Renal artery stenosis: evaluation with colour duplex ultrasonography

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Abstract

Background. Detection of renal artery stenoses (RAS) by means of duplex Doppler ultrasound with direct scanning of the main renal arteries is subject to numerous limitations. Using semiquantitative analysis of the Doppler curve, which can be recorded from intrarenal arteries, it is possible to detect renal US unaffacted by the problems of direct Doppler scanning of the renal arteries.

Methods. Both angiography of the renal arteries and colour duplex ultrasonography (US) of the interrenal vessels (interlobar arteries) were performed in 214 patients (53.2 ± 14.1 years) with severe arterial hypertension. Angiography was used as ‘gold standard’ in the diagnosis of RAS and the Doppler results were compared with the subsequent findings on angiography. At angiography, the reduction of diameter > 70% was assessed as haemodynamically effective RAS. For the duplex Doppler diagnosis of RAS the following parameters were calculated: (a) resistive index (RI) of each kidney, and (b) side-to-side differences of the resistive indices (∆RI) between the right and left kidney.

Results. Angiography demonstrated 59 RAS (>70%) in 53 patients, including six with bilateral RAS. By means of duplex US we found a significant difference of RI between kidneys with RAS (0.48 ± 0.11) and without RAS (0.63 ± 0.08; P < 0.001). In addition, a significant difference of the ∆RI was noted in patients with RAS (24.4% ± 12.5%) and the controls without RAS (3.6% ± 2.7%). Using a combination of both RI and ∆RI, threshold values of RI = 0.45 resp. ∆RI = 8% yields a sensitivity of 92.5% and a specificity of 95.7% in the detection of haemodynamically effective RAS.

Conclusions. Colour duplex US with calculation of the RI and ∆RI of intrarenal arteries is a valuable non-invasive test assessing the haemodynamic effects of a RAS. Low costs and safety support the use of the Doppler technique in screening for renovascular disease.

Key words: colour duplex ultrasonography; renal artery stenosis; renovascular hypertension; resistive index

Introduction

Renal artery stenosis is seen as a cause of arterial hypertension in some 1% of all hypertensive patients [1]. Identification of a haemodynamically effective renal artery stenosis (RAS) is the prerequisite for curative therapy of renovascular hypertension by surgical correction or angioplasty. The objectives for these interventions are the improvement of blood pressure control and renal function and the prevention of renal artery occlusion.

Various diagnostic methods are available for identification of RAS, with intraarterial angiography as the gold standard for morphological visualization of unilateral and bilateral renal artery stenoses. In angiography, the haemodynamic significance of a stenosis can only be estimated from the reduction of diameter of the renal artery. Owing to its invasive character and the substantial costs involved, angiography cannot be used as a screening method for low-prevalence RAS.

Given suitable test conditions, duplex ultrasonography (US) can also be used to identify a RAS from the enhanced flow velocity and the altered flow characteristics in the stenotic segment of the renal artery [2–5]. The frequency of artery variants, lengthy examination times and technically inadequate test conditions limit the use of the direct duplex US detection of a RAS. Disagreement exists concerning the sensitivity, specificity, and predictive value of various duplex US parameters in the evaluation of RAS [6–10]. There is no consensus on how to evaluate the waveforms from duplex Doppler examination of the renal arteries.

Animal experiments have shown that duplex Doppler US of segmental and interlobar arteries can detect haemodynamic changes in the presence of a RAS, reducing pulsatility and lowering post-stenotic vessel resistance [11]. Previous Doppler US studies in hypertensive patients also showed significant signal changes (as measured with acceleration index and resistive index) in intrarenal vessels distal to a haemodynamically effective RAS. This Doppler approach to diagnosis of RAS avoids the drawbacks of direct duplex sonographic identification of RAS [12–15].

The following study was intended to validate the use of color duplex US as a diagnostic method for indirect identification of haemodynamically effective
Renal artery stenosis: duplex Doppler evaluation

RAS (>70% diameter reduction in angiography) in a population with severe arterial hypertension, and to discuss its suitability as a screening method.

Methods

Subjects

Over a 2-year observation period, all patients with severe hypertension who were to undergo renal artery angiography were evaluated with renal sonography and examination of intrarenal arteries by means of duplex US.

Patients with chronic renal diseases, single kidneys, or renal artery occlusion were excluded from the study. Additionally, the colour duplex US tests were performed only if the heart rate was between 50 and 100/min and there was no arrhythmia. Examinations using colour duplex US and angiography techniques were performed at a maximum interval of 8 weeks. A total of 214 patients (105 female, 109 male; 53.2 ± 14.1 years; minimum 16 years; maximum 84 years) were included in the study (Table 1).

At least one of the following hypertension criteria was met:

1. Hypertension with diastolic blood pressure (BP) values ≥110 mmHg (before initiation of antihypertensive drug therapy);
2. Hypertension refractory to multiple drug therapy (diastolic BP ≥95 mmHg under a combination of three antihypertensive drugs);
3. Arterial hypertension in individuals younger than 30 years;
4. Sudden deterioration in kidney function in association with a known hypertension;
5. Hypertension in association with a sonographically detected size difference of the kidneys (>1.5 cm);
6. Acute onset of hypertension or significant deterioration of pre-existing hypertension.

Angiographic reference methods

Angiography was used as ‘gold standard’ in the diagnosis of RAS and the Doppler results were compared with the subsequent findings on angiography. In all patients angiography was carried out by means of intravenous (n=78) or intra-arterial digital subtraction angiography (n=91) (DSA). In 45 cases, the renal arteries were visualized within a coronary angiography. Positive or technically insufficient intravenous DSA results were additionally investigated with intra-arterial DSA.

At angiography the renal artery diameter reduction (D%DR) was calculated after measurement of the normal (D) and the minimal diameter (d) by \( \text{D%DR} = \frac{(D-d)}{D} \times 100 \). According the angiographic findings the reductions of diameter >70% were assessed as haemodynamically effective RAS irrespective of their localization, length or X-ray morphology. Patients with atherosclerotic (n=43) and fibrodysplastic RAS (n=10) were also taken into account in the study.

B-scan US and colour duplex US

Colour duplex US examinations were performed by two experienced observers prior to the angiography. All examinations were performed with a Toshiba SSA 270A (Toshiba, Tokyo, Japan; 3.75 MHz sector/curved array transducer) with the patient lying in the supine position using a lateral or posterolateral approach. No special measures were taken to improve sonographic test conditions. Following sonographic examination of both kidneys in the B-scan mode, kidney size in the longitudinal axis was determined. The intrarenal arteries were visualized in the colour duplex mode. Settings for the colour display were optimized individually.

Using imaging guidance of the colour signal, the sample volume (3 mm) for the Doppler US test was placed in at least three different positions within the renal parenchyma (Figure 1), the signals were registered over at least three heart cycles from the interlobar arteries (wall filter 100 Hz). The Doppler frequency spectra were analysed by the implemented measuring

Table 1. Basic patient data

<table>
<thead>
<tr>
<th></th>
<th>Angiogram</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No stenosis</td>
</tr>
<tr>
<td>Patients</td>
<td>161</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>86</td>
</tr>
<tr>
<td>Female</td>
<td>75</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.6 ± 14.1</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>88.9 ± 27.1</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>202 ± 31</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>119 ± 14</td>
</tr>
</tbody>
</table>

Fig. 1. B-scan US of a right kidney with the Doppler sample volume within the renal parenchyma; correct position of the Doppler sample volume is controlled by colour Doppler mode.
equipment and the following parameters determined: maximum systolic flow velocity (V\textsubscript{sys}), end-diastolic flow velocity (V\textsubscript{dias}) and heart rate. The resistive index (RI) was calculated according to the algorithm

\[ RI = \frac{(V\text{sys} - V\text{dias})}{V\text{sys}}. \]

An average value of all determinations of the RI was calculated for each kidney.

Blood pressure at the time of testing was not taken into account. All tests were performed without reference to the use of antihypertensive medication.

**Duplex US stenosis criteria**

Duplex US diagnosis of a RAS was made on the basis of the dampened downstream Doppler signal curves recorded from the interlobar arteries. RAS causes a decreased RI in the intrarenal arteries of the affected kidneys (‘pulsus parvus’) [13,14,16].

For the duplex Doppler diagnosis of RAS the following parameters were evaluated and compared retrospectively with the angiographic findings:

(a) individual resistive index (RI) of each kidney, and
(b) side-to-side differences of the resistive indices (ΔRI) between the right and left kidney, indicating a RAS on the side with the relatively lower RI.

The ΔRI\% was calculated by the following algorithm:

\[ ∆RI\% = 100\times(\frac{RI\text{max} - RI\text{min}}{RI\text{max}}), \]

(\(RI\text{max}\): RI of the kidney with the higher RI; \(RI\text{min}\): RI of the kidney with the lower RI).

Different threshold values for RI (0.40, 0.45, 0.50) and ΔRI\% (5–11\%) were tested in receiver operating characteristic (ROC) analysis to compare their diagnostic efficacies in detection haemodynamically effective RAS.

The study was not aimed at a complete visualization in the Doppler sonographic examination of the main renal arteries.

**Documentation and statistics**

The measured and calculated data were stored in a database. The SPSSPC statistic program (SPSS GmbH Software, Munich, Germany) was used for statistical data analysis. The mean values and standard deviations were calculated and were compared using the Wilcoxon or t test. A value of \(P<0.05\) was considered statistically significant. Sensitivity, specificity, and predictive values were calculated for the different RI and ΔRI\%.

From this data the ROC curve was constructed.

**Results**

A total of 214 patients with arterial hypertension were examined in the study. Angiographically, 59 RAS with a lumen reduction >70\% were detected in 53 patients (Table 1). In six patients there were bilateral RAS >70\% located before the branching of the renal arteries into the segment arteries. All unilateral stenoses affected the main renal artery; no stenoses were observed in the region of an accessory renal artery.

With all patients, it was possible to visualize both kidneys in the B-scan US and we obtained adequate Doppler studies in all patients. Interlobar arteries in various parenchyma segments of both kidneys could be visualized within a test period of <20 min using colour duplex US, and Doppler frequency spectra could be inferred for more than three heart cycles from different renal parenchyma segments.

Figure 2 presents the typical duplex US findings in a patient with a left-sided RAS. The individual data for RI and ΔRI\% of all patients are demonstrated in Figure 3. In addition, B-scan and duplex US test results are summarized in Table 2.

Sensitivities and specificities for different threshold values of the RI and ΔRI\% were calculated and the ROC curves were constructed from these data (Figure 4).

By comparison of the different threshold values, the 8\% cut-off point for the ΔRI\% combined with the 0.45 cut-off point of the RI yields favourable sensitivity and specificity for the Doppler method to select patients with haemodynamically effective RAS (Tables 3, 4).

Fifty-one (86.4\%) of all 59 unilateral and bilateral RAS were identified correctly using the above cut-off values for RI and ΔRI\%. In seven (4.3\%) of 161 patients positive duplex US tests were found, while the main renal arteries appeared normal in the angiography (Table 3). In one 25-year-old patient, the right kidney was supplied by two arteries both of which showed a >70\% stenosis indicating a fibrodysplasia. The left main renal artery was supplied by three vessels.

**Table 2. B-scan and duplex US results (214 patients/428 kidneys)**

<table>
<thead>
<tr>
<th>Angiogram</th>
<th>No stenosis</th>
<th>RAS</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney size (cm)</td>
<td>11.3 ± 1.0</td>
<td>10.3 ± 1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(n=369)</td>
<td>(n=59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RI (all kidneys)</td>
<td>0.63 ± 0.08</td>
<td>0.48 ± 0.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean</td>
<td>0.90</td>
<td>0.83</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>0.47</td>
<td>0.29</td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>0.00</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>(n=369)</td>
<td>(n=59)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔRI% Mean</td>
<td>0.02 ± 0.02</td>
<td>0.16 ± 0.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum</td>
<td>0.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n=161)</td>
<td>(n=53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔRI% Mean (%)</td>
<td>3.6 ± 2.7</td>
<td>24.4 ± 12.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum (%)</td>
<td>12.5</td>
<td>48.4</td>
<td></td>
</tr>
<tr>
<td>Minimum (%)</td>
<td>0.0</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>(n=161)</td>
<td>(n=53)</td>
<td></td>
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</tr>
</tbody>
</table>
artery also showed a significant stenosis. A further anatomical variant was a left lower pole artery without stenosis. Duplex US revealed an RI of 0.40 in all parenchyma segments of the right kidney. The RI was

Fig. 2. Doppler velocity flow signals from intrarenal arteries in a hypertensive patient with a left sided RAS; (A), right kidney; RI = 0.63; (B), left kidney; RI = 0.38.

Fig. 3. Scatterplot of the RI and side-to-side differences of the RI (ΔRI%) obtained from all 214 patients with and without RAS. Each symbol represents one patient. The lower RI from intraindividual comparison of both kidneys is shown for each patient. The threshold values are marked with asterisks. *ΔRI% = 8%; **RI = 0.45.

Fig. 4. Detection of a >70% RAS by means of duplex Doppler examination. The receiver operating characteristic (ROC) curve shows the sensitivity and specificity for the different cut-off values of ΔRI. The least total error was calculated for the 8% threshold value.
Discussion

Previous studies have shown that duplex US can be used to detect stenoses of the renal arteries directly from the accelerated blood flow in the stenosed vessel segment. Apart from qualitative signal modifications (spectral broadening of the Doppler frequency band, high systolic and diastolic Doppler frequencies, poststenotic flow turbulence, colour aliasing), a raised systolic velocity in the stenotic vessel segment is given as diagnostically indicative [4,7,17–19].

However, results for duplex sonographic diagnosis of RAS produced contradictory findings, due to various technical modifications, variable test regimes and evaluation parameters. In particular, the method demands ideal sonographic test conditions, which are limited by frequent air overlapping of the abdomen and adiposity. Frequent vessel variants of the renal vascular flow path (accessory arteries, aberrant arteries) can seldom be detected by duplex US. Finally, duplex US and colour duplex US require long examination times for a complete visualization of the main renal arteries, even when sufficiently experienced staff are used, apparently limiting the suitability of duplex US as a practical screening method [4,10]. As compared to conventional duplex US, colour duplex US facilitates visualization of the renal vessels. However, the available studies indicate no superiority of this method for the direct detection of RAS [9,10].

Several researchers have examined the indirect detection of a stenosis by means of duplex US of intrarenal arteries as a technical modification of the test [12–15]. Patriquin et al. [13] were able to demonstrate that the Doppler signals of intrarenal arteries (interlobar, interlobular arteries) with preceding stenoses have a reduced pulsatility based on stenosis-induced changes of internal haemodynamics. These results agree with animal and clinical results concerning Doppler sonographic modifications in the post-stenotic renal flow path [11–13]. Apart from quantifiable modifications of the diagnostically established pulsatility parameters (acceleration index, acceleration time), the consequences of haemodynamically effective stenoses include an absolute or relative reduction of the RI [12] and a prolongation of the acceleration time [11,13].

In the present study, a selected population of hypertension patients was used to examine whether the diagnosis of haemodynamically effective stenosis (diameter reduction >70%) in a renal artery can be achieved through Doppler sonographic determination of the RI of intrarenal vessels. Intra-arterial DSA or conventional angiography was used as reference technique in 136 patients including all patients with RAS. Intravenous DSA, which is considered inappropriate in the diagnosis of moderate RAS or stenosis in renal vascular variants, was accepted as reference in 78 patients with technically sufficient investigation.

Patients with arterial hypertension caused by chronic renal failure were excluded from the study. Our study shows an RI variation of between 0.47 and 0.90 for an interindividual comparison of nonstenosed kidneys. The intraindividual lateral comparison shows only a small difference in the RI for the two kidneys (0.02 ± 0.02). Age-dependent changes in vessel elasticity [20], heart rate and cardiac factors [21–23] are documented as influencing variables for the interindividual variance.

In the present study the Doppler sonographic diagnosis of a RAS rests on detection of an intraindividual, significant reduction of the ipsilateral RI exceeding different tested threshold values (>5–10%) by comparison with the contralateral kidney or significant reduction of the ipsilateral RI to less than 0.45. This relative method of observation ensures that haemodynamic factors which affect only the unilateral kidney and which are responsible for the interindividual variance of the RI are detected. By comparison of the different threshold values in a ROC analysis, the cut-off point of 8% yields favourable sensitivity (92.5%) and specificity results (97.5%) for the method of detecting >70% RAS. Using our Doppler US criteria moderate RAS (≤70%) may account for some false positive US test results in our study.

In an angiographically-controlled study Schwerk et al. [14] have shown that lateral comparison of the resistive indices is suitable for duplex sonographic detection of stenoses. The authors demonstrated a correlative relationship between Doppler sonographic and angiographic findings. RAS >50% show significant lateral differences (ΔRI% >5%) as compared to resistive indices with unilateral RAS.

Because of the frequency of bilateral RAS, the duplex US method has to be adapted by introducing
additional criteria for the detection of bilateral changes in the renal arteries. Since the absolute RI values of the interlobar arteries were also reduced in the majority of angiographically detected RAS, this fact was exploited in the present study as a supplementary stenosis criterion to detect bilateral RAS which have led to pronounced intrarenal perfusion disturbances on both sides. By including RI values $< 0.45$ as a supplementary stenosis criterion we were able to diagnose bilateral RAS in four of six patients.

False positives with low RI on both sides must be expected, especially with young patients or in cases of tachycardia, where reduced resistive indices are measured [21,22]. Diagnosis of a bilateral RAS should therefore be approached in a critical spirit, taking the effective influencing variables into account.

Using combined evaluation of the above-noted stenosis criteria ($\Delta RI% > 8\%$ and/or $RI < 0.45$), we overlooked a total of 6 RAS in four patients, including false negative test results in two with bilateral RAS. False negatives with bilateral RAS must therefore be estimated as the most important error source of the method.

False negative duplex tests may provide false reassurance that a RAS is absent in patients who should be selected for interventional therapy. As a consequence, in a high-prevalence population (prevalence $>20\%$) patients should undergo angiography as the safest diagnostic procedure. However, in a lower-prevalence population angiography is not justified, and investigators are interested in a non-invasive screening for RAS. Colour duplex US may be an useful screening procedure because it can predict the presence or absence of severe RAS with high degree of accuracy. According to this, larger duplex US studies are needed in a low-prevalence population to evaluate colour duplex US as screening procedure.

Determination of intrarenal RI detects stenoses in all locations, with no ability to differentiate positions in the main renal artery. Differentiation of morphological (eccentric, concentric) or pathogenetic attributions (fibrodysplastic, atherosclerotic) of a stenosis is impossible. Stenoses affecting only a segment artery or an accessory artery may lead to intrarenal $\Delta RI$ and can be localized coarsely.

Doppler sonographic detection of stenosis-induced changes in renal haemodynamics through the reduced RI is based on the functional effectiveness of the existing stenoses. Duplex US testing should therefore be regarded as a functional diagnostic method allowing lateral localization in cases of unilateral RAS. According to Schwerk et al.’s studies, it is possible to grade the extent of the RAS [14]. Given sufficient experience, the test procedure is relatively undemanding and can in our experience be carried out reliably and reproducibly within less than 20 min. The technique described in the paper is of comparable value to other diagnostic methods for detecting a RAS such as captopril test or DTPA scintigraphy with ACE inhibition and therefore offers a simple diagnostic alternative for the detection of a haemodynamically effective RAS.

In a recently published study the combination of intrarenal and extrarenal Doppler scanning has acquired considerable importance as a screening method for the diagnosis of both moderate and severe RAS [24].

In addition, newer data suggests that the application of the captopril test to renal Duplex ultrasonography increases the sensitivity in detecting renal artery stenosis by inducing the pulse tardus distal to significant stenosis [25,26]. This may provide further pathophysiological informations, which are useful and efficient for identification of patients with renovascular hypertension.

References

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