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Original Article

Assessment of diagnostic value of a new Doppler index for renal artery stenosis and comparison with conventional methods

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Abstract: This study aimed to assess a new Doppler parameter for diagnosis of renal artery stenosis (RAS), the bilateral renal ratio (BRR). Fifty-nine patients with suspicion of RAS were evaluated. The BRR, defined as the ratio of renal artery peak systolic velocities between the affected side and healthy side, was measured, and its sensitivity and specificity were compared to those of four conventional parameters. The best cutoff value for the new BRR was 2.05 with a sensitivity of 98.1% and specificity of 99%. The new BRR exhibited significant improvement compared to conventional parameters and thus, is a useful index for more accurate diagnosis of RAS.

Keywords: Renal artery stenosis (RAS), color Doppler ultrasonography (CDUS), new Doppler index

Introduction

Renal artery stenosis (RAS) is one of the main causes of secondary high blood pressure, possibly accounting for 1% to 5% of all hypertension cases. RAS has a hidden onset; development is rapid and prognosis is poor, ultimately leading to end-stage kidney disease. Renovascular hypertension can be treated by surgical reconstruction with or without stenting. Early RAS responds to aggressive treatment that can help in correcting high blood pressure and protecting kidney function from damage. Hence, early diagnosis of RAS and differential diagnosis are particularly important [1].

There are three main types of RAS [2]: 1. Atherosclerotic RAS represents approximately 90% of cases and is commonly seen in older men. Most lesions occur at the proximal portion of the main renal artery. 2. Fibromuscular dysplasia involves not only damage to the renal artery, but also to the iliac artery, mesenteric artery, and head-arm arterial trunk and is most commonly seen in young women. 3. Takayasu arteritis leads to decreases in renal function in about 60% of cases, and 87% of the constriction in the renal artery is located at the beginning of the artery. This type of RAS is often seen in women around 30 years old.

Ultrasound examination is currently considered the primary diagnostic tool for RAS screening owing to its non-invasiveness, convenience, low cost, and repeatability [3]. It is difficult to have a unified diagnostic standard, and, therefore, a comprehensive analysis based on patient conditions is used to evaluate the findings.

Direct parameters obtained using ultrasonic diagnosis of RAS include the maximal renal artery peak systolic velocity (RPSV), the renal-aortic ratio (RAR), the renal-renal ratio (RRR), and the renal interlobar ratio (RIR). The bilateral renal ratio (BRR) is a new parameter measured by the direct Doppler method that is defined as the ratio of the RPSV on the stenotic side of the renal artery to that on the contralateral side. RPSV, RAR, RRR, and RIR are currently considered good single index parameters. Indirect method parameters include the tardus-parvus wave form of the intrarenal artery, acceleration time, acceleration, and resistance index difference.

This clinical study was designed to determine whether BRR, a new direct Doppler ultrasonic parameter, can be used to diagnose severe RAS. For evaluation, we compared sensitivity and specificity of BRR for diagnosis of RAS with those of other conventional ultrasonic parameters, namely the RPSV, RAR, RRR, and RIR.

Materials and methods

Study methods

Between January 2012 and June 2016, 59 patients with severe hypertension and a diagnosis of unilateral RAS in our hospital were evaluated by renal color Doppler ultrasonography (CDUS). All patients were enrolled consecutively and examined by digital subtraction arteriography (DSA) within three months of the Doppler study. The patients with bilateral RAS and renal artery occlusion were excluded from the study. The study protocols were approved by the Ethics Committee of the First Hospital of Jilin University. All patients provided written informed consent prior to participation in the study.

Instrumentation

The GE LOGIQ 9 and PHILIPS IU22 models of ultrasonographic instruments were used at a center frequency of 3.5 MHz or 5 MHz with a convex array probe. The acoustic beam and blood flow direction angle were adjusted to less than 60°, and efforts were made to achieve minimum angle correction. The sampling gate size was in the mid-lumen of the arteries. The abdominal aortic blood flow velocity was initially measured in the abdominal aorta 1 cm below the superior mesenteric artery. Subsequent measurements were carried out as deep as possible in the region of the right abdominal rib or costal margin followed by crosscut scanning. The velocities of renal arterial blood flow (proximal, middle, and distal segments) were recorded. Finally, velocities were measured adjacent to the medullary pyramids to obtain the interlobar artery index, and these measurements were used to calculate RAR, RRR, RIR, and BRR values [4, 5].

DSA was performed via the trans-femoral arterial route using a 5-French pigtail catheter. Images were taken in the anteroposterior (AP) and left and right anterior oblique positions (LAO and RAO, respectively) [6].

Statistical analysis

Statistical analysis was performed using the SPSS software package (version 10.0; SPSS Inc., Chicago, IL, USA). The diagnostic performance of the four conventional parameters (RPSV, RAR, RRR, and RIR) as well as the new parameter, BRR, was evaluated in terms of sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively). The sensitivity was calculated by dividing the number of true positive results detected using CDUS by the number of positive results detected using DSA. The specificity was calculated by dividing the number of true-negative results detected using CDUS by the number of negative results detected using DSA.

In addition, receiver operating characteristic (ROC) curves were constructed to compare these CDUS parameters in detecting RAS. The ROC curves were created by plotting sensitivity against one minus specificity (1 - specificity). The different CDUS parameters were compared by the chi-square test. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant.

Results

Among the 59 cases, there were 38 male patients and 21 female patients, aged 16-79 years old. Renal artery angiography results revealed unilateral RAS in 54 patients and normal renal arteries in 5 patients. Among the 54 cases with unilateral RAS, 41 were atherosclerotic, 9 had Takayasu arteritis, and 4 had fibromuscular dysplasia.

Comparison of results for the new BRR and conventional parameters

Based on ROC curve analysis, the areas under the curves for RPSV, RAR, RRR, RIR, and BRR were 0.980, 0.881, 0.902, 0.872, and 0.996, respectively. The best estimated cutoff values for RPSV, RAR, RRR, and RIR, were 222.5 cm/s, 2.3, 2.85, and 4.95, respectively (**Figure 1**). The best cutoff value for BRR was 2.05, based on the maximum combined sensitivity and specificity.

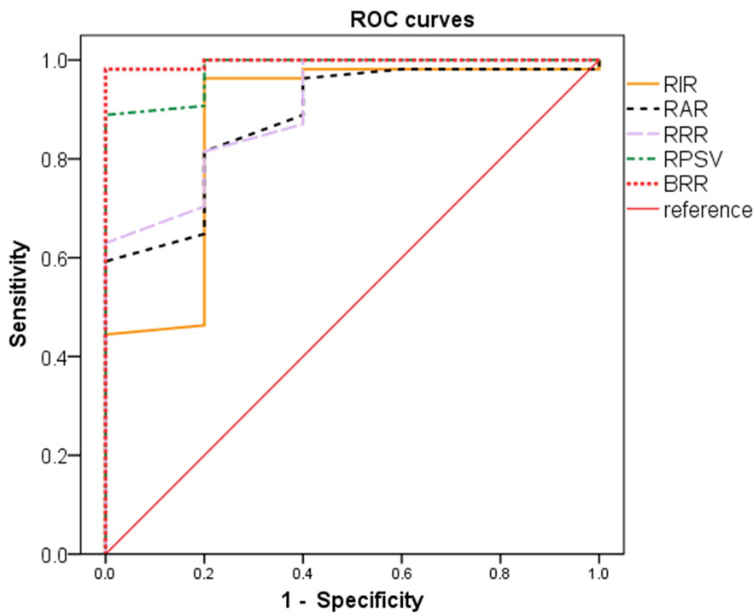

Figure 1. ROC curves for BRR. BRR exhibited the largest area under the curve (AUC = 0.996) compared to the four conventional parameters RPSV (AUC = 0.980), RAR (AUC = 0.881), RRR (AUC = 0.902), and RIR (AUC = 0.872, suggesting BRR has the greatest diagnostic value.

Table 1. Diagnostic performance of BRR and conventional parameters

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
RPSV > 222.5 cm/s	88.9	98.3	98.1	45.6
RAR > 2.3	81.5	80	97.8	28.6
RRR > 2.85	63.0	98.1	98.3	20.0
RIR > 4.95	96.3	80	98.1	66.7
BRR > 2.05	98.1	99	99.1	83.3

Diagnostic performance of BRR and conventional Doppler parameters

The results for the sensitivity and specificity of the BRR and conventional Doppler parameters (RPSV, RAR, RRR, and RIR) for the diagnosis of RAS are presented in **Table 1**.

RPSV > 222.5 cm/s showed a sensitivity of 88.9% and a specificity of 98.3%, with a PPV and NPV of 98.1% and 45.6%, respectively. RAR > 2.3 offered a sensitivity of 81.5% and a specificity of 80%, with a PPV and NPV of 97.8% and 28.6%, respectively. RRR > 2.85 produced a sensitivity of 63% and a specificity of 98.1%, with a PPV and NPV of 98.3% and 20%, respectively. RIR > 4.95 had a sensitivity of 96.3% and a specificity of 80%, with a PPV and NPV of 9 8.1% and 66.7%. BRR > 2.05 showed a sensitivity of 98.1% and a specificity of 99%, with a PPV and NPV of 99.1% and 83.3%, respectively (**Table 1**).

The sensitivity of the new parameter BRR (98.1%) was much higher than that of RPSV, RAR, and RRR ($P < 0.005$), but was similar to that of RIR. The specificity and PPV of BRR was superior to that of RAR and RIR ($P < 0.005$), but was similar to that of RRR and RPSV. The NPV of BRR was 83.3%, which was much higher than that of RPSV, RAR, RRR and RIR ($P < 0.005$).

Discussion

Chain *et al.* [7] reported a best cut-off value of 200 cm/s for RPSV with a sensitivity of 97% and a specificity of 72%. Other authors use RPSV > 150 cm/s to diagnose RAS with a sensitivity and specificity of 87.3% and 91.5%, respectively [7, 8]. Our study offers a superior cut-off value at 222.5 cm/s with a sensitivity of 88.9% and a specificity of 98.3%. Several investigators have reported higher values for the diagnostic threshold of RAR of 1.2-3.7 [7-12]. In the present study, the best threshold value was an intermediate value of 2.3. Chain *et al.* [7] reported a cut-off value 2.7 for RRR, which is similar to the 2.85 found in our study, with a sensitivity of 97% and a specificity of 96%, which are considerably higher than the values found in the present study. The present study demonstrated a RIR cut-off value of 5.0 with a sensitivity of 94.6% [12, 13]. Where differences in values exist, they may be due to the different types of cases seen, the renal arteriography procedure used, or the color Doppler flow imaging (CDFI) testing method [13].

Our study found that the performance of the new parameter BRR is superior to that of the current measures RPSV, RAR, and RRR and similar to that of RIR. The hypothesis on which the new parameter BRR is based is that the bilateral renal artery blood flow velocity increases as the blood flow velocity in RAS increases. In this study, the best cut-off value for BRR was observed to be 2.05.

Comparison of BRR and RPSV: To a certain extent, BRR should not be influenced by differences between individual patients. Any other existing disorder may also exert a secondary effect on the renal artery flow velocity, such as in patients with hyperthyroidism in whom renal artery flow is relatively increased. Similarly, abdominal aortic aneurysmal oppression can cause renal artery opening velocity to increase [7, 14, 15]. Thus, the BRR has higher specificity and NPV than RPSV.

Comparison of BRR and RAR: On the one hand, the renal artery flow velocity does affect the results of RAR due to the influence of individual differences. RAR is also influenced by abdominal aorta velocity, which is affected by heart, pelvic, and lower limb artery disease. Therefore, the sensitivity and specificity of RAR are also low [15]. In contrast, BRR is less influenced by individual differences and is not affected by interference from the abdominal aorta velocity.

Comparison of BRR and RRR: The diagnostic basis of RRR is the increased blood flow velocity in RAS and poor distal velocity, although these changes are not proportional. Considering the influence of the narrow space and the high-speed jet of downstream artery flow velocity on the RRR, there is a tendency for false negative cases [7, 10]. To a certain extent, BRR can overcome the influence of jet to distal arteries. Compared to RRR, the sensitivity and NPV of BRR are much higher.

In earlier studies, RIR was considered to be the best single diagnostic index for RAS [10]. Our study shows that BRR has a sensitivity and specificity similar to those of RIR. The diagnostic value of RIR is also based on the increase in velocity due to narrowing of the artery and low velocity at the distal end. However, the changes were not as proportional as expected. The changes are influenced by many other factors, especially other systemic diseases, which cause the proportionality of the changes to disappear. This in turn can adversely affect the diagnostic accuracy of RIR. Diabetes, atherosclerosis, and other diseases that are associated with peripheral vascular disease increase the peripheral circulation resistance due to vascular hardness. All these factors affect the diagnostic value of RIR. However, we observed that BRR is not affected by interference from the above-mentioned factors. In this study, 90% of the cases involved arteriosclerosis, yet BRR was not affected by resistance due to peripheral circulation and vascular hardness. Hence, a high degree of diagnostic sensitivity and specificity was achieved.

BRR is a valuable parameter for diagnosis of unilateral RAS. Hence, a limitation of this study is that only unilateral and not bilateral RAS cases were included. Additionally, comparisons were not made between the diagnostic accuracy of BRR and other methods, such as computed tomography angiography (CTA), DSA, and others.

In conclusion, the new parameter BRR, with a best cut-off value of 2.05, showed significant improvement in sensitivity and specificity compared to conventional direct parameters. Values obtained for the conventional parameters were: RPSV > 222.5 cm/s, RAR > 2.3, RRR > 2.85, and RIR > 4.95. BRR and RIR proved to have the best sensitivity and specificity as single indices. BRR should not be influenced by systemic factors or individual patient differences. Thus, BRR proved to be a useful index to improve diagnostic accuracy for RAS.

Disclosure of conflict of interest

None.

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