

The Value of Color Doppler Ultrasound in the Diagnosis of Atherosclerotic Renal Artery Stenosis

Yang Bai^{1, a}, Guanghong Han^{2, b}, Ying Sun^{1, c}, and Ying Xu^{3, d, *}

¹Department of Ultrasound, the First Hospital of Jilin University, Changchun 130021, China

²Department of Oral Geriatrics, School and Hospital of Stomatology, Jilin University, Changchun 130021, China

³Department of Nephrology, the First Hospital of Jilin University, Changchun 130021, China

^ay_bai@126.com, ^bhangh@jlu.edu.cn, ^cyingsunjdy@126.com, ^djlujdy@126.com

*Corresponding author

Keywords: angiography, renal artery stenosis, ultrasonography, atherosclerosis, ARAS, Doppler, renal artery obstruction

Abstract: Objective: To explore the diagnostic function of color Doppler ultrasonography for senile arteriosclerotic renal artery stenosis (RAS). Methods: We selected 85 patients suffered from atherosclerotic hypertension and analyze ultrasound parameters of renal artery, which include peak systolic velocity (PSV), end diastolic velocity (EDV), resistance index (RI), accelerate time (AT) and acceleration (AC). We calculated the PSV ratio of the renal artery to the abdominal aorta (RAR), the PSV ratio of the renal artery to the interleaf artery (RIR). Double blind method was used in this study and renal arteriography was used as the gold standard. Result: Color Doppler ultrasound is a useful diagnostic technique for atherosclerotic RAS. $PSV \geq 160$ cm/s, $RAR > 2.3$ is an indicator of stenosis $\geq 50\%$, while interlobular artery $AT > 0.07$ s suggests more than 75% of RAS.

1. Introduction

RAS is a morphological lesion, which refers to the narrowing of the inner diameter of the trunk or main branch of the renal artery due to various reasons, and the resulting hemodynamic changes. When the degree of stenosis is $\geq 60\%$, the hemodynamic changes in the kidney are obvious, which may induce hypertension, lead to accelerated deterioration of kidney function and the deterioration of renal function in turn aggravates the changes the internal environment, further aggravating the progression of renal artery disease [1], thus forming a vicious circle. In recent years, with the change of lifestyle and accelerated population aging, more and more people have atherosclerotic renal artery stenosis (ARAS). Currently, ARAS has gradually become the most common type of renal artery stenosis for about 70%, the causes of aortitis, fibrosis and dysplasia are relatively few. Previous studies by several scholars have suggested a close relationship between renal vascular stenosis and secondary hypertension, and have been widely recognized by clinicians. However, Wheatley K et al. [2] compared ARAS drug therapy with interventional therapy. Randomized controlled trials showed no significant differences in renal function improvement and hypertension control between the two groups. Textor.SC [3] and other studies on ARAS revascularization have shown that 25%-30% of patients have a certain degree of recovery of renal function, 19%-25% of patients' renal function is getting worse and worse, and other patients have no obvious changes. The difference in efficacy between different populations shows the complexity of pathophysiological changes after renal artery stenosis. Clinicians should understand the pathophysiology of ischemic nephropathy and the potential risk of vascular reconstruction in diffuse atherosclerotic disease. The complete regulatory mechanism remains to be studied. Therefore, the recanalization of renal artery stenosis remains a hot spot for clinicians. However, with the deep understanding of the renal endocrine function of ARAS patients in the past few decades, the function of renin - angiotensin - aldosterone system (RAAS) in

hypertension has been gradually affirmed. Atherosclerosis and renal vascular stenosis are the cause and effect of each other [4], so this study used renal angiography as the gold standard to explore the diagnostic value of Color Doppler ultrasound for ARAS, and analyzed the relevant parameters.

2. Materials and Methods

2.1 Object

From March 2014 to February 2016, 85 patients with hypertension and atherosclerotic disease in our hospital underwent renal angiography and renal artery color Doppler ultrasonography, excluding multiple Aortic arteritis, fibromuscular dysplasia, and renal artery stenosis caused by dissecting aneurysms. The patients were 40 to 82 years old, with an average of (63.52 ± 11.23) years old, 57 males and 28 females with serum creatinine (100.2 ± 38.6) $\mu\text{mol/L}$.

2.2 Equipment and methods:

Ultrasound and angiography examination were performed by the same operator, respectively, and the results of ultrasound and renal angiography were double-blind.

Renal artery CDFI examination: using GE logiq E9 color Doppler ultrasound system, convex array probe, frequency 2.8 ~ 5.0MHz. The sonographer has more than 10 years of work experience, and the number of cases of renal artery examination is more than 2000 cases per year. According to the specific conditions of each subject, select the appropriate probe frequency, adjust the focus area, wall filtering 50Hz ~ 200Hz, sampling volume 2 ~ 3mm, the angle between the sound beam and the direction of blood flow is less than 60° . The fasting was performed after 20:00 the day before examination, and an ultrasound examination was performed in the next morning. The patient is supine for 5 minutes to ensure that the heart rate and breathing are in a stable state, then take the supine or lateral position, measure the kidney diameter, and examine the abdominal aorta (AO), renal artery (RA) trunk, segmental artery, Interlobular artery and record the hemodynamic parameters. The location of the hemodynamic parameters was selected on the abdominal aorta, 10-20 mm from the distal end of the superior mesenteric artery; the renal artery is examined at the initial, middle and distal segments; the intrarenal artery is selected from the upper part of the kidney, the lower part and the middle part, and the resistance index was calculated from three places [5, 6]. Hemodynamic parameters including PSV, EDV, RI, AT, AC, and calculation of renal artery PSV and renal artery horizontal segment Arterial PSV ratio (RAR) and renal artery trunk PSV to intertrochanteric artery PSV ratio (RIR).

Renal angiography: selective or non-selective renal angiography via femoral artery puncture. The contrast agent was selected for Omnipaque, the injection speed was 15 ml/s, the dose was 25-30 ml, and the recording frame was 25 p/s. According to the degree of reduction of renal artery diameter, they were divided into 4 groups: group1: stenosis degree 0~49%, groups2: stenosis degree 50%~74%, groups3: stenosis degree 75%~99% and group4: stenosis degree 100% completely occluded.

3. Statistical Analysis

We used SPSS 19.0 software for data aggregation analysis, drawn ROC curves and evaluate the differences in hemodynamic parameters in the diagnosis of stenosis. The measurement data were expressed as $m \pm sd$, the statistical methods were analyzed by one-way ANOVA and non-parametric tests. Rank sum test.

4. Result

1) Renal angiography results: 85 patients, a total of 170 kidneys, congenital developmental abnormalities of the kidney and renal artery dysplasia are not included in this study. There are 121 branches in group 1, 24 branches in groups 2, 20 branches in groups 3, and 5 branches in groups 4.

There were 42 patients diagnosed with renal artery stenosis $\geq 50\%$ (27 males and 15 females), in which 35 persons with unilateral and 7 patients with bilateral stenosis. In the 49 stenotic arteries, 25 stenosis on the right side, 24 stenosis on the left side. The lesion is located in the initial segment of 42, in the middle segment of 2, and occlusion in 5 branches. There were no significant differences in age, gender, and renal function between stenotic and non-stenotic patients.

2) CDFI examination Results: The success rate of CDFI examination was 96.5% (164/170), and 6 renal arteries were from 3 male subjects, which were not detected due to obesity. According to the group determined by renal angiography, the measurement parameters (PSV, EDV, RI, AC, RA R, RIR) between the groups were compared.

In the parameters of PSV, EDV, RAR and RIR of renal artery, significant differences were found between group 1 and 2, between 1 and 3 respectively ($P < 0.05$); There was a significant difference in RI PSV, AT, AC of intrarenal artery between groups 3 and 1, the group 3 and 2, respectively ($P < 0.05$), (Table 1). The diameter stenosis rate $\geq 50\%$ was used as the threshold for RAS, and the ROC curve was made for the parameters with different parameters, thereby screening out the index for diagnosing the stenosis degree of ARAS $\geq 50\%$ (Table 2). The diameter stenosis rate $\geq 75\%$ was used as the standard for RAS, and the ROC curve was used to distinguish the parameters between the groups, thereby screening out the index for diagnosing ARAS stenosis $\geq 75\%$ (Table 3).

Table.1. Stenosis grouping and comparison of parameters between groups

Stenosis grouping	number	Renal artery				Interlobe artery			
		PSV	EDV	RAR	RIR	PSV	RI	AC	AT
Group 1	121	80.80±30.01	39.87±11.23	1.83±0.39	3.21±1.42	27.35±5.12	0.73±0.09	3.60±1.42	0.05±0.01
Group 2	24	174.96±50.23	58.76±30.23	2.90±0.84	8.05±2.34	25.25±8.14	0.74±0.07	3.45±1.80	0.07±0.03
Group 3	20	236.05±88.76	98.87±53.21	3.72±1.43	15.88±8.12	20.14±10.11	0.64±0.07	1.52±1.73	0.14±0.07
Group 4	5	-----	-----	-----	-----	-----	-----	-----	-----

Note: group 1 stenosis degree 0~49%, group 2 stenosis degree 50%~74%, group 3 stenosis degree 75%~99% and group 4 100% complete occlusion; PSV: peak systolic flow velocity; EDV: end diastolic velocity; AT: acceleration time; AC: acceleration; RI: resistance index; RAR: ratio of peak flow velocity of renal artery to abdominal aorta during systole; RIR: ratio of peak velocity of systolic phase of renal artery to interlobular artery. Comparison between groups in each group, $P < 0.01$

Table.2. Area under the ROC curve with a diameter stenosis rate $\geq 50\%$

parameter	Area under the ROC curve	95% confidence interval
PSV ≥ 160 cm/s	0.945	0.912~0.978
RAR ≥ 2.3	0.939	0.909~0.969
RIR ≥ 5.5	0.912	0.871~0.953
AT ≥ 0.07 s	0.652	0.554~0.750
RI ≤ 0.67	0.741	0.651~0.831

Table.3. Area under the ROC curve with a diameter stenosis rate $\geq 75\%$

parameter	Area under the ROC curve	95% confidence interval
PSV ≥ 190 cm/s	0.948	0.921~0.975
AT ≥ 0.07 s	0.942	0.913~0.971
RI ≤ 0.60	0.801	0.736~0.866

5. Discussion

ARAS often occurs in the elderly, and research [7] shows that the prevalence of ARAS in older people over 65 years old is greater than 7%. ARAS is a progressive disease, Because of its occult and potential hazards, early diagnosis of ARAS, timely and effective treatment have important clinical significance for improving patients' quality of life and prognosis. Although renal angiography is regarded as the gold standard for the diagnosis of RAS, its clinical application has

been limited due to its invasive and expensive. Therefore, finding a simple and non-invasive inspection method has always been a topic of concern. In 1984, Norris CS et al first used PSV as a diagnostic criteria for RAS \geq 60% (sensitivity 83%, specificity 97%) [[8]. Two years later, Kohler TR [9] used RAR \geq 3.5 as threshold of RAS \geq 60% (sensitivity 91%, specificity 95%). Hoffmann et al [10] used the PSV (\geq 180cm/s) of the renal artery as the threshold for the stenotic renal artery, the diagnostic sensitivity reached 95%, and the specificity was 90 %. In the hemodynamic analysis, when the diameter of renal arteriosclerosis reaches 60%, the blood flow begins to decrease, and the hemodynamic changes begin to have clinical significance. So the diagnosis of severe RAS is essential in order to take effective treatment. Some scholars have proposed that the imaging diagnosis methods including Doppler ultrasound and angiography examination have over-diagnosis for the RAS [11].

In this study, the trend of research related to international peers is similar, but the results of this study are low, with PSV and RAR being the most obvious. This may be related to the age composition of the subject and the type of clinical disease. This study is a patient with ARAS, the age is older, the average age is 63.52 years, and the youngest is 40 years old. The heart pump function gradually decreases. Increased blood viscosity, arteriosclerosis further aggravated hemodynamic resistance, ARAR patients often combined with atrial fibrillation, resulting in spectral amplitude fluctuations. Therefore, compared with the experimental results of aortic inflammation and fibromuscular dysplasia as the main research object [12], the assignment of PSV and RAR is relatively low. The threshold of renal artery PSV \geq 160cm/s, the sensitivity was 85.2%, the specificity was 94.3%, and the threshold of renal artery PSV \geq 190cm/s, the sensitivity was 66.1% and specificity was 9.63%. The results of this study are similar to those of previous scholars [13, 14].

In this study, RAR \geq 2.3 was used as the threshold, sensitivity was 80.1%, and specificity was 90.5%, in order to be more suitable as a screening index. We chose a lower threshold to increase sensitivity. However, when the abdominal aorta is extensively atherosclerotic and stenosis, the blood flow is turbulent, the spectral envelope is not smooth, and the abdominal aorta PSV is increased. At this time, the RAR will become smaller [15]. It is not appropriate to use RAR to analyze the kidney blood flow and the degree of stenosis.

AT predicts non-severe stenosis, the effect is not ideal, the area under the ROC curve is 0.625, which may be related to the factors of small slow wave, such as the degree of RAS, the resistance of distal vascular segment, vascular compliance, age and renal artery, etc. related. According to the mechanism of small slow wave, the resistance of the stenotic artery and vascular compliance are the main factors affecting the small slow wave in the case of constant arterial pressure in the stenosis. The better the compliance of the downstream blood vessels, the lower the index RI. The more obvious the change of slow wave [14]. The intrarenal artery of ARAS usually has higher resistance and poor compliance, and its small slow wave is not as obvious as non-atherosclerotic RAS [16] and it is believed that the use of intrarenal hemodynamics alone will increase the false negative rate of diagnosis.

When ARAS \geq 75% stenosis, the phenomenon of Tardus-Parvus waveform appears in the kidney [17], because the obvious stenosis affects the hemodynamic state, causing the vascular pressure of the stenosis to decrease, and the pulsation characteristics of the blood flow are weakened, according to The formula $R = 8\eta L/\pi r^4$, the blood vessel radius is reduced by 50%, the blood flow resistance will be increased by 16 times, the length of the stenosis segment is doubled, and the resistance will be doubled, so in the case of severe RAS and long segment stenosis, the blood flow resistance will increase significantly, the pulsation will be weakened, and the typical Tardus-Parvus waveform phenomenon will appear. The increase of blood flow in the stenosis segment is not obvious, so when the renal artery color Doppler ultrasonography is used to detect RAS, especially for suspected severe RAS, it's not possible to rely solely on the renal artery blood flow velocity to make a diagnosis, but at the same time combine its changes in spectrum morphology and intrarenal indicators. Among the Tardus-Parvus waveform related parameters, the intersegmental artery AT is the most stable and reliable. Statistical analysis showed that the area under the ROC curve of the inter-arterial artery was 0.942, which was better than the AC, PSV and RI of the inter-arterial artery. Although RI has a

certain predictive value, it is often difficult to measure accurately, RI was affected by factors such as low flow rate, weak pulsation, and changes in spectral envelope burr-like changes. The authors believe that ARAS, especially for the patients with impaired renal function, RI application is limited.

6. Summary

Color Doppler ultrasound is suitable as a method for atherosclerotic RAS screening. Asian human body type is significantly thinner than Westerners, and the renal artery display rate is correspondingly improved. PSV is well displayed in the case of renal artery. ≥ 160 cm / s, RAR > 2.3 is an indicator of stenosis $\geq 50\%$, while inter-arterial artery AT > 0.07 s suggests more than 75% of renal artery stenosis.

Acknowledgements

This study was supported by the Finance Department of Jilin Province (Application of Contrast-Enhanced Ultrasound in the Diagnosis of Renal Artery Stenosis and Evaluation of Hemodynamic Changes in Patients with Vena Cava Obstructive Budd-Chiari Syndrome by Contrast-Enhanced Ultrasound).

* Correspondence to: Dr. Ying Xu, Department of Nephrology, the First Hospital of Jilin University, No. 71, Xinmin Street, Changchun 130021, Jilin Province, China E-mail: jlujdy@126.com

References

- [1] Chade AR, Lerman A, Lerman LO. Kidney in early atherosclerosis. *Hypertension*. 2005. 45 (6): 1042-9.
- [2] Wheatley K, Ives N, Gray R, et al. Revascularization versus medical therapy for renal-artery stenosis. *N Engl J Med*. 2009. 361 (20): 1953-62.
- [3] Textor SC. Ischemic nephropathy: where are we now. *J Am Soc Nephrol*. 2004. 15 (8): 1974-82.
- [4] Fava C, Minuz P, Patrignani P, Morganti A. Renal artery stenosis and accelerated atherosclerosis: which comes first. *J Hypertens*. 2006. 24 (9): 1687-96.
- [5] Malatino LS, Polizzi G, Garozzo M, et al. Diagnosis of renovascular disease by extra- and intrarenal Doppler parameters. *Angiology*. 1998. 49 (9): 707-21.
- [6] Krumme B, Blum U, Schwertfeger E, et al. Diagnosis of renovascular disease by intra- and extrarenal Doppler scanning. *Kidney Int*. 1996. 50 (4): 1288-92.
- [7] Hansen KJ, Edwards MS, Craven TE, et al. Prevalence of renovascular disease in the elderly: a population-based study. *J Vasc Surg*. 2002. 36 (3): 443-51.
- [8] Norris CS, Pfeiffer JS, Rittgers SE, Barnes RW. Noninvasive evaluation of renal artery stenosis and renovascular resistance. Experimental and clinical studies. *J Vasc Surg*. 1984. 1 (1): 192-201.
- [9] Kohler TR, Zierler RE, Martin RL, et al. Noninvasive diagnosis of renal artery stenosis by ultrasonic duplex scanning. *J Vasc Surg*. 1986. 4 (5): 450-6.
- [10] Hoffmann U, Edwards JM, Carter S, et al. Role of duplex scanning for the detection of atherosclerotic renal artery disease. *Kidney Int*. 1991. 39 (6): 1232-9.
- [11] Drieghe B, Madaric J, Sarno G, et al. Assessment of renal artery stenosis: side-by-side comparison of angiography and duplex ultrasound with pressure gradient measurements. *Eur Heart J*. 2008. 29 (4): 517-24.

- [12] Chaudhry MA, Latif F. Takayasu's arteritis and its role in causing renal artery stenosis. *Am J Med Sci.* 2013. 346 (4): 314-8.
- [13] Hélénon O, el RF, Correas JM, et al. Color Doppler US of renovascular disease in native kidneys. *Radiographics.* 1995. 15 (4): 833-54; discussion 854-65.
- [14] Conkbayir I, Yücesoy C, Edgüer T, Yanik B, Yaşar AU, Hekimoğlu B. Doppler sonography in renal artery stenosis. An evaluation of intrarenal and extrarenal imaging parameters. *Clin Imaging.* 2003. 27 (4): 256-60.
- [15] Soares GM, Murphy TP, Singha MS, Parada A, Jaff M. Renal artery duplex ultrasonography as a screening and surveillance tool to detect renal artery stenosis: a comparison with current reference standard imaging. *J Ultrasound Med.* 2006. 25 (3): 293-8.
- [16] Demirpolat G, Ozbek SS, Parildar M, Oran I, Memiş A. Reliability of intrarenal Doppler sonographic parameters of renal artery stenosis. *J Clin Ultrasound.* 2003. 31 (7): 346-51.
- [17] Kotval PS. Doppler waveform parvus and tardus. A sign of proximal flow obstruction. *J Ultrasound Med.* 1989. 8 (8): 435-40.