Original Article

Decrease of Glomerular Filtration Rate may be Attributed to the Microcirculation Damage in Renal Artery Stenosis

Yao-Jian Dong, Cheng Huang, De-Mou Luo, Jing-Guang Ye, Jun-Qing Yang, Guang Li, Jian-Fang Luo, Ying-Ling Zhou

Department of Cardiology, Guangdong Cardiovascular Institute, Guangdong General Hospital, Guangdong Academy of Medical Sciences, Guangzhou 510100, China

Abstract

Background: The decrease of glomerular filtration rate has been theoretically supposed to be the result of low perfusion in renal artery stenosis (RAS). But the gap between artery stenosis and the glomerular filtration ability is still unclear.

Methods: Patients with selective renal artery angiogram were divided by the degree of renal artery narrowing, level of estimated glomerular filtration rate (eGFR), respectively. The different levels of eGFR, renal microcirculation markers, and RAS severity were compared with each other, to determine the relationships among them.

Results: A total of 215 consecutive patients were enrolled in the prospective cohort study. Concentrations of microcirculation markers had no significant difference between RAS group (RAS ≥ 50%) and no RAS group (RAS < 50%) or did not change correspondingly to RAS severity. The value of eGFR in RAS group was lower than that in the no RAS group, but it did not decline parallel to the progressive severity of RAS. The microcirculation markers presented integral difference if grouped by different eGFR level with negative tendency, especially that plasma cystatin C (cysC) and urinary microalbumin to creatinine ratio (mACR) increased with the deterioration of eGFR, with strong ($r = -0.713$, $P < 0.001$) and moderate ($r = -0.580$, $P < 0.001$) correlations. In the subgroup analysis of severe RAS (RAS ≥ 80%), the levels of plasma cysC and urinary mACR demonstrated stronger negative associations with eGFR, ($r = -0.827$, $P < 0.001$) and ($r = -0.672$, $P < 0.001$) correlations, respectively.

Conclusions: Severity of RAS could not accurately predict the value of eGFR, whereas microcirculation impairment may substantially contribute to the glomerular filtration loss in patients with RAS.

Key words: Glomerular Filtration Rate; Renal Artery Stenosis; Renal Microcirculation

Introduction

Currently, the golden standard investigation of renal artery stenosis (RAS) remains catheter selective angiography, as it provides visually anatomical information of artery trunk, an assessment of renal perfusion and the option of measuring the pressure gradient across the functional significance of the lesion. The decrease of glomerular filtration rate has been theoretically thought to be the result of low perfusion in RAS. But angiography has been proven insensitive by means of defining which moderate artery stenosis is hemodynamically significant in renal studies. And the gap between artery stenosis and the glomerular filtration ability is unclear. The severity of atherosclerotic renal artery narrowing has little correlation with blood flow, kidney function, and renal structural damage.[1-3] The essential renal impairment depends on the degree of renal parenchyma microcirculation damage. However, the relationships among anatomically stenosis of renal artery, estimated glomerular filtration rate (eGFR), and microcirculation function status are still unknown. The present study aimed to lineate counter relations about the anatomy, eGFR, and microcirculation in RAS disease and explores the gap between them.

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.152483

Methods

Patients

A single-center prospective cohort study with retrospectively analyzed was conducted. A total of 215 consecutive patients were enrolled by catheter selective angiography of renal artery and coronary simultaneously during October 2013 to September 2014. Peripheral venous blood samples and urine samples were collected and analyzed before the catheter intervention. The coronary and renal arteries patency was assessed by two independent investigators, blinded for laboratory data. eGFR, $ml \cdot min^{-1} \cdot 1.73\ m^{-2}$ was calculated by the Cockroft–Gault formula for renal function assessment. The concentrations of serum β2-microglobulin (β2-MG),

Address for correspondence: Dr. Ying-Ling Zhou, Department of Cardiology, Guangdong Cardiovascular Institute, Guangdong General Hospital, Guangdong Academy of Medical Sciences, Guangzhou 510100, China
E-Mail: donghaojian@sina.com

urinary β2-MG, cystatin C (cysC), uric acid (UA), and urinary microalbumin to creatinine ratio (mACR) were collected as the markers for renal microcirculation function. Patients were divided by the degree of renal artery anatomic narrowing and level of eGFR, respectively. The levels of microcirculation markers mentioned above were compared with each other in different groups. Written informed consent was obtained from all recruited participants, and this study protocol was approved by the local Ethics Committee.

- For men: eGFR = ([140 − age] × body weight)/(serum creatinine concentration [mg/dL] ×72)
- For women: eGFR = ([140 − age] × body weight)/(serum creatinine concentration [mg/dL] ×72) ×0.85.

Intervention procedure

Renal artery and coronary selective angiography was performed by femoral or radial artery approach. Heparin was infused to achieve an activated clotting time of at least 200s during the procedure. And the angiographic procedure was finished with Juckins left and right catheters or multi-purpose catheter. Coronary and RAS was measured as the percentage of decrease in luminal diameter. Coronary significant stenosis was defined and confirmed in two vertical views: >40% narrowing for left main coronary artery and >70% narrowing for other main branches. The presence of a renal artery significant stenosis was defined as having a stenosis ≥50%, criteria from the stenting in renal dysfunction caused by atherosclerotic RAS.[4] Further, according to laboratory and clinical researches of RAS,[5,6] patients would be graded as severe lesion (RAS ≥ 80%), moderate lesion (50%≤RAS < 80%), mild lesion (50%>RAS > 0), and normal artery (RAS = 0), respectively.

Statistical analysis

Statistical analyses were performed using SPSS version 13.0 (SPSS Inc., USA) for windows software. The descriptive data are expressed as means ± standard deviation. Differences between groups were calculated by Student's *t*-test for continuous variables, and Chi-square test was used to assess differences in categorical variables. The differences between groups were analyzed using analysis of variance. The power of relations between was assessed by Spearman's rank correlation method. Probability values of <0.05 were considered statistically significant.

Results

Clinical characteristics

Baseline demographic, clinical and laboratory characteristics of the patients, divided up by the presence or absence of RAS, are provided in Table 1. The overall prevalence of RAS in the present population was 38.6%, with an average stenotic rate (77.28% ± 16.01%). The distribution of triple vessel coronary disease was not significantly different between RAS group and no RAS group (31.3% vs. 45.5%, $P = 0.108$). Majority (96.4%) of RAS group patients had a history of hypertension, which was much markedly more than no RAS group ones. Left ventricular ejection fraction by echo in RAS group was also higher, while the value of N-terminal of the prohormone brain natriuretic peptide did not differ significantly between two groups. Prevalence of chronic renal dysfunction (eGFR < 60 ml·min^{-1}·1.73 m^{-2}) was more common in the RAS group than that in the other one. In terms of the renal microcirculation function status, the levels of serum and urinary β2-MG, cysC, UA and urinary mACR did not present statistical difference between RAS group versus no RAS group.

Renal microcirculation function and renal artery stenosis severity

Divided by stenotic degree of renal artery, the overall prevalence of different RAS severity was 28.4% (61/215)

Table 1: Clinical characteristics of the patients with and without significant RAS

Variables	RAS (RAS ≥ 50%) (n = 83)	No RAS (RAS < 50%) (n = 132)	Total (n = 215)	*T*	*P*
Age (years)	69.51 ± 8.95	64.63 ± 11.21	66.55 ± 10.62	2.859	0.005
Male, *n* (%)	46 (55.4)	93 (70.5)	139 (64.7)	3.386	0.066
Triple coronary vessel disease, *n* (%)	26 (31.3)	60 (45.5)	86 (40.0)	6.083	0.108
Bilateral RAS, *n* (%)	21 (25.3)	–	–	–	–
Stenosis rate of renal artery (%)	77.28 ± 16.01	–	–	–	–
eGFR (min^{-1}·1.73 m^{-2})	48.63 ± 24.94	59.36 ± 27.40	55.14 ± 26.90	−2.466	0.015
Chronic renal dysfunction (eGFR<60 ml· min^{-1}· 1.73 m^{-2}), *n* (%)	61 (73.5)	74 (56.1)	135 (62.8)	4.810	0.028
Hypertension, *n* (%)	80 (96.4)	100 (75.8)	180 (83.7)	12.278	0.000
Diabetes mellitus, *n* (%)	34 (41.0)	55 (41.7)	89 (41.4)	0.004	0.95
LVEF (%)	61.79 ± 11.36	57.03 ± 12.68	58.90 ± 12.36	2.374	0.019
NT-pro BNP (pg/ml)	1629 ± 4187.43	2156.57 ± 4547.03	1949.22 ± 4402.75	−0.727	0.469
Serum β2-MG (mg/L)	3.43 ± 2.67	3.05 ± 1.88	3.20 ± 2.22	1.018	0.310
Urinary β2-MG (mg/L)	4.11 ± 10.09	3.21 ± 8.09	3.56 ± 8.90	0.607	0.545
CysC (mg/L)	1.36 ± 0.85	1.31 ± 0.59	1.33 ± 0.70	0.428	0.669
UA (μmol/L)	411.24 ± 124.57	394.43 ± 121.52	401.04 ± 122.60	0.834	0.406
Urinary mACR (mg/gCr)	157.16 ± 304.68	159.47 ± 441.33	158.56 ± 392.16	−0.036	0.972

LVEF: Left ventricular ejection fraction; β2-MG: β2-microglobulin; CysC: Cystatin C; UA: Uric acid; Urinary mACR: Urinary microalbumin to creatinine ratio; RAS: Renal artery stenosis; eGFR: Estimated glomerular filtration rate; NT-pro BNP: N-terminal of the prohormone brain natriuretic peptide.

with severe lesion (RAS ≥ 80%), 10.2% (22/215) with moderate lesion (50% ≤ RAS < 80%), 24.2% (52/215) with mild lesion (50% > RAS > 0), and 37.2% (80/215) with normal artery (RAS = 0), respectively. The level of serum β2-MG in severe group was higher than those in the normal artery group (RAS = 0) ($P = 0.011$), with a weak positive associations to the severity of RAS ($r = 0.172$, $P < 0.05$), but it did not differ significantly in the three groups once lesions existed. Although they also lineated a positive relation trend, urinary mACR and other indexes of the microcirculation function did not make significantly variable no matter how the severity of RAS was Table 2.

Renal microcirculation function and estimated glomerular filtration rate level

Patients were grouped by eGFR into different renal functions status [Table 3]. More than half of the overall patients (62.8%, 135/215) had chronic renal dysfunction (eGFR < 60 ml·min^{-1}·1.73 m^{-2}). The microcirculation markers mentioned above presented integral difference between normal function group (eGFR ≥ 90 ml·min^{-1}·1.73 m^{-2}) versus severe dysfunction group (eGFR < 30 ml·min^{-1}·1.73 m^{-2}). The values of microcirculation markers, however, were not significantly different between patients with normal (eGFR ≥ 90 ml·min^{-1}·1.73 m^{-2}) and mild (90 > eGFR ≥ 60 ml·min^{-1}·1.73 m^{-2}) impairment of renal function. The concentrations of urinary mACR and cysC increased with the deterioration of eGFR, with which they had moderate ($r = -0.580$, $P < 0.001$) and strong ($r = -0.713$, $P < 0.001$) correlations, respectively. In the subgroup analysis of patients with severe RAS (RAS ≥ 80%), all the microcirculation markers had significantly negative relation with eGFR level. Among them, levels of plasma cysC and urinary mACR demonstrated even stronger negative associations with eGFR, ($r = -0.827$, $P < 0.001$) and ($r = -0.672$, $P < 0.001$) correlations, respectively [Table 4].

Table 2: Renal microcirculation markers in different RAS severity

Variables	RAS ≥ 80% (n = 61)	50% ≤ RAS < 80% (n = 22)	0 < RAS < 50% (n = 52)	RAS = 0 (n = 80)	Statistical value H	P
Serum β2-MG (mg/L)	3.93 ± 3.20*	2.59 ± 0.88*,†	2.87 ± 1.60*,†	3.09 ± 1.95†	11.23	0.011
Urinary β2-MG (mg/L)	5.10 ± 12.14	2.48 ± 4.74	5.42 ± 13.79	2.59 ± 5.65	4.68	0.196
CysC (mg/L)	1.54 ± 1.02	1.07 ± 0.29	1.34 ± 0.58	1.30 ± 0.59	4.85	0.183
UA (μmol/L)	419.57 ± 130.99	400.75 ± 116.25	374.87 ± 97.23	398.73 ± 126.77	1.136	0.768
Urinary mACR (mg/gCr)	167.15 ± 322.17	146.93 ± 284.47	147.88 ± 245.78	160.47 ± 479.13	0.018	0.997

RAS: Renal artery stenosis; β2-MG: β2-microglobulin; CysC: Cystatin C; UA: Uric acid; Urinary mACR: Urinary microalbumin to creatinine ratio. Superscript letters *,† stand for a subset of the column group; different letter meant statistically different statistic values between groups, no statistical difference between with the same letter.

Table 3: Renal microcirculation markers in different levels of eGFR in the total population

Variables	eGFR ≥ 90 ml·min^{-1}·1.73 m^{-2} (n = 25)	90 > eGFR ≥ 60 ml·min^{-1}·1.73 m^{-2} (n = 54)	60 > eGFR ≥ 30 ml·min^{-1}·1.73 m^{-2} (n = 99)	eGFR < 30 ml·min^{-1}·1.73 m^{-2} (n = 37)	Statistical value H	P
Serum β2-MG (mg/L)	2.15 ± 0.53*	2.26 ± 0.73*	3.18 ± 1.29†	5.39 ± 4.17‡	15.474	0.000
Urinary β2-MG (mg/L)	0.77 ± 0.58*	1.63 ± 4.03*	3.31 ± 8.10*	9.07 ± 15.28†	4.877	0.003
CysC (mg/L)	0.84 ± 0.21*	0.95 ± 0.19*	1.33 ± 0.42†	2.23 ± 1.10‡	34.936	0.000
UA (μmol/L)	320.99 ± 107.59*	373.13 ± 127.52*,†	414.21 ± 109.41†,‡	461.89 ± 125.79‡	6.218	0.001
Urinary mACR (mg/gCr)	16.77 ± 20.28*	69.58 ± 179.15*	164.92 ± 350.53*,†	372.57 ± 689.02†	4.301	0.006

eGFR: Estimated glomerular filtration rate; β2-MG: β2-microglobulin; CysC: Cystatin C; UA: Uric acid; Urinary mACR: Urinary microalbumin to creatinine ratio. Superscript letters *, †, ‡ stand for a subset of the column group; different letter meant statistically different statistic values between groups, no statistical difference between with the same letter.

Table 4: Renal microcirculation markers in different levels of eGFR in severe RAS (RAS ≥ 80%)

Variables	eGFR ≥ 90 ml·min^{-1}·1.73 m^{-2} (n = 5)	90 > eGFR ≥ 60 ml·min^{-1}·1.73 m^{-2} (n = 12)	60 > eGFR ≥ 30 ml·min^{-1}·1.73 m^{-2} (n = 28)	eGFR < 30 ml·min^{-1}·1.73 m^{-2} (n = 16)	Statistical value H	P
Serum β2-MG (mg/L)	1.82 ± 1.03*	2.16 ± 0.96*	4.32 ± 0.59†	7.39 ± 3.84‡	18.519	0.000
Urinary β2-MG (mg/L)	1.91 ± 0.74*	2.98 ± 3.23*	6.64 ± 4.18†	15.43 ± 15.28†	9.649	0.000
CysC (mg/L)	0.92 ± 0.13*	1.34 ± 0.18†	2.22 ± 0.57‡	3.23 ± 0.76§	28.749	0.000
UA (umol/L)	356.47 ± 95.11*	388.63 ± 131.49*	436.26 ± 116.31†	543.84 ± 123.19‡	7.361	0.000
Urinary mACR (mg/gCr)	32.57 ± 18.39*	102.71 ± 72.35†	384.13 ± 293.66‡	548.96 ± 423.68§	11.873	0.000

β2-MG: β2-microglobulin; CysC: Cystatin C; UA: Uric acid; Urinary mACR: Urinary microalbumin to creatinine ratio; eGFR: Estimated glomerular filtration rate; RAS: Renal artery stenosis. Superscript letters *, †, ‡, § stand for a subset of the column group; different letter meant statistically different statistic values between groups, no statistical difference between with the same letter.

Severity of renal artery stenosis and renal function

The level of eGFR in RAS ≥ 80% group was significantly more impaired than that in the normal artery group (RAS = 0) (44.50 ± 27.88 vs. 60.09 ± 28.17 ml·min·1.73 m^{-2}, $P = 0.011$). And eGFR value did not have a significant difference in other groups comparisons, which indicated a weak negative associations between eGFR level and severity of RAS ($r = -0.234$, $P < 0.001$) [Figure 1].

Discussion

Our study demonstrates that the stenotic extent of renal artery trunk, which was the golden diagnostic standard for RAS, was not that strongly related to the renal function impairment as theoretically conceived. The renal microcirculation markers presented as connection with RAS severity and renal function. Severity of microvascular damage and loss may determine the frontier before eGFR by promoting the progression of renal functional and structural damage.

The renal microcirculation has unique anatomical and functional characteristics. The renal artery small branching order afferent arterioles lead to the glomerular capillaries and the distal ends of the capillaries of each glomerulus join together to form the efferent arterioles, followed by a second capillary network constituted by the peritubular capillaries surrounding renal tubules.[7] The changes in tone in afferent and efferent arterioles and glomerular capillary pressure are the main determinants of GFR. The decrease in the availability of small vessels in the kidney can transiently or permanently deteriorate renal blood flow, glomerular filtration ability, and tubular function, which was suggested as a possible starting point of RAS.[8-10]

The reduction in renal perfusion attributable to RAS was acknowledged to be the essential cause of ischemic renal disease. Nevertheless, the results of revascularization of RAS were disconcerting that resolution of hypertension and mainly, improvements in renal function are still at best modest. The difficulty lies in that a high degree of stenosis may not correlate with deteriorative renal function or deserve refractory hypertension.[11,12] And reasons for this gap between the success rate and outcomes are mainly in the microvascular disease and parenchyma damage distal to the stenosis. In addition to diagnosis confirmed, it could be more important to interpret the "significant" and "reversible" RAS, including the complex relation between anatomy and function

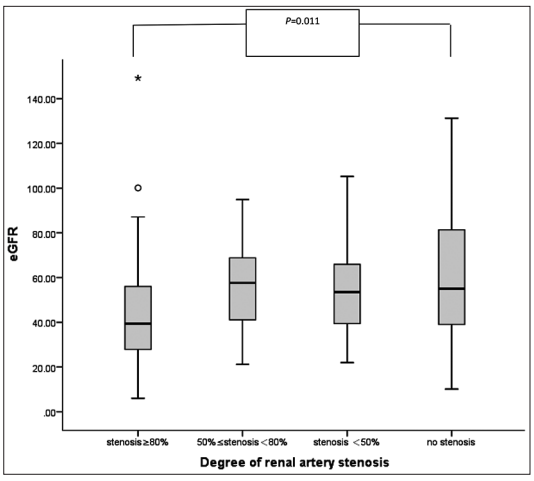

Figure 1: Comparison of estimated glomerular filtration rate in patients divided by increasing severity of renal artery stenosis.

Although one could hypothesize that RAS would be associated with lower perfusion and more severe renal function impairment, we found only a weak negative association between eGFR level and severity of RAS in the study. Since GFR is determined by both renal blood flow and glomerular capillary hydrostatic pressure, the severity of RAS displayed only weak association with eGFR. The rising systemic blood pressure triggered by renin-angiotensin-aldosterone system could compensate the hemodynamic effects of stenotic lesions, regulation of afferent, and efferent arteriole could temporary maintain the glomerular filtration ability, not every RAS would then lead in renal ischemia and influence the eGFR result. Resolution of the stenosis did not always recover renal function, which had been observed in human and experimental studies.[13,14] For the overall population in the present study, all microcirculation markers presented variable degree of difference between normal function group versus severe dysfunction group, whereas not significant difference was observed between normal renal function group and mild renal dysfunction group. It indicated that in the early impairment of eGFR, the renal parenchyma loss was still limited, and RAS or the microvascular disease deserves aggressive treatment. The deterioration of eGFR may be reversed by the reconstruction of perfusion. However, in patients with moderately to severely impaired eGFR, microcirculation biomarkers would negatively correlate with eGFR. Furthermore, in the subgroup analysis of patients with severe RAS (RAS ≥ 80%), microcirculation biomarkers presented even more prominent negative association with all eGFR level, indicating the potential causal relationship between reduced glomerular filtration ability and microcirculation dysfunction in patients with RAS, especially for those with severe RAS. With the more severe stenotic lesion in renal artery, there would be more diffuse disease in the microvascular and more loss of the renal parenchyma.

Renal microvasculature remodeling and damage could directly compromise the perfusion of glomerulus and mesenchymal, leading to the glomerular sclerosis and interstitial fibrosis.[15,16] Functional abnormalities in the microcirculation of the renal parenchyma distal to the stenosis in RAS contribute to the pathophysiology of ischemic renal real injury.[17,18] Although assessment of the severity of RAS could be technically resolved with the use of the clinically available high-resolution imaging techniques (e.g., computed tomography angiography, selective angiography), the assessment and quantification of renal microcirculation

damage are, on the other hand, the most difficult problem to sort out. Stromski *et al*. had found out missing pulse steady state free precession as a powerful tool for the noninvasive measurement of slow fluid flows in different regions of the kidney about renal microcirculation,[19] while some laboratory indexes recently are adopted as the detection of microvasculature damage in renal microcirculation dysfunction, like 24 h microalbuminuria (mALB), transferrin, β2-MG, urinary retinal binding protein, urinary N-acety1-β-D-glucosamine, cysC, UA, and urinary mACR. Notably, all the microcirculation markers in our study had prominent elevation by increasing severity of eGFR. CysC is a new and promising biomarker for kidney microcirculation dysfunction. Because of its low molecular weight, cysC is freely filtered at the glomerulus and is almost completely reabsorbed and catabolized, but not secreted by tubular cells. The elevation of cysC concentration, not influenced by inflammation, age or sex, reflected the early decrease of glomerular filtration rate. Given these characteristics, cysC concentration may be superior to creatinine concentration in detecting renal function impairment. In the present study, the cysC could not differentiate the RAS group from no RAS group, but it showed a strong relation with eGFR. Meanwhile, the term mALB was coined to describe a small increase in the level of albumin of normal urine protein,[20] which represented the early impairment of endothelial function and renal microcirculation. Previous data had revealed that spot urinary mACR accurately reflects the total 24 h level of urine albumin excretion and the mACR has been shown to be superior to a 24 h urine collection in predicting renal events in patients with type 2 diabetes and nephropathy.[21,22] Likewise, mACR level was not significantly different in the RAS and no RAS group, the level of mACR, however, also had apparent relation to eGFR. Both of cysC and mACR indicated that microvascular disease was not absolutely parallel to the main trunk lesion, and the mere application of stenotic rate of renal artery could not accurately represent the real deterioration status. Microcirculation presented as the conjunction between the eGFR and RAS severity, adding more comprehensive information to the RAS.

Deterioration of the renal microcirculation in the chronically stenotic kidney could play a pivotal role in defining the "significant" RAS. The presence of functional microcirculation impairment may indeed represent the initial steps of renal injury. Beyond the stenotic degree of artery, serum cysC and urinary mACR emerged as compromising biomarkers in RAS systemic evaluation and could complement information for clinical management.

References

1. Mukherjee D. Renal artery revascularization: Is there a rationale to perform? JACC Cardiovasc Interv 2009;2:183-4.
2. Textor SC, Lerman LO. Reality and renovascular disease: When does renal artery stenosis warrant revascularization? Am J Kidney Dis 2014;63:175-7.
3. Lao D, Parasher PS, Cho KC, Yeghiazarians Y. Atherosclerotic renal artery stenosis – Diagnosis and treatment. Mayo Clin Proc 2011;86:649-57.
4. Bax L, Woittiez AJ, Kouwenberg HJ, Mali WP, Buskens E, Beek FJ, *et al.* Stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function: A randomized trial. Ann Intern Med 2009;150:840-8, W150.
5. Dieter RS. The functional assessment of renal artery stenosis. Expert Rev Cardiovasc Ther 2005;3:369-70.
6. Cooper CJ, Murphy TP, Cutlip DE, Jamerson K, Henrich W, Reid DM, *et al.* Stenting and medical therapy for atherosclerotic renal-artery stenosis. N Engl J Med 2014;370:13-22.
7. Chade AR. Renal vascular structure and rarefaction. Compr Physiol 2013;3:817-31.
8. Basile DP. Rarefaction of peritubular capillaries following ischemic acute renal failure: A potential factor predisposing to progressive nephropathy. Curr Opin Nephrol Hypertens 2004;13:1-7.
9. Bobik A. The structural basis of hypertension: Vascular remodelling, rarefaction and angiogenesis/arteriogenesis. J Hypertens 2005;23:1473-5.
10. Urbieta-Caceres VH, Syed FA, Lin J, Zhu XY, Jordan KL, Bell CC, *et al.* Age-dependent renal cortical microvascular loss in female mice. Am J Physiol Endocrinol Metab 2012;302:E979-86.
11. Dworkin LD, Murphy T. Is there any reason to stent atherosclerotic renal artery stenosis? Am J Kidney Dis 2010;56:259-63.
12. De Bruyne B, Manoharan G, Pijls NH, Verhamme K, Madaric J, Bartunek J, *et al.* Assessment of renal artery stenosis severity by pressure gradient measurements. J Am Coll Cardiol 2006;48:1851-5.
13. Textor SC, Wilcox CS. Renal artery stenosis: A common, treatable cause of renal failure? Annu Rev Med 2001;52:421-42.
14. Eirin A, Zhu XY, Urbieta-Caceres VH, Grande JP, Lerman A, Textor SC, *et al.* Persistent kidney dysfunction in swine renal artery stenosis correlates with outer cortical microvascular remodeling. Am J Physiol Renal Physiol 2011;300:F1394-401.
15. Pei F, Li XY, Fang Y, Shi HY, Diao HJ. Cardiac and renal arteriolar pathological changes in the autopsied elderly hypertensive patients with left ventricular hypertrophy (in Chinese). Chin J Cardio 2008;36:872-7.
16. Kang DH, Kanellis J, Hugo C, Truong L, Anderson S, Kerjaschki D, *et al.* Role of the microvascular endothelium in progressive renal disease. J Am Soc Nephrol 2002;13:806-16.
17. Futrakul N, Butthep P, Laohareungpanya N, Chaisuriya P, Ratanabanangkoon K. A defective angiogenesis in chronic kidney disease. Ren Fail 2008;30:215-7.
18. Prewitt RL, Chen II, Dowell R. Development of microvascular rarefaction in the spontaneously hypertensive rat. Am J Physiol 1982;243:H243-51.
19. Stromski ME, Brady HR, Gullans SR, Patz S. Application of missing pulse steady state free precession to the study of renal microcirculation. Magn Reson Med 1991;20:66-77.
20. Svendsen PA, Oxenbøll B, Christiansen JS. Microalbuminuria in diabetic patients – A longitudinal study. Acta Endocrinol Suppl (Copenh) 1981;242:53-4.
21. Lambers Heerspink HJ, Gansevoort RT, Brenner BM, Cooper ME, Parving HH, Shahinfar S, *et al.* Comparison of different measures of urinary protein excretion for prediction of renal events. J Am Soc Nephrol 2010;21:1355-60.
22. Price CP, Newall RG, Boyd JC. Use of protein: Creatinine ratio measurements on random urine samples for prediction of significant proteinuria: A systematic review. Clin Chem 2005;51:1577-86.

Received: 16-12-2014 **Edited by:** Yi Cui

How to cite this article: Dong YJ, Huang C, Luo DM, Ye JG, Yang JQ, Li G, Luo JF, Zhou YL. Decrease of Glomerular Filtration Rate may be Attributed to the Microcirculation Damage in Renal Artery Stenosis. Chin Med J 2015;128:750-4.

Source of Support: This work was supported by Guangdong Provincial Natural Scientific Grant for 2012 (No. S2012010009532). **Conflict of Interest:** None declared.