisation leads to a fall in blood pressure, and an improvement or stabilisation of renal function in a large number of hypertensive patients. These effects are more evident in patients with atheromatous renal artery stenosis in a single functioning kidney and in those with renal dysfunction, in whom medical therapy is generally ineffective.

Keywords: renal artery stenosis, stent, hypertension, creatinine

Introduction

Currently there is a great interest in renal artery stenosis as a cause of hypertension, impaired renal function, or both, as well as recurrent pulmonary oedema or apparent heart failure [1-5]. Treatment of the stenosed renal artery by revascularisation techniques (surgery or angioplasty) provides the opportunity to stabilise or reverse all the above, thereby reducing cardiovascular morbidity and mortality and delaying the need for renal replacement therapy [6].
Whereas in patients with fibromuscular dysplasia the results of percutaneous transluminal angioplasty (PTA) are uniformly good [7-8], in patients with atherosclerotic disease the benefits and efficacy of PTA are not nearly as good [9-10]. Furthermore, it is not clear from the various studies which patients with atheromatous renal artery stenosis undergoing PTA are more likely to have improvement in blood pressure and/or renal function, and no recommendations could be made as to when renal PTA should be performed.
We studied thirty patients who were electively referred for renal PTA. Our aim was to assess the long term (47.5±35.4 months follow-up) benefits of renal artery PTA with stent placement, and identify the hypertensive patients more likely to have improvement in blood pressure and/or renal function.

Patients and methods

Between 1998 and 2006, thirty consecutive patients with hypertension and renal artery stenosis were referred electively for renal PTA. Of these, 18 patients were male. The mean age (± SD) was 69.0 ± 7.6 years (age rage 59-81). Supine blood pressure was recorded three times, two minutes apart, using a semi-automated ultrasound sphygmoma-nometer (Arteriosonde, Roche) 2 days before renal PTA and at the end of follow up period thereafter. Venous blood was also collected for determination of serum creatinine 2 days before PTA, and at the end of follow-up period. The mean follow-up was 47.5±35.4 (range 29-58) months. The mean values of all three measurements of blood pressure and serum creatinine before PTA and at the end of follow up were included in the analysis.
Percutaneous angioplasty with stent replacement was performed in 33 renal arteries. All patients had atheromatous renal artery disease. Seventeen patients had unilateral stenosis, 8 had bilateral disease (in 3 of them there was bilateral stent replacement), and 5 patients had stenosis in a solitary kidney. Sixteen patients had ostial lesions and the remaining fourteen non ostial lesions. Prior to PTA-stent average BP was 177.6/88.3 ± 26.8/17.1 mmHg, and serum creatinine level was 251.8±145.7 μmol/L. Renal function was considered abnormal if serum creatinine was greater than 124 μmol/L (> 1.5 mg/dl) on two separate occasions prior to renal PTA. Twenty five

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patients (83.3%) had serum creatinine > 124 μmol/L (mean serum creatinine 278.2±140.5 μmol/L). Hypertension was considered cured if diastolic blood pressure was 90 mmHg or less without treatment, and improved if diastolic pressure was less than 90mmHg after administration of an equal or reduced dose of medication. Hypertension was also considered improved if diastolic pressure was > 90mmHg and < 110mmHg, associated with a fall of at least 15mmHg whilst on the same or reduced antihypertensive therapy. Hypertension was considered unchanged if the above two criteria were not fulfilled [6-7]. The renal function was considered improved if serum creatinine fell by 20 % compared to the pre PTA level, and worsened if increased by 20% or more. During follow-up, one patient had further renal angiography due to strong clinical suspicions of restenosis.

Statistical analysis

Results are expressed as mean±SD, or as percentages where appropriate. Comparison between paired variables such as blood pressure or serum creatinine levels was performed with paired-t-test. The un-paired t-test was used to compare the means between groups. To determine the statistical significance of the differences (pre and post PTA) between groups, we used the Mann-Whitney rank-sum test. A p value of less than 0.05 was considered as statistically significant.

Results

The clinical and demographic data of patients who underwent renal PTA are shown in Table 1. Our results demonstrate that in follow-up period after renal PTA, out of 30 patients, hypertension was completely cured in 1 (3.4%) patients, improved in 21(68.9%) and failed to improve in 8 patients (27.5%), (Table 2). In the group as a whole there was a significant reduction in both systolic and diastolic BP: 20.6/8.3 mm Hg, p<0.001, p<0.003 respectively.

Furthermore, out of the 30 patients, the renal function improved in 10 patients (34.4%), was unchanged in 9 (27.5%), and worsened in 11 patients (37.9%), (Table 3). No significant difference was found between the pre and post PTA serum creatinine (p=0.2). The reduction on medication post PTA was statistically significant (p<0.03) in all patients.

Table 1. Clinical, demographic and angiographic characteristics of 30 hypertensive patients who underwent renal PTA (results are mean ± SD)

Variable	Number [%] or Mean pre PTA	End of follow up	P value
Sex (M/F)	18/12		
Age	69.0±7.6		
SBP (mmHg)	177.6 ±26.8	157.0±18.4	p<0.05
DBP (mmHg)	88.3 ± 17.1	80.0±10.5	p<0.05
Serum Creatinine (μmol/l)	251.8±145	265.4±139	NS
No of hypertensive drugs	2.4±1.1	2.1±1	p<0.05
Unilateral RAS	17(56.6%)		
Bilateral RAS	8 (26.6%)		
Single Functioning Kidney	5 (16.6%)		
Renal impairment	25(83.3%)		

The BP (mean value) measurements and mean number of antihypertensive drugs prior to PTA and post PTA at the end of follow up were as follows: pre PTA 177.6/88.3 ± 26.8/17.1 mm Hg (2.4±1.1), and at the end of follow up 157.0/80.0 ± 18.4/10.5 mm Hg (2.1±1). The serum creatinine prior to PTA and at the end of follow up was 251.8±145 and 265.4±139 μmol/l respectively.

Ostial and non ostial

Technical success and long term patency rates were not significantly different between ostial and non ostial lesions (Table 2, 3).

Table 2. Number of patients (%) in whom Blood Pressure was cured, improved, or failed to improve following renal PTA with stent placement

Blood Pressure	n	Ostial	Non ostial	Unilateral	Bilateral	Solitary Kidney
Cured	1 (3.4%)	0	1 (7.7%)	1 (5.88%)	1 (12.5%)	1 (20%)
Improved	21(68.9%)	11(68.7%)	10 (69.2%)	12 (70.5%)	5 (62.5%)	3 (60%)
Failure to Improve	8 (27.5%)	5 (31.2%)	3 (23%)	4 (23.5%)	2 (25%)	1 (20%)
Total	30	16	14	17	8	5

Table 3. Number of patients (%) in whom serum creatinine improved, was unchanged or worsen following renal PTA

Serum Creatinine	n	Ostial	Non ostial	Unilateral	Bilateral	Solitary Kidney
Improved	10 (34.4%)	6 (37.5%)	4 (28.5%)	5 (29.4%)	1 (12.5%)	4 (80%)
Unchanged	9 (27.5%)	4 (25%)	5 (35.7%)	6 (35.3%)	4 (50%)	0
Worse	11 (37.9%)	6 (37.5%)	5 (35.7%)	6 (35.3%)	3 (37.5%)	1 (20%)
Total	30	16	14	17	8	5

There were not statistically significant differences in the reduction of blood pressure, serum creatinine and medication between to the two groups.

Unilateral vs. Bilateral renal PTA vs. Single functioning kidney

In patients with unilateral stenosis there were 5.8% cured of hypertension and the reduction of SBP was statistically significant (p<0.03). In patients with bilateral stenosis there were 12.5% cured of hypertension. There were better results in patients with single functioning kidney. In 5 patients who had renal PTA to a solitary kidney, 1(20%) of

them was with completely regulated hypertension and 3 (60%) with improved blood pressure control. Four of them (80%) had improved serum creatinine.
The reduction in both SBP and DBP was statistically significant in patients of that group ($p<0.01$ and $p<0.05$ respectively). In the same group of patients we observed greater reduction in serum creatinine (mean Cr difference 159.1±16.6 μmol/l) compared to other patients (bilateral: mean Cr difference 31.8±64.5, unilateral: mean Cr difference16.2±88.2 μmol/l). This difference between the groups was not statistically significant ($p=0.4$, $p=0.3$). In patients also with stenosis to a solitary kidney there was higher number of patients whose serum creatinine improved after renal PTA than in those with bilateral or unilateral disease (80% and 12.5%, 29.4% respectively) (Table 3).

Renal impairment

None of the patients with renal impairment was cured of hypertension but in 18 (72%) improved. Sixteen patients (64%) with renal insufficiency had unchanged (24%) or improved (40%) serum creatinine following renal PTA and in 9 (36%) patients serum creatinine worsened (Table 4).

Table 4. The effect of renal PTA on Blood Pressure and serum creatinine in patients with (serum creatinine >124 μmol/l) and without renal impairment

	Serum Creatinine			**Blood Pressure**	
	Renal impairment prior to PTA			**Renal impairment prior to PTA**	
	YES	**NO**		**YES**	**NO**
Improved	10(40%)	0	Cured	0	1(20%)
Unchanged	6(24%)	3(60%)	Improved	18(72%)	3(60%)
Worsen	9(36%)	2(40%)	Failure to improve	7(28%)	1(20%)
Total	25	5		25	5

Events

Initial technical success was achieved in all patients. In 4 patients we recorded the following minor and major events: two patients developed a local haematoma but none required blood transfusion, two patients developed cholesterol embolisation and one of them transient acute renal impairment. In one patient (3%) repeat angiography during the follow-up demonstrated renal artery re-stenosis (ostial lesion).

Discussion

Renal artery stenosis has been thought to be a rare cause of hypertension. It is now being realised that in patients with vascular disease elsewhere, atherosclerotic narrowing of the renal artery is extremely common. Indeed, renal artery stenosis is the most common curable cause of hypertension and impaired renal function. It is also a rare cause of acute, recurrent pulmonary oedema [3] and apparent congestive heart failure [4-5] in patients without overt coronary or valvular heart disease. The ability to stabilise or reverse all the above through revascularisation techniques has increased the clinical awareness of atherosclerotic renal artery stenosis. Renal PTA with stent replacement has become the treatment of choice in these patients. The main objectives of this procedure are to normalise blood pressure and to delay loss of renal function.
However, the long-term outcomes of this approach on blood pressure and progression to renal failure have not been investigated. Probably the weak point of our study is that there is no control group of patients who are treated only medically. However but the length of the follow up period is sufficient to lead in some conclusions. Our results clearly demonstrate that renal PTA with stenting leads to a large long-term fall in blood pressure in patients with atheromatous disease.
Renal revascularization can result in improvement or stabilization of renal status especially in patients with single functioning kidney and in those with renal insufficiency, in whom medical therapy is generally ineffective [6-7]. The benefit rate of PTRA in renal status is usually lower than that in hypertension, because of evolution of the underlying nephropathy [8]. This was observed also in our study where no significant difference was found between the pre and post PTA serum creatinine ($p=0.2$). In 65.4% of patients serum creatinine remained unchanged or worsened but we had significant reduction in blood pressure and in antihypertensive medication.
Despite antihypertensive therapy and PTA, atherosclerotic lesions tend to progress leading to renal ischaemia, loss of renal mass and ultimately possibly occlusion of the renal artery [9]. Improvement in renal function after renal revascularisation has been reported in 25-53% of all patients with unilateral or bilateral disease [10-11]. In our study the 47.5 months (4 years) follow-up confirm previous findings of improved renal function in 34.4% patients.
In patients with stenosis in a single functioning kidney there was an even greater percentage of patients whose control of hypertension improved or cured and serum creatinine decreased (80% and 80% respectively) following renal PTA with stenting. Shannon HM *et al.* [12], reported that in 21 patients (serum creatinine > 150 μmol/L) who had PTA and stent implantation to a stenosis in a solitary kidney serum creatinine improved or stabilised in all but six patients led to return. Similar results were also reported by other investigators [13]. This can be explained by the fact that in stenosis in a single functioning kidney there is haemodynamically significant reduction to renal flow with resultant retention of sodium and water.
In our study, in bilateral renal artery disease there was a larger fall in blood pressure following renal PTA when compared to unilateral disease, and a greater number of patients had improved serum creatinine.
In patients with renal impairment there was a smaller improvement in blood pressure control and a decrease in serum creatinine following PTA when compared to patients with normal renal function (3.0 % and 20.0%, respectively). This is explained by the fact that hypertension in patients with renal failure has multiple aetiologies and is maintained as long as the renal damage is not reversible.

More importantly, however, in 64% of patients with renal impairment (mean Cr: 278, 2±140 μmol/L), serum creatinine improved or remained stable in 24% and 40% respectively during follow-up. This shows the efficacy of this procedure even in patients with at least moderate to severe renal failure [14]. This finding is clinically important, because atheromatous renovascular disease is a common cause of end stage renal failure accounting for 7.5-27% of patients older than 50 years undergoing renal dialysis [15-16]. Stent restenosis is a result of myointimal hyperplasia and is usually smooth and concentric, involving the proximal and middle portions of the stent. Restenosis seems to be a major problem, occurring in 20%-38% of the cases after 1 year or 16% reported during short-time follow-up by other investigators [17-18]. The incidence of restenosis is higher in ostial lesions and with the use of the articulated Palmaz stent the percentage of restenosis is about 11% [19].

Our restenosis rate (3%) was considerably lower than those in other studies; in one patient with stenosis in ostial lesion. Angiographic follow-up is required only in this patient where there was strong suggestion of restenosis. We were aware of the risk of missing subjects but it was difficult to propose that annual follow-up intrarterial angiography.

Cholesterol embolisation is a well-known complication of both aortography and renal angioplasty as a complication of stent placement from 1987 [20]. According to the literature this happens in 3-6% of patients [21]. This complication was observed in two (6.6%) patients in our series.

Conclusion

Our results clearly demonstrate that renal PTA with stenting leads to a long term improvement in blood pressure, and an improvement or stabilisation of renal function in a large number of hypertensive patients. These effects are more evident in patients with atheromatous renal artery stenosis in a single functioning kidney and in those hypertensive patients who present with bilateral stenosis. It is suggested therefore that hypertensive patients with atheromatous renal artery stenosis with or without mild to moderate impairment in renal function, or signs of sodium and water retention in the absence of overt cardiac disease, should be considered for renal artery revascularisation (PTA) with stent replacement. It seems that, at least one third of them will have a benefit in renal function and more of them better control of blood pressure for a long term.

Conflict of interest statement. None declared.

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