Efficacy of percutaneous transluminal renal angioplasty with stent in elderly male patients with atherosclerotic renal artery stenosis

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Objectives: Percutaneous transluminal renal angioplasty with stent implantation (PTRAS) has become the treatment of choice for atherosclerotic renal artery stenosis (ARAS). This study evaluates the long-term effects of PTRAS on hypertension and renal function in elderly patients with ARAS.

Methods: We conducted a retrospective cohort study of all patients who underwent PTRAS in the geriatric division of a tertiary medical center during the period 2003–2010. The clinical data were extracted from the medical records of each patient. Changes in blood pressure, antihypertensive treatment, and estimated glomerular filtration rate were analyzed before and after PTRAS.

Results: Eighty-six stents in 81 elderly patients were placed successfully. The average age of the patients was 76.2 years (65–89 years). Mean follow-up was 31.3 months (range 12–49 months). There was a significant decrease in both systolic and diastolic blood pressure at the third day after the PTRAS procedure and the reduction in blood pressure was constant throughout the follow-up period until 36 months after PTRAS. However, there was no marked benefit to renal function outcome during the follow-up period. The incidence of contrast-induced nephropathy was 9.9% in this study group. The rate of renal artery restenosis was 14.8%. The survival rate was 96.3% for 4 years after the procedure.

Conclusion: It is beneficial to control blood pressure in elderly patients with ARAS up to 36 months after a PTRAS procedure. However, their renal function improvement is limited.

Keywords: angioplasty, hypertension, renal function, elderly, renal artery stenosis

Introduction

Atherosclerotic renal artery stenosis (ARAS) is a common problem and is more prevalent in the elderly. It is estimated to occur in 0.5%–1.0% of all patients with hypertension, 5.5% of patients with chronic kidney disease (CKD),¹ and 6.8%–7% of patients over 65 years old.² ARAS is one of the major causes of secondary hypertension, ischemic nephropathy, and chronic renal insufficiency in the elderly.¹ Researchers have suggested a significant negative correlation between the severity of renal artery stenosis and the survival of patients.^{3,4} Percutaneous transluminal renal angioplasty with stent implantation (PTRAS) has become the predominant intervention for ARAS. The assumption was that restoring renal blood flow would improve both blood pressure (BP) control and renal function. However, comparing PTRAS versus medical therapy alone, no benefit was demonstrated in PTRAS groups in three recent randomized trials, the Dutch Renal Artery Stenosis Intervention Cooperative (DRASTIC) trial,⁵ the Stent Placement in Patients with Atherosclerotic Renal Artery Stenosis (STAR)

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trial, and the Angioplasty and Stent for Renal Artery Lesions (ASTRAL) trial. Other research showed that PTRAS only had benefits for BP,^{6,7} but not for renal function or long-term survival, and there were even adverse effects in some cases if contrast-induced nephropathy (CIN) occurred.^{6–8} The ASTRAL trial concluded that there was no significant advantage of PTRAS in maintaining renal function, decreasing the average systolic BP, or long-term survival, but these results are widely questioned because of their loose inclusion criteria (some patients didn't have critical clinical manifestation of renal artery stenosis, etc).⁹

Studies conducted in China usually have a small sample size and short follow-up, and no widely recognized conclusions can be drawn.¹⁰ As a result, the best intervention for ARAS is still not clear. The aim of our study was to examine the clinical features and the clinical outcome of the procedure, focusing on changes in renal function and BP control in the elderly with ARAS.

Methods

Patients

This retrospective study related to elderly patients with ARAS at the geriatric department in a tertiary medical center during the period January 2003 to January 2010. All the patients met the procedure criteria: (1) age ≥ 65 years, (2) hypertensive, (3) diagnosed as ARAS by percutaneous angiography, (4) severity of renal artery stenosis $\geq 70\%$, (5) cross-stenosis difference of systolic pressure > 20 mmHg, (6) treated by PTRAS and technical procedures successful, (7) examined by Doppler ultrasonography every 6 months after procedure, and at least 18 months' follow-up after the procedure.

Data collection

The clinical data were collected from clinical medical records and included age at the time of intervention, atherosclerotic risk factors, comorbid conditions, BP, serum creatinine (SCr), and antihypertensive treatment before and after PTRAS and during the follow-up period.

BP measurement was according to the guidelines of the Joint National Committee seventh report.¹¹ Resting BP was measured three times during each visit, with an interval of at least 5 minutes between measurements and with the patient in a sitting position, and the average of the two last readings was recorded. We classified the antihypertensive medications into six kinds: calcium-channel blocker, diuretic, angiotensin converting-enzyme inhibitor or angiotensin-receptor blocker,

α -blockers, β -blocker, and others. Refractory hypertension was defined as failure to reach target BP with treatment of at least three antihypertensive medications in adequate doses.

Estimated glomerular filtration rate (eGFR) calculated by the Chronic Kidney Disease Epidemiology Collaboration formula¹² was adopted as assessment of baseline renal function. Improvement of renal function after the procedure was defined as a consistent 20% decrease in serum creatinine from the baseline value, deterioration as a consistent 20% increase above baseline, and values within 20% of baseline were considered stabilized.^{13–15}

Diagnostic criteria for CIN were: SCr increase of 0.5 mg/dL (44.2 μ mol/L) or 25% of baseline value and SCr ≥ 110 μ mol/L within 48 hours after receiving iodinated contrast injection in the procedure of renal arteriography. Hydration rate was the percentage of patients who had been given intravenous fluid hydration with normal saline just after the PTRAS procedure.

The definition of restenosis after PTRAS was in-stent stenosis of renal artery $> 50\%$ determined by renal arteriography. During the follow-up period, if the restenosis was suspected by Doppler sonography, the renal arteriography would be applied to confirm the diagnosis of restenosis.

Statistical analysis

Statistical analysis was performed using SPSS version 13.0 (IBM, Armonk, NY). The descriptive data are expressed as means $\pm$ standard deviation. Differences between groups were calculated by Student's *t*-test for continuous variables and by contingency tables for nominal variables. Probability values of <0.05 were considered statistically significant.

Multivariate logistic regression analysis for the presence of CIN after procedure, renal function deteriorating within 12 months postprocedure, and restenosis were evaluated on the following factors: age, preprocedural SCr, preprocedural BP, having diabetes or not, received postprocedural hydration treatment, bilateral renal artery stenosis, complete release of stenosis. The study was approved by the ethics committee of our hospital.

Results

For the period 2003–2010, of the 136 patients with ARAS who received PTRAS, 55 were excluded from the study due to not meeting the procedural inclusion criteria. A total of 81 patients met the procedural criteria of the study, and the mean period of follow-up was 31.3 ± 12 months.

Table 1 Baseline characteristics of the elderly ARAS patients

	Patients	Unilateral ARAS	Bilateral ARAS	P-value
Patients, n (%)	81	45 (55.6)	36 (44.4)	
Age, years	76.2 ± 5.1	76.4 ± 5.2	76 ± 4.1	
SCr, µmol/L	129.6 ± 56.3	125.7 ± 51.5	133.8 ± 57.9	0.76
eGFR, mL/minute/1.73 m ²	53.1 ± 20.9	54.1 ± 22.4	52 ± 19.5	
Systolic pressure, mmHg	155.9 ± 22.8	151 ± 24	158 ± 23.2	0.19
Diastolic pressure, mmHg	79.3 ± 10.8	77.3 ± 11.8	79.8 ± 11.3	0.56
Number of antihypertensive medications	2.28 ± 1.18	2.23 ± 1.25	2.35 ± 1.16	0.79
Refractory hypertension, n (%)	37 (45.5)	16 (43.2)	21 (56.8)	0.21
Degree of stenosis, %	84.5 ± 10.1			
Diabetes mellitus, n (%)	29 (35.8)	14 (31.1)	15 (41.7)	0.53
Coronary heart disease, n (%)	57 (70.4)	28 (62.2)	29 (80.6)	0.39
eGFR < 60 mL/minute, n (%)	58 (71.6)	31 (68.9)	27 (75)	0.78
eGFR < 30 mL/minute, n (%)	13 (16)	8 (17.8)	5 (13.9)	0.71
Stroke, n (%)	8 (9.9)	4 (8.9)	4 (11.1)	0.62
Hyperlipidemia, n (%)	10 (12.3)	4 (8.9)	6 (16.7)	0.29

Note: Data are presented as means ± standard deviation.

Abbreviations: ARAS, atherosclerotic renal artery stenosis; SCr, serum creatinine; eGFR, estimated glomerular filtration rate.

Clinical characteristics

We analyzed the data in a total of 86 transluminal stents placed in 81 patients. The baseline characteristics of the 81 patients are shown in Table 1. All PTRAS procedures were successful. There was no procedure-related death or major complications. Compared with patients who had unilateral RAS, the patients with bilateral RAS had higher systolic BP and were more likely to have complications such as diabetes mellitus, coronary heart disease, and stroke. The difference was not significant.

Blood pressure outcome

Changes in BP in the pre-PTRAS and follow-up periods are demonstrated in Table 2. BP was measured at the following time intervals: preprocedure, the third day, 12, 24, and 36 months after the procedure. Compared to the pre-PTRAS procedure, there was a significant decrease in BP levels (both systolic and diastolic pressure) from the third day after the PTRAS ($P < 0.05$). Regardless of refractory hypertension or

common hypertension before PTRAS, there was the same tendency (Table 3). The decrease in BP was sustained throughout the 36 months of the follow-up period. The kind of antihypertensive medications taken by patients who had the procedure for BP was reduced, but the differences were not statistically significant.

Renal function outcome

Mean follow-up was 31.3 ± 12 months. Three patients died, and three patients reached end-stage renal failure, requiring initiation of hemodialysis. The patients died because of pulmonary infection around the 30th month post-PTRAS. The patients who reached end-stage renal failure had more advanced renal insufficiency at the time of PTRAS (CKD stage 3b with eGFR < 45 mL/minute) and showed a more rapid decline in renal function after stenting. The renal function outcome in the entire group of patients is shown in Table 2. The renal function outcome in different hypertensive groups of patients is shown in Table 3. Compared to

Table 2 Blood pressure and renal function outcome

	Patients (n)	Blood pressure			Renal function		
		Systolic pressure (mmHg)	Diastolic pressure (mmHg)	Antihypertensive medications	Better %	Same %	Worse %
Preprocedure	81	155.9 ± 22.8	79.3 ± 10.8	2.3 ± 1.1			
Postprocedure: 3 days	81	130.3 ± 14.5**	66.7 ± 8.9**	2.1 ± 1.0			
12 months	80	136.7 ± 15.1**	69.3 ± 8.7**	2.2 ± 1.0	15	61.3	23.8
24 months	69	137.9 ± 10.2**	70.3 ± 7.9**	2.2 ± 1.1	10.1	65.2	24.6
36 months	47	135.1 ± 14.7**	68.3 ± 10.2**	2.1 ± 1.0	17	55.3	27.7

Notes: Compared with baseline values, ** $P < 0.01$; differences between the values at different follow-up periods were not significant ($\chi^2 = 3.585$, $P = 0.352$); no significant differences between any two groups of renal function. Data are presented as means ± standard deviation.

Table 3 Blood pressure and renal function outcome in different preprocedure BP of patients

Patients n, %	Blood pressure (mmHg)			Renal function postprocedure (12 months)		
	Preprocedure	Postprocedure (12 months)	Postprocedure (24 months)	Better n, %	Same n, %	Worse n, %
Refractory hypertension						
37 (45.7)						
SBP	169.6 ± 23.1	139.5 ± 14.4**	145.7 ± 16.2**	6 (16.7)	21 (58.3)	9 (25)
DBP	81.3 ± 14.5	71.5 ± 8.9*	72.2 ± 6.4*			
Common hypertension						
44 (54.3)						
SBP	141 ± 14.4	131.8 ± 14.9*	129.3 ± 12.3*	5 (11.3)	29 (66)	10 (22.7)
DBP	76.4 ± 7.4	68.3 ± 7.2*	69 ± 8.2*			

Notes: Compared with baseline values, * $P < 0.05$; ** $P < 0.01$; $\chi^2 = 5.623$, $P = 0.673$, no significant difference between any two groups of renal function. Data are presented as means ± SD.

Abbreviations: BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; SD, standard deviation.

that of those who had common hypertension preprocedure, the renal outcome of patients with refractory hypertension preprocedure had no significant difference. The results of multivariate logistic regression analysis for the risk of renal function deteriorating within 12 months postprocedure are shown in Table 4. These show preexisting diabetes significantly increased the risk of deterioration of renal function. The difference in renal function outcome among the different eGFRs in the pre-PTRAS is shown in Table 5.

Eight patients (9.9%) developed CIN on the third day after PTRAS. The results of multivariate logistic regression analysis for the risk of CIN are shown in Table 6. Preexisting diabetes, eGFR of the pre-PTRAS < 30 mL/minute and systolic blood pressure ≥ 180 mmHg significantly increased the risk of CIN, and immediate hydration therapy after PTRAS significantly lowered the risk of CIN.

Twelve (14.8%) patients with restenosis were detected by color Doppler ultrasonography during follow-up and then determined by renal arteriography. Logistic regression analysis suggested that there was no significant relevance between the restenosis and risks such as preoperative renal functions, BP, and complications.

Table 4 Multivariate logistic regression analysis of renal function deteriorating within 12 months postprocedure

Factor	P-value	OR	95% CI
Preprocedural diabetes	0.0234	5.99	1.274–28.128
Preprocedural refractory hypertension	0.6279	1.40	0.359–5.458
Hydration therapy immediately after procedure	0.7632	0.75	0.111–5.018

Abbreviations: OR, odds ratio; CI, confidence interval.

Discussion

In the current study, we demonstrated that PTRAS improved BP control, and this improvement was maintained during the follow-up period of 36 months in elderly patients with ARAS, of whom 45.5% had refractory hypertension. From 3 days up to 36 months after PTRAS, the BP of the patients decreased significantly and was easier to control within normal range, although there was no change in the kinds of antihypertensive medications. This result is similar to that of other studies.^{16,17} Renal artery reconstruction – by eventually relieving renal hemodynamic obstacles, resulting in decreased secretions of the local neuroendocrine system and significant drop in BP – could notably improve the malignant hypertension caused by renovascular abnormality in elderly people, which presumably will reduce the occurrence of cardiovascular and cerebrovascular events. This may have contributed to the low mortality during the 4-year follow-up period. Antihypertensive medication was still required after PTRAS, because many patients showed systemic atherosclerosis. The prevalence of multiple use of antihypertensive medication and application of angiotensin converting–enzyme inhibitors/angiotensin-receptor blockers in recent years may have caused the insignificant decrease of antihypertensive medication.

In our study, for about 3 years after PTRAS, renal function improved in 10.2%–17%, stabilized in 61.3%–55.3%, and worsened in 23.7%–27.7%. This suggests that PTRAS did not significantly affect renal function in the elderly patients. Other studies also reported the deterioration rate of renal function range from 14% to 39% after PTRAS.¹⁶

Table 5 Renal function outcome classified with preprocedural eGFR

Preprocedural eGFR (mL/minute/1.73 m ²)	Patients, n	Hydration rate, n (%)	Follow-up length	Patients, n	Better, n (%)	Same, n (%)	Worse, n (%)
60–90	23	13 (56.5)	12 months	22	1 (4.5)	15 (68.2)	6 (27.3)
			24 months	18	0	13 (72.2)	5 (27.8)
			36 months	15	0	9 (60.0)	6 (40.0)
45–59	17	14 (82.4)	12 months	17	2 (11.8)	12 (70.6)	3 (17.6)
			24 months	14	3 (21.4)	7 (50)	4 (28.6)
			36 months	10	2 (20)	7 (70)	1 (10)
30–44	28	26 (92.9)	12 months	28	7 (25)	13 (46.4)	8 (28.6)
			24 months	24	3 (12.5)	16 (41.7)	5 (20.8)
			36 months	14	5 (35.7)	6 (42.8)	3 (21.5)
<30	13	12 (92.3)	12 months	13	2 (15.4)	9 (69.2)	2 (15.4)
			24 months	13	1 (7.7)	9 (69.2)	3 (23.1)
			36 months	8	1 (12.5)	4 (50.0)	3 (37.5)

Abbreviation: eGFR, estimated glomerular filtration rate.

Recently, a few prospective randomized clinical trials (DRASTIC, STAR, and ASTRAL) have been completed, and all failed to demonstrate benefits of PTRAS on renal outcomes compared with medical therapy alone. The ASTRAL trial^{18–20} even reported that there were no beneficial effects of PTRAS on ARAS patients, including renal function and BP. Compared with patients treated by medication only, patients treated by PTRAS had more complications after the procedure. However, many researchers thought that the main pitfall of those clinical trials was the inclusion of patients whose stenosis was not critical (50% of patients in the STAR trial had mild stenosis and 41% of patients in the ASTRAL trial had stenosis less than 70%).^{20,21} In our study, all patients' renal artery stenosis was more than 70%, and the BP cross-stenosis difference was more than 20 mmHg. All patients were treated by PTRAS and the technical procedures were successful. However, in our study 71.6% patients were in CKD stage 3 and 16% in CKD stage 4 before PTRAS. In addition, 70.4% patients had experienced coronary heart disease. PTRAS alone could hardly improve renal function in elderly patients with ARAS.

Table 6 Multivariate logistic regression analysis of post-procedural CIN

Factor	P-value	OR	95% CI
Preprocedural diabetes	0.0069	14.25	2.08–91.62
Preprocedural eGFR < 30 mL/minute	0.0002	457.81	19.83–11381
Preprocedural systolic pressure ≥ 180 mmHg	0.0156	8.57	1.53–121.52
Hydration therapy immediately after procedure	0.0215	0.15	0.01–0.89

Abbreviations: CIN, contrast-induced nephropathy; OR, odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate.

In our study, statistical analysis showed that preexisting refractory hypertension and class of renal function were not independent predictive factors of the deterioration of renal function post-PTRAS. However it was shown that preexisting diabetes significantly increased the risk of deterioration of renal function. The reason may be that the preexisting diabetes can worsen the ischemic nephropathy, which developed slowly during the long process of ARAS in elderly patients. The pathologic changes of ischemic nephropathy included renal arteriole sclerosis, tubular atrophy, and interstitial fibrosis. Local renal artery revascularization could not be effective to change glomerular hyperperfusion in diabetes and could not change the wide renal arteriole sclerosis and other irreversible pathological changes.

PTRAS may bring about potential damage to the kidney, such as contrast-induced renal impairment and small cholesterol crystal embolization. In this study, eight patients (9.9%) got CIN after PTRAS, and 66.7% of them appeared to have renal function damage. According to multivariate logistic regression analysis, preexisting diabetes, eGFR < 30 mL/minute and systolic blood pressure ≥ 180 mmHg were risk factors for CIN. Hydration therapy immediately after PTRAS procedure was able to lower the risk significantly in the elderly patients with ARAS.

In our study, 13.8% of the patients developed restenosis after PTRAS, which was similar to the average restenosis rate of 15%–17% at 1 year after PTRAS reported by other studies.^{22,23} Risk factors for restenosis may include the experience of vascular intervention and the use of antiplatelet agents after PTRAS.

We conclude that the main effect of PTRAS is on BP control, but it could hardly bring benefits to renal outcome in

elderly patients with ARAS. Individualized risk assessment before PTRAS, hydration therapy after the procedure, and the control of blood glucose are very important. Further prospective, randomized studies with larger samples of patients are needed to validate our observation.

Acknowledgments

The authors appreciate that the manuscript was edited and proofread by Ms Nancy B Martin. This study was funded by grants from the National Natural Science Foundation of China (No 30772296 and No 81170312) and supported by the Beijing Natural Science Foundation (No 7122163).

Disclosure

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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