Percutaneous renal artery stenting reduces arterial blood pressure, but what about renal function? A single-center experience

Perkütan renal arter stent uygulaması arteryel kan basıncını düşürür, fakat böbrek fonksiyonlarına etkisi nedir? Tek merkezin deneyimi

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Abstract

Objective: To assess the effects of percutaneous transluminal angioplasty and stenting (PTRA/S) on arterial blood pressure and renal function.
Methods: A retrospective chart review of patients undergoing PTRA/S at our institution between December 2003 and September 2006 was done. Follow-up data were derived from hospital records. Estimated glomerular filtration rate (EGFR) was used as the marker of renal function. To evaluate the pre- and post-procedure values in individual patients the paired t test and Wilcoxon signed-rank tests were used.
Results: Thirty-six patients (16 women, 30 men; mean age 59±15 years, range: 25-83 years) underwent 43 PTRA/S interventions at our institution. The mean duration of follow-up was 9.3±8.6 (range 2-28) months. We observed no significant change in EGFR from pre-procedure to that obtained at follow-up (71.4±40.2 mL/min vs.73.3±39.0 mL/min; p=0.483). Mean arterial blood pressure (MABP), however, was reduced significantly: pre-procedure MABP-123±22 mmHg; post-procedure follow-up value of 101±14 mmHg (p <0.001). The mean number of antihypertensive medications used at the time of intervention was 2.1±1.0 (range: 0-4), whereas at follow-up, this number had decreased to 1.3±1.0 (range: 0-4; p<0.001). In patients with renal impairment (EGFR ≤59 mL/min), 41% showed improvement, 29% showed no change and 29% demonstrated deterioration in EGFR.
Conclusion: PTRA/S may preserve renal function, especially in patients with pre-procedural impaired renal function.
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Key words: Hypertension, percutaneous transluminal renal angioplasty, renal artery stenosis, renal failure, stent, glomerular filtration rate

Özet

Amaç: Bu çalışmanın amacı, perkütan transluminal anjiyoplasti ve stent (PTRA/S) uygulamasının arteryel kan basıncı ve böbrek fonksiyonları üzerine olan etkilerinin araştırılmasıdır.
Yöntemler: Aralık 2003 ile Eylül 2006 tarihleri arasında hastanemizde PTRA/S uygulanan hastaların dosyaları geriye dönük olarak incelenmiştir. Hastaların takip verileri dosya kayıtlarından elde edilmiştir. Böbrek fonksiyonlarını değerlendirmek için tahmini glomerüler filtrasyon hızı (GFR) kullanılmıştır. İşlem öncesi ve işlem sonrasında elde edilen verilerin karşılaştırılmasında eşleştirilmiş t testi ve Wilcoxon işaret sıralama testleri kullanılmıştır.
Bulgular: Hastanemizde 36 hastaya (16 kadın, 20 erkek; ortalama yaş 59±15, R: 25-83) toplam 43 PTRA/S işlemi uygulanmıştır. Hastaların işlem sonrası ortalama takip süresi 9.3±8.6 (R: 2-28) ay olarak bulunmuştur. İşlem sonrasında, tahmini GFR değerinde işlem öncesine göre anlamlı bir değişiklik saptanmamış (71.4±40.2 mL/dak karşı 73.3±39.0 mL/dak; p=0.483), ancak ortalama arteryel kan basıncında işlem öncesine göre belirgin düşüş gözlenmiştir (işlem öncesi: 123±22 mmHg; işlem sonrası: 101±14 mmHg; p < 0.001). İşlem öncesinde kullanılan ortalama antihipertansif sayısı 2.1±1.0 (R: 0-4) iken işlem sonrasındaki takip süreci sonunda bu sayı 1.3±1.0'a (R: 0-4) düşmüştür (p<0.001). Böbrek fonksiyonları bozuk olan hastalara (GFR ≤59 mL/dak) uygulanan girişimsel tedavi sonrası %41'inde böbrek fonksiyonlarında iyileşme görülürken, %29'unda stabil seyir izlenmiş ve %29'unda ise kötüleşme tespit edilmiştir.
Sonuç: PTRA/S uygulaması, özellikle işlem öncesi böbrek fonksiyonlarında bozulma olan hastalarda böbrek fonksiyonlarını koruyabilir.
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Anahtar kelimeler: Hipertansiyon, perkütan transluminal renal anjiyoplasti, renal arter darlığı, böbrek yetmezliği, stent, glomerüler filtrasyon hızı

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Introduction

Renovascular hypertension is caused by atherosclerotic renal artery stenosis (RAS) or fibromuscular dysplasia. Atherosclerotic RAS alone is the most common cause of secondary hypertension, accounting for 1% to 5% of cases, and frequently leads to progressive renal ischemia and loss of renal function (1). Once a stenotic lesion causing renovascular hypertension is found and proven to be functionally significant, three choices are available for treatment: medical therapy, angioplasty and surgical revascularization (2). Percutaneous transluminal renal angioplasty (PTRA), first introduced by Gruntzig in 1978 (3), has been a cornerstone in the treatment of renovascular hypertension. Stent implementation following PTRA is a less invasive technique than surgery, yet also has a high rate of correction of the stenosis (4).

Many studies have demonstrated the efficacy of PTRA with stenting (PTRA/S) for control of renovascular hypertension (5-7), but the success of PTRA/S regarding maintenance of renal function in these patients with normal or impaired renal function is still controversial. Several studies have demonstrated the efficacy of successful PTRA/S on improving or preserving renal function in patients with ischemic nephropathy (8-12). However, a recent meta-analysis of three randomized trials in which the effects of balloon angioplasty with medical therapy were compared in a total of 210 patients showed no consistent differences in changes in renal function (1).

In this study, we assessed the effects of PTRA/S on renal function and renovascular hypertension in patients who were followed-up in our tertiary university hospital nephrology and hypertension clinic.

Methods

Patient population

After approval was obtained by the university medical centre's Medical Records Review Committee, charts were reviewed of non-dialysis dependent patients over 18 years of age who had undergone percutaneous renal artery angioplasty with stenting (PTRA/S) for unilateral or bilateral renal artery stenosis between December 2003 and September 2006 and who had a minimum of two months follow-up. Patients with renal lesions due to fibromuscular dysplasia were also included. Patients were excluded if they had an estimated glomerular filtration rate (EGFR) <15 mL/min or if they did not attend regular follow-up visits. Successful PTRA/S was defined as a residual renal artery stenosis of <20% in the absence of a complication.

Our interventional radiology colleagues considered renal artery lesions for stenting if the diameter of the stenosis (measured by duplex ultrasonography, magnetic resonance angiography or conventional angiography) exceeded 50% in a patient with hypertension (systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg) or impaired renal function (serum creatinine concentration (Cr_s) >1.4 mg/dL). Lesions were defined as 'ostial' if a nondiseased arterial segment could not be identified between the renal ostium and the lesion on angiography.

Preoperative demographic data were obtained, including age, gender, risk factors, and symptoms. Clinical factors included presence of diabetes mellitus, hypertension, coronary artery disease (CAD), hyperlipidemia, cerebrovascular disease, peripheral vascular disease, and tobacco usage. Antihypertensive medications prescribed previously were also checked. Multiple agents of a single class (e.g. angiotensin-converting enzyme inhibitors, beta-adrenergic antagonists) were coded as one agent unless they have recognized clinical utility in combination (eg, calcium channel antagonists). No patients were receiving medications such as cimetidine, trimethoprim or amiloride, which can affect the EGFR by altering plasma creatinine concentration (13).

Follow-up data were derived from hospital records. Follow-up blood pressure was measured by both oscillometric and manual techniques. Mean arterial pressure was calculated. Our measure of renal function was the estimation of glomerular filtration rate, calculated using the Cockroft and Gault formula (14) using the Cr_S (mg/dL), weight (kg), age (years) and gender of the patient as follows:

EGFR in males (mL/min)=[(140-age)xbody weight] / (Cr_sx72)

EGFR in females (mL/min)=Value for malesx0.85.

An EGFR of ≤59 mL/min was considered evidence for the presence of moderate to severe renal impairment (15). Renal function was considered "improved" if the EGFR had increased ≥15% at follow-up, and "worsened" if the EGFR had decreased ≥15%, and "unchanged" if the change in EGFR was less than 15%.

Stent procedure technique

In all patients, a right femoral approach was preferred for access with Seldinger method. After a 7F sheath introducer was placed, a 7F double curve renal guiding cathether was introduced via a 0.018 guidewire. The lesions were predilated and then Vascular Express SD stent system (Boston Scientific Corporation, Natick, MA, USA) was hand-crimped on the same balloon and inflated at 8-12 atm pressure. For osteal lesions, the proximal part of the stent protruded 1-2 mm into the aorta. A total of 50-70 cc non-ionic contrast material was used for the diagnostic and treatment procedures, and all patients were started on an anticoagulation protocol.

Statistical analysis

Statistical analyses were performed using SPSS version 10.0 for Windows® software (SPSS Inc., Chicago, USA). Data are expressed as mean±standard deviation (SD). The normality of data distributions were determined by Kolmogorov-Smirnov test. To evaluate the pre- and post-procedure values in individual patients, for normally distributed data, the paired *t* test was used. For non-normally distributed data (diastolic blood pressure and number of antihypertensive medications), the Wilcoxon signed-rank test was used. P values less than 0.05 were considered statistically significant.

Results

Thirty-six patients (16 women, 20 men; mean age 59±15 years, range 25-83 years) underwent 43 PTRA/S interventions at our institution from December 2003 through September 2006. Of these, seven patients had bilateral PTRA/S. Fourteen (39%) of the patients had diabetes, 15 (42%) had ischemic heart disease, 13 (36%) had peripheral arterial disease, 15 (42%) were hyperlipidemic, and 18 (50%) were smokers. The indication for PTRA/S was isolated hypertension in 20 (56%), impaired renal function in 3 (8%), and both hypertension and impaired renal function in 13 (36%).

Thirty-seven (86%) renal artery stents were placed for ostial stenosis and six (14%) for non-ostial lesions. Stenosis was due to atherosclerotic disease in 37 (86%) and due to fibromuscular dysplasia in 6 (14%) lesions. The mean length of the stenotic segment at the time of intervention was 1.2±0.8 cm (range 0.5-4.0), whereas mean stenosis degree (percent of diameter) was 77±17% (range 50-99). The stenting procedure was successful in all attempts. No procedural deaths occurred nor were any emergency renal surgical procedures performed.

The mean duration of follow-up was 9.3±8.6 months (range, 2-28 months). The systolic, diastolic and mean arterial blood pressures after stent implantation were significantly lower compared to pre-procedure levels (Table 1). The mean number of antihypertensive medications used at the time of intervention was 2.1±1.0 (range, 0-4), whereas at follow-up, this number had decreased to 1.3±1.0 (range, 0-4; p <0.001).

We observed no significant change in EGFR between the pre-procedure and follow-up values (71±40 mL/min vs. 73±39 mL/min; p=0.483; Fig. 1). Renal function at follow-up was categorized as better, unchanged, or worse and is shown in Table 2. In patients with renal impairment (EGFR ≤59 mL/min), 41% showed improvement, 29% showed no change and 29% demonstrated deterioration in EGFR. In patients with an EGFR ≥60 mL/min, 74% showed no change and only two patients (10%) experienced deterioration.

Table 1. Mean blood pressures pre-procedure and at a mean of follow-up 9.3 months after percutaneous renal artery angioplasty with stenting

Variables	Pre-stent	Follow-up	p
Systolic BP, mmHg	174±34	138±22	<0.001*
Diastolic BP, mmHg	98±18 (95; 83-108)	84±12 (80; 80-90)	<0.001**
Mean BP, mmHg	124±22	101±14	<0.001*
Number of antihypertensives	2.1±1.0 (2; 1-3)	1.3±1.0 (1; 1-3)	<0.001**

Values are also expressed as mean±SD, median (25%-75% percentiles).
*p value significance by paired t test, ** p value significance by the Wilcoxon signed-rank test
BP - blood pressure

Table 2. Percent change from pre-procedure estimated glomerular filtration rate at a mean of 9.3 months after percutaneous renal artery angioplasty with stenting*

Variables	N	Better (%)	Unchanged (%)	Worse (%)
Pre-stent EGFR ≤59 mL/min	17	7 (41)	5 (29)	5 (29)
Pre-stent EGFR ≥60 mL/min	19	3 (16)	14 (74)	2 (10)
All patients	36	10 (28)	19 (53)	7 (19)

*Better = >15% increase in EGFR; Unchanged = <15% change (better or worse); Worse = >15% decrease in EGFR
EGFR - estimated glomerular filtration rate

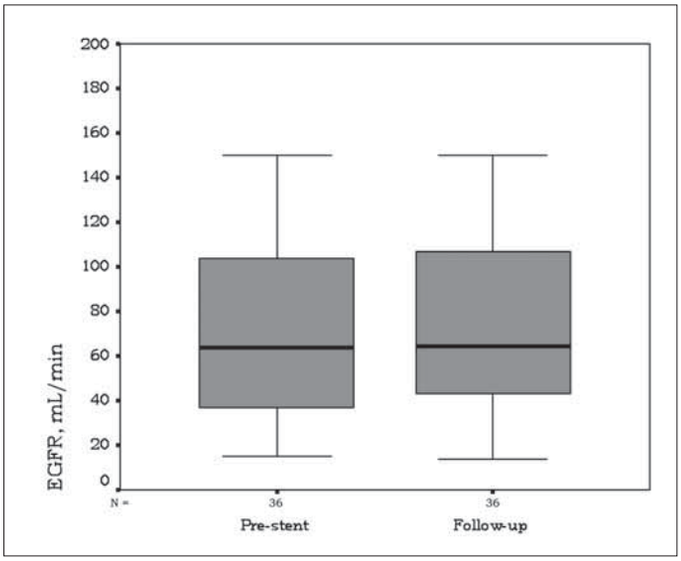

Figure 1. Estimated glomerular filtration rate (EGFR) values pre-procedure and at a mean of follow-up 9.3 months after percutanenous renal artery angioplasty with stenting

Discussion

In this retrospective investigation of patients who underwent PTRA/S, we observed a significant improvement in blood pressure control and a reduction in the requirement for antihypertensive medications at a mean follow-up of 9.3 months. Furthermore, this beneficial effect was accompanied by renal function preservation (improved or unchanged) particularly in patients with impaired renal functions (EGFR ≤59 mL/min). Thus, about one-third of the patients with impaired renal function did not benefit from the stent procedure.

With respect to the effect of the intervention on changes in renal functions, these results were compared with the previous studies which have been performed retrospective in nature (16, 17). In 1999, Rocha-Singh et al. (16) reported changes in blood pressure and renal function after PTRA/S in 150 patients with 180 renal artery lesions. Of these, 71 had a serum creatinine level of >1.4 mg/dL, and at 13 month follow-up, renal function was preserved or improved in 87%, while the mean arterial blood pressures decreased significantly in all patients. Lederman et al. (17) retrospectively evaluated 300 patients who were treated with PTRA/S. Using serum creatinine as a marker of renal function, they found that among patients who had renal insufficiency at baseline (101 of 300), renal function was preserved at follow-up in 73%. They also found an improvement in or cure of arterial hypertension in 71% of patients after a

median follow-up of 16 months. Similar to these findings, we observed that 71% of patients with impaired renal function benefited from the PTRA/S procedure.

The above studies used serum creatinine levels as a marker of pre- and post-PTRA/S renal function. Serum creatinine is a laboratory measurement which may be altered by many factors, including muscle mass, which diminishes with age (13). Instead, we used EGFR, which is a more sensitive marker of renal function and can be used more accurately in determination of renal insufficiency (18).

Preservation of renal function after PTRA/S has been prospectively observed in other studies as well. In a recent study (19), the impact of stent-supported angioplasty on renal function and blood pressure control was prospectively evaluated in 215 patients. At one-year follow-up, median S_{Cr} had decreased significantly (p=0.047) from 1.21 mg/dL to 1.10 mg/dL in 52% of the patients, and creatinine clearance in the entire cohort had increased by 2.3±15.1 mL/min (p=0.028). Importantly, the decrease in serum creatinine concentration tended to be larger in patients with higher baseline serum creatinine (>1.5 mg/dL). As in previous studies, the authors found that mean arterial blood pressure decreased significantly (from 102±12 mmHg at baseline to 92±10 mmHg after stenting, p<0.001). In another study of 105 patients, in which the renal function and outcome of PTRA/S for atherosclerotic renal artery stenosis was prospectively examined, a significant increase in EGFR (from 33±10 to 54±24 mL/min) was observed in the subgroup of patients with an initially lower EGFR (<50 mL/min) (4). Our results, and those of previous studies, demonstrate that beneficial effects of PTRA/S on renal function may be anticipated in selected patients, especially those with a low EGFR.

Correction of hemodynamically relevant stenoses of the renal artery can lead to an improvement in, or cure of, arterial hypertension (20). A recent meta-analysis comparing medical therapy and balloon angioplasty (without stenting) in a total of 210 renal artery stenosis patients from the three randomized trials found that balloon angioplasty was more effective in reducing arterial blood pressure than pharmacologic therapy alone (1). The weighted mean difference between the two treatment modalities was -7 mmHg (95% CI: -12 to -1 mmHg) for systolic blood pressure and -3 mmHg (95% CI: -6 to -1 mmHg) for diastolic blood pressure. However, meta-analysis of these trials found no significant change in renal function between the angioplasty and medical-therapy groups. The methods for evaluating changes in renal function were not uniform though, and these trials did not include patients in whom renal artery stents were placed.

Since PTRA/S techniques are widely used over the last decade, predictive factors of long-term survival of these patients are also defined (21). In a very recent study by Bates et al. increased mortality was found to be associated with comorbid chronic obstructive pulmonary disease and congestive heart failure. Baseline azotemia was found to be the strongest independent predictor of all cause mortality (21).

In the current study we found that in patients with moderate to severe renal impairment (EGFR ≤59 mL/min), 29% demonstrated deterioration in EGFR within the mean duration of 9.3 months. This finding emphasizes that there was a subgroup of patients who did not benefit from the stenting procedure. Nearly one third of patients with impaired renal function had further deterioration, which makes us think that this might not be a good therapeutic option for these patients. The lack of instances where the stenting procedure resulted in acute problems such that would require emergency surgery suggests that it, per se, did not cause an accelerated decline in renal function in the acute setting.

Limitations of the study

This retrospective chart review includes limitations inherent to such studies. Blood pressure recordings were extracted from hospital records. The timing of clinical follow-up was not standardized and was left to the preference of the treating physician. The small number of patients (n=36) and inclusion of patients with both atherosclerotic disease and fibromuscular dysplasia in our study makes generalizing our results to larger patient populations difficult.

Conclusion

In conclusion, blood pressure is significantly lower after PTRA/S in patients with renovascular hypertension at a mean follow-up of 9.3 months. In these patients, estimated glomerular filtration rate was mainly preserved, especially in patients with impaired renal function. The benefits and complications of PTRA/S should be determined over a longer period of follow-up, so that patients and clinicians can have more accurate prognostic information for treatment decisions.

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References

1. Nordmann AJ, Woo K, Parkes R, Logan A. Balloon angioplasty or medical therapy for hypertensive patients with atherosclerotic renal artery stenosis? A meta-analysis of randomized controlled trials. Am J Med 2003; 114: 44-50.
2. Kaplan NM, Flynn JT. Kaplan's clinical hypertension. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.
3. Gruntzig A, Kuhlmann U, Vetter W, Lutolf U, Meier B, Siegenthaler W. Treatment of renovascular hypertension with percutaneous transluminal dilatation of a renal artery stenosis. Lancet 1978; 1: 801-2.
4. Ramos F, Kotliar C, Alvarez D, Baglivo H, Rafaelle P, Londero H, et al. Renal function and outcome of PTRA and stenting for atherosclerotic renal artery stenosis. Kidney Int 2003; 63: 276-82.
5. Sos TA, Pickering TG, Sniderman K, Saddekni S, Case DB, Silane MF, et al. Percutaneous transluminal renal angioplasty in

renovascular hypertension due to atheroma or fibromuscular dysplasia. N Engl J Med 1983; 309: 274-9.
6. Tegtmeyer CJ, Kellum CD, Ayers C. Percutaneous transluminal angioplasty of the renal artery. Results and long-term follow-up. Radiology 1984; 153: 77-84.
7. Dorros G, Prince C, Mathiak L. Stenting of a renal artery stenosis achieves better relief of the obstructive lesion than balloon angioplasty. Cathet Cardiovasc Diagn 1993; 29: 191-8.
8. Harden PN, Macleod MJ, Rodger RS, Baxter GM, Connell JM, Dominiczak AF, et al. Effect of renal-artery stenting on progression of renovascular renal failure. Lancet 1997; 349: 1133-6.
9. Beutler JJ, Van Ampting JM, Van De Ven PJ, Koomans HA, Beek FJ, Woittiez AJ, et al. Long-term effects of arterial stenting on kidney function for patients with ostial atherosclerotic renal artery stenosis and renal insufficiency. J Am Soc Nephrol 2001; 12: 1475-81.
10. Rocha-Singh KJ, Ahuja RK, Sung CH, Rutherford J. Long-term renal function preservation after renal artery stenting in patients with progressive ischemic nephropathy. Catheter Cardiovasc Interv 2002; 57: 135-41.
11. Arthurs Z, Starnes B, Cuadrado D, Sohn V, Cushner H, Andersen C. Renal artery stenting slows the rate of renal function decline. J Vasc Surg 2007; 45: 726-31.
12. Bates MC, Campbell JE, Broce M, Lavigne PS, Riley MA. Serum creatinine stabilization following renal artery stenting. Vasc Endovascular Surg 2008; 42: 40-6.
13. Horio M, Orita Y, Fukunaga M. Assessment of renal function. In: Johnson RJ, Feehally J, editors. Comprehensive Clinical Nephrology. 2nd ed. Spain: Elsevier Limited; 2003. p.27-34.
14. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976; 16: 31-41.
15. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. Am J Kidney Dis 2002; 39: 1-266.
16. Rocha-Singh KJ, Mishkel GJ, Katholi RE, Ligon RA, Armbruster JA, McShane KJ, et al. Clinical predictors of improved long-term blood pressure control after successful stenting of hypertensive patients with obstructive renal artery atherosclerosis. Catheter Cardiovasc Interv 1999; 47: 167-72.
17. Lederman RJ, Mendelsohn FO, Santos R, Phillips HR, Stack RS, Crowley JJ. Primary renal artery stenting: characteristics and outcomes after 363 procedures. Am Heart J 2001; 142: 314-23.
18. Kashyap VS, Sepulveda RN, Bena JF, Nally JV, Poggio ED, Greenberg RK, et al. The management of renal artery atherosclerosis for renal salvage: does stenting help? J Vasc Surg 2007; 45: 101-8.
19. Zeller T, Frank U, Muller C, Burgelin K, Sinn L, Bestehorn HP, et al. Predictors of improved renal function after percutaneous stent-supported angioplasty of severe atherosclerotic ostial renal artery stenosis. Circulation 2003; 108: 2244-9.
20. Uder M, Humke U. Endovascular therapy of renal artery stenosis: where do we stand today? Cardiovasc Intervent Radiol 2005; 28: 139-47.
21. Bates MC, Campbell JE, Stone PA, Jaff MR, Broce M, Lavigne PS. Factors affecting long-term survival following renal artery stenting. Catheter Cardiovasc Interv 2007; 69: 1037-43.