How to diagnose renal artery stenosis correctly using ultrasound? Evaluation of results of renal arteries duplex ultrasonography examinations

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Abstract

Aim: Renal artery duplex ultrasonography (RDU) is an effective and non-invasive screening test in diagnosing renal artery stenosis. The discordance of results in multiple RDU is common. We aim to evaluate the discordance and the reasons for discordance between diagnoses and measurements from multiple RDU examinations. Material and method: A retrospective study was performed in 64 examinations of renal arteries from 32 patients that were referred for two or more RDU examinations and renal artery digital subtraction angiography (DSA) within six months, between August 2013 and January 2016. Using DSA as gold standard, we divided the renal arteries into three groups: discordant (one diagnosis of RDU was correct and one was wrong), misdiagnosed (neither RDU diagnosis was correct) and correct (both RDU diagnoses were correct) groups. We evaluated the discordance and reasons for discordance of diagnoses and measurements from multiple RDU examinations. Results: Among 64 renal arteries included in this study, 37 renal arteries had two correct diagnoses, 19 renal arteries had two discordant diagnoses, and eight renal arteries were misdiagnosed twice by RDU. The discordance of peak systolic velocity (PSV), the ratio between PSV in the renal artery with stenosis and PSV in the aorta (RAR), and tardus-parvus waveform measurements were clearly higher in the discordant diagnoses group than in the correctly diagnosed group. The most common reason for a discordant diagnosis was failure in obtaining correct tardus-parvus waveforms of the interlobar artery (26.31%). The most common reason for misdiagnosis was the presence of an extremely severe stenosis with an atrophic kidney (31.25%). Overall, 87.50% of patients underwent RDU examinations had correct diagnoses of stenosis or occlusion at least once (including location and degree), as confirmed by DSA. Conclusions: Our study indicates that standard operating procedures and improvements in examination technique by ultrasound doctors could reduce the discordance between multiple tests.

Keywords: renal artery stenosis; duplex ultrasonography; misdiagnosis; discordance

Introduction

Renal artery stenosis (RAS) is the largest cause of secondary hypertension, affecting 25% to 35% of the patients with secondary hypertension [1]. In China, renal artery duplex ultrasonography (RDU) is a widely available screening examination. However, RDU can be a technically demanding imaging technique and also an operator-dependent technique [2] and frequently discordance of diagnosis between RDU and digital subtraction angiography (DSA) and among different RDU examinations can be seen. DSA is the reference standard for the diagnosis of RAS and now is used as confirmatory imaging (the diagnosis accuracy is approximately 100%) prior to further treatment [3]. Compared with DSA, RDU has a sensitivity of 67-98% and a specificity of 54-99% for detecting RAS [4-8]. Previous studies showed that many
reasons could lead to the discordance of diagnoses, such as interobserver disagreement [9] and vessel tortuosity [10].

The aim of our study was to evaluate the accuracy and discordance between RDU examinations. Furthermore, to determine the possible reasons for discordant RDU diagnoses and/or misdiagnosis, in order to guide the standardization of RDU investigation.

Material and methods

Patients

A retrospective study was performed on 178 patients referred for two or more RDU examinations to Peking Union Medical College Hospital between August 2013 and January 2016. The study was approved by the medical ethics committee. Neither patient approval nor informed consent was required for the review of medical records or radiologic images. The inclusion and exclusion criteria are shown in figure 1. Stenosis (reduction of the lumen between 50% and 99%) was diagnosed if the measured values of renal arteries fit one of the following criteria: 1) peak systolic velocity (PSV) ≥150 cm/s [11]; 2) the ratio between PSV in the renal artery with stenosis and PSV in the aorta (RAR) ≥2.5 [12]; 3) the existence of a tardus-parvus waveform [13]; and 4) occlusion (100% reduction of the lumen), with neither blood flow signal nor frequency spectrum detectable in the renal artery [14].

From 178 patients only 32 patients (16 men and 16 women, mean age 42 years) who had two or more RDU examinations were eligible for inclusion. These 32 patients had 68 renal arteries: 2 patients had one accessory renal artery, and 2 patients had one bypassed renal artery, respectively. The bypassed renal arteries and the ipsilateral renal arteries were excluded from the study. Finally, 64 renal arteries were included in the study. Twenty-four of the renal arteries had no stenosis, 30 had stenosis, and 10 were occluded. Though some of the included patients had three or more RDU examinations in 6 months before DSA, only two RDU examinations right before DSA were compared and analyzed (in order to shorten the time span between RDU and DSA and to reduce the influence of disease progression for making a unified analysis). Clinical, laboratory, and imaging examination data, including time interval between the two RDU tests, a complete physical examination, medical history, blood and urine tests, were collected to evaluate kidney function and imaging assessment.

Ultrasonography

RDU was performed by 15 registered ultrasound doctors. Patients were required to fast for at least eight hours before testing. RDU was performed using a 3.5-MHz or 5.0-MHz curvilinear array transducer by LOGIQ 9 (GE Medical Systems, Milwaukee, WI) or IU22 (Philips Medical Systems, Bothell, Wash). Patients were scanned in the supine or decubitus position. Real-time gray-scale ultrasonography was performed initially to assess morphology. The evaluation of blood vessels began with the supra-renal abdominal aorta. The aortic PSV was obtained at the level of 1 cm below the superior mesenteric artery to assess RAR. The renal arteries were scanned using three approaches: transverse scanning from the mesogastric-epigastric area, flank coronal scanning, and intercostal or subcostal transverse scanning. Color Doppler imaging was used to search for turbulence in the renal arteries. The PSV in the renal artery spectra were recorded in the proximal (including the origins of renal artery), middle, and distal parts of the renal artery. The highest PSV was chosen to assess RAR. The spectral Doppler analysis was performed in the upper, middle and lower pole interlobar arteries. The morphology change of the normal early systolic peak was recorded. PSV, acceleration time of early systole (AT), and the resistance index (RI) were recorded from each waveform. The AT was measured from the onset of systole to the first systolic peak. The RI was determined using the built-in calculation software of the ultrasound systems. If an accessory renal artery was visualized, all the parameters would also be measured for the accessory renal artery.

Digital subtraction angiography

The DSA examination included an aortogram of the abdominal aorta using a 5F pigtail catheter (Cordis, Johnson & Johnson, Miami, Florida, USA) with a transfemoral approach. A non-ionic contrast agent (Ultravist, 370 mg of iodine per mL, Bayer-Schering HealthCare, Germany) was injected into the aorta at a rate of 4 ml/sec. These were performed by board-certified vascular surgeons or board-certified vascular interventional radiologist. The point of greatest stenosis was measured using the digital caliper technique with multiple projections and was compared with the normal renal arterial diameter. The degree of stenosis was determined by manual measurement of the narrowest diameter of the stenotic segment (A) compared with a normal segment (B) and calculated by $100 \times (1-A/B)$. 

Fig 1. Participant flow chart
The definition of a correct diagnosis was that the RDU examination correctly defines the existence and location (proximal, middle, distal part or whole trunk) of the stenosis compared with DSA. Additionally, correct RDU examination had to accurately determine the presence and the degree of stenosis (normal, stenotic, or occluded). According to the result of DSA and diagnosis of RDU examinations, we divided the subjects into three categories, as shown in figure 2: discordant, misdiagnosed and correct diagnoses. We further divided the three categories into five groups according to the measurement of all parameters in the RDU results, as shown in figure 2. We evaluated the discordance of measurements between discordant diagnoses and misdiagnoses groups. The discordance of PSV and RAR were defined as differences between the PSV and RAR of two RDU of greater than 25%. The discordance of interlobular frequency spectra was defined as presence or absence of the tardus-parvus waveform as reported by RDU examiners. In several examinations, some of the measurements were unable to be obtained by examiners which will be further explained in the results. These measurements were excluded from the analysis. Moreover, if the renal artery PSV in misdiagnosed RDU was lower than 25% that in the correctly diagnosed RDU, the former PSV was defined as suspicious inauthentic low PSV. On the contrary, it was defined as suspicious inauthentic high PSV. According to this definition, we speculate possible reasons for misdiagnoses.

**Statistical analyses**

The statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS version 19.0; SPSS Inc., Chicago, IL, USA). The values were expressed as the mean ± standard deviation (SD) or as a percentage. To compare the intergroup differences of PSV, tardus-parvus waveform and RAR measurement discordance between discordant diagnoses and misdiagnoses groups, Chi-square was used and a p value of <0.05 was considered significant. All findings were separately and blindly evaluated before DSA was performed.

### Results

Patient baseline characteristics are shown in Table I. The mean time interval between first and second RDU examination was 61.29±29.86 days and the mean time interval between second RDU examination and DSA was 19.56±10.08 days.

Among the 128 RDU examinations of 64 renal arteries, renal artery PSV could not be evaluated 22 times in 15 renal arteries (once in 8 renal arteries and twice in 7 renal arteries). The reasons for the failures were: occlusion of 7 renal arteries (not detected twice), excessive bowel gas and/or obesity that impaired renal artery visualization in 4 renal arteries, renal atrophy with extreme stenosis that impaired renal artery visualization in 3 arteries, and RDU performed in the emergency room in 2 renal arteries. Visualization of one renal artery was impaired by both excessive bowel gas and extreme stenosis simultaneously. RAR was not obtained 20 times in 20 renal arteries: 16 renal arteries PSV and 4 aortic PSV were unable to be obtained. The interlobar artery frequency spectrum was not obtained 14 times in 12 arteries. Interlobar artery frequency spectra were not detected 8 times. Additionally, sharp and large interlobar artery frequency spectra could not be obtained 6 times in order to acquire the correct measurements.

Among the 64 renal arteries included in this study, 37 renal arteries had two correct diagnoses, 19 renal arteries had two discordant diagnoses, and 8 renal arteries were misdiagnosed twice by RDU. Comparing with DSA, RDU in this study had a sensitivity of 74.0% and a specificity of 65.5% for detecting RAS. As explained before, some of the measurements were unable to be obtained.

### Table I. Baseline characteristics of the 32 included patients

| Age (years) | 42.15±21.45 |
| Male | 16(50) |
| Disease | |
| Atherosclerosis | 13(40.62) |
| Takayasu’s arteritis | 16(50) |
| Fibromuscular dysplasia | 3(9.38) |
| BMI | 23.67±4.01 |
| Blood pressure (mmHg) | |
| Systolic pressure | 151±30.97 |
| Diastolic pressure | 91±22.48 |
| Serum creatine (μmol/L) | 110.38±68.86 |
| BUN (mmol/L) | 6.63±2.72 |
| eGFR (mL/min/1.73m2) | 49.03±27.06 |
| History of hypertension | 25(81.25) |
| Duration of hypertension (years) | 6.68±9.91 |

The results are expressed as number (%) or mean±standard deviation. BMI: body mass index; BUN: blood urea nitrogen; eGFR: estimated glomerular filtration rate.
We excluded the failure of measurements of all the parameters to evaluate the discordance among these three groups. This exclusion is shown in Table II. In the correctly diagnosed group, the discordance rates of PSV, tardus-parvus waveform, and RAR were 6.06%, 3.33%, and 16.67%, respectively. In the discordant diagnoses group, the discordance rates of PSV, tardus-parvus waveform, and RAR were 11.76%, 35.71%, and 85.71%, respectively. According to the Chi-square test, the p values of the intergroup differences of PSV, tardus-parvus waveform and RAR measurement discordance were 0.597, 0.009, and 0.001 respectively. In other words, the discordances of tardus-parvus waveforms and RAR measurements were clearly higher in the discordantly diagnosed group comparing with the correctly diagnosed group.

Regarding the evaluation of diagnosis, there were two patients in our study that each had one accessory renal artery. RDU detected none of the accessory renal arteries. Two patients had one bypassed renal artery. One of the bypassed arteries was misdiagnosed, while the other had two discordant diagnoses. There was one patient with stenosis at the proximal part of the renal artery and a post-stenotic aneurysm at the middle part. The patient was misdiagnosed at first RDU (the examiner interpreted the aneurysm as a stenosis and the upstream stenosis was not identified). There was also one misdiagnosed patient with two eccentric stenosis. The excessive intestinal gas and/or obesity were the causes for not visualizing four renal arteries during the first RDU. Overall, 87.50% of patients underwent RDU examinations had correct diagnoses of stenosis or occlusion at least once (including location and degree), as confirmed by DSA.

The large angle of velocity which is close to 60° could also lead to incorrect measurement as shown in figure 3. We listed possible reasons for discordant diagnoses and misdiagnoses in Table III. Some of the misdiagnoses occurred for multiple reasons.

**Discussions**

We evaluated the concordance and accuracy of different RDU examinations, as DSA has been considered to
be the gold standard for the diagnosis of RAS. We also evaluated the concordance of RDU parameter measurements from multiple examinations and determined possible reasons for discordance in diagnosis and measurement. In this study, a total of 27.94% renal arteries had two discordant diagnoses. Regarding the measurement of RDU parameters, the table II indicates that the discordantly diagnosed group had greater discordance than the correctly diagnosed group. The discordance of measurement may be an essential reason of the discordance of diagnosis.

Obtaining an incorrect PSV of the renal artery is a major reason for misdiagnosis. Seven arteries were measured incorrectly in the discordant group. Three of them were caused by obtaining incorrectly low velocities, and four of them were produced by obtaining incorrectly high velocities. To obtain accurate PSV, the examiners should scan the entire renal artery to define the highest velocity. As turbulent flow masks the stenosis site, high pulse repetition frequency is suggested to decrease the range of turbulent flow and reveal the stenosis more clearly. Increasing pulse repetition frequency could guide the examiner in placing the sample gate on the right place (the most stenotic site), so the highest velocity of renal artery can be obtained. The sample gate should be placed at the most stenotic site under the guidance of color Doppler imaging. For complicated cases, multiple sampling is necessary. Examiners have to search for the white or yellow color flow code through the entire cardiac cycle or systolic period and measure the highest velocity at turbulent flow accordingly. Ding-Yu et al [15] reported in a flow dynamics experiment that at a further distance downstream, there is a tendency for the velocity to remain slightly peaked, although it shifts away from the flow divider. Peak velocities are increased at 1 diameter downstream due to a weak jet effect at the constricted plug. In other words, the peak velocity may not be generated at the stenosis site, but rather, it is generated closely downstream. This alteration of velocity is a possible contributor to discordant PSV measurement. Furthermore, the angle of insonation should be maintained at 60° or less. Large angles of insonation could contribute to inaccurately high peak velocities. Multiple scan sections and scan planes are necessary to find a lower angle of insonation [16]. Moreover, the sample line should be parallel to the flow vector instead of the arterial wall, especially in patients with eccentric stenosis or post-stenotic aneurysm [17]. We found that larger angles (close to 60°), especially combined with other factors such as obesity, vessel tortuosity, and deeply located renal arteries, could lead to a difficulty in sampling and could easily cause inaccurately high velocities. In this study, a patient with a post-stenotic aneurysm was misdiagnosed by the first doctor, who mistakenly diagnosed the aneurysm as a stenosis and did not find the upstream stenosis. When turbulence is measured, it is essential to scan the entire renal artery to find the highest velocity and correctly determine whether it is a stenosis or an aneurysm. A patient with two eccentric moderately stenosed renal arteries, as defined by DSA, was misdiagnosed by two different examiners. Eccentric stenosis, opposite to concentric stenosis is defined as asymmetric stenosis of vessel lumen. When wall thickening is clearly limited to one side of the arterial wall, or if circumferential wall thickening is noted, the thinnest part of the wall is estimated to be less than 50% of the thickest point of the basilar artery wall under visual inspection [18]. Traditionally, only diameter measurements have been used to evaluate stenosis in DSA. The projection image should be generated at an angle that allows measurement of the minimum luminal diameter. This dimension may be unmeasurable in cases of eccentric stenosis with images generated at suboptimal

<table>
<thead>
<tr>
<th>Reason</th>
<th>discordant diagnoses (N=19)</th>
<th>misdiagnoses (N=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Too much intestinal gas or obesity</td>
<td>4(21.05)</td>
<td>2(12.50)</td>
</tr>
<tr>
<td>Extremely severe stenosis of artery lumen</td>
<td>4(21.05)</td>
<td>5(31.25)</td>
</tr>
<tr>
<td>with an atrophy kidney</td>
<td>2(10.52)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Obtaining suspicious inauthentic high</td>
<td>4(21.05)</td>
<td>0(0)</td>
</tr>
<tr>
<td>velocity of renal artery</td>
<td>2(10.52)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Accessory renal artery</td>
<td>0(0)</td>
<td>4(25)</td>
</tr>
<tr>
<td>Segmental artery stenosis</td>
<td>2(10.52)</td>
<td>1(12.50)</td>
</tr>
<tr>
<td>Eccentric stenosis</td>
<td>0(0)</td>
<td>4(25)</td>
</tr>
<tr>
<td>Poststenotic aneurysm</td>
<td>1(5.26)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Obtaining incorrect tardus-parvus of interlobar artery</td>
<td>5(26.31)</td>
<td>0(0)</td>
</tr>
<tr>
<td>Wrong description of stenotic location</td>
<td>1(5.26)</td>
<td>3(18.75)</td>
</tr>
<tr>
<td>Wong judgment of stenosis with authentic measurement</td>
<td>1(5.26)</td>
<td>0(0)</td>
</tr>
</tbody>
</table>

The results are expressed as number(%); N – number of patients.
ultrasound-guided procedures. In our study, four renal adjacent bowel gas is a factor contributing to the failure of excessive intestinal gas and/or obesity are important reasons for misdiagnosis. For example, Zachrissonet al [27] reported that RAR is a more sensitive criterion than traditional RDU criteria when screening patients with clinical suspicion of RAS. Additionally, factors other than RAS, such as left heart insufficiency, mitral valve disease, and aortic disease, could affect the results of PSV and RAR. Therefore, indirect parameters are useful indicators for the detection of a hemodynamically significant RAS [16]. Our previous studies showed that the five hemodynamic parameters (RPSV, RAR, RIR, AT, and RI) may comprehensively reflect the hemodynamic changes in RAS [17,28]. Moreover, we found discordant measurement in multiple RDU examinations, even by the same operator examining the same patient. To solve this problem, other parameters besides traditional ones, such as renal morphology evaluation or ARI, are suggested in RDU examinations to potentially increase diagnostic accuracy [29].

In our study, the mean time interval between RDU examinations was 60.19 days. There is no widely accepted guidance regarding follow-up intervals for patients with renal artery stenosis. In China, rheumatologists and vascular surgeons typically suggest a follow-up interval for examination of the renal artery of 3 to 6 months to re-evaluate the renal artery and adjust therapy accordingly. Efficiency and swiftness are major factors in the choice of the imaging procedure. RDU most frequently is the first choice because the RDU study report can be obtained by clinical doctors within one day in China.

To the best of our knowledge, this is the first study to evaluate multiple RDU examinations for diagnosing renal artery stenosis. This is also one of the few studies to evaluate the reasons for misdiagnosis of RAS. There are still several limitations of this study. First, this is a single-center retrospective study, which may be susceptible to a biased result. Moreover, we set up a time limitation of 6 months for all examinations to detect disease progression. However, there is no globally accepted standard for this time limitation. Research has shown at one year, the cumulative incidence of progression from normal to ≥60% RAS was 0% and from <60% to ≥60% RAS was 30% [30]. In other research, the reported cumulative incidence of progression at one year was 3%, 11%, and 18% for renal arteries initially classified as normal, <60% stenosis, and ≥60% stenosis, respectively [31]. Davis et al [32] used multiple RDU to evaluate the RAS progression. They found out that regardless of the presence or absence of baseline disease, a small percentage of patients de-
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...demonstrated anatomic progression of RAS during RDU examination, with a total of 9.1% demonstrating anatomic progression and 2.3% progressing to occlusion over a mean follow-up of 34.4±25.1 months. Furthermore, the patients involved in this study had a rather low activity of Takayasu’s arteritis. The ESR and CRP of patient had to be maintained at low levels before surgery or intervention treatment. Therefore, the possibility of morphology change of renal artery during three examinations was low. Some researches established a reported time limitation of three months to eliminate the effect of disease progression [33]. For patients in our hospital, however, only a few of them repeated RDU examinations at three months. Therefore, to balance disease progression and the recruitment of patients, we established a time limitation of 6 months.

In conclusion, to increase the success of RDU, the examiners should scan the entire renal artery to define the highest velocity with standard technique and multiple approaches. Moreover, the renal artery PSV, RAR, RIR, AT, and RI have to be measured in a standardized manner. Also, the examiners should be aware of the regular and irregular hemodynamic changes and combine various criteria correctly to diagnose the existence of RAS and its severity.

Conflict of interest: none

References:


