The pulsatility index and the resistive index in renal arteries. Associations with long-term progression in chronic renal failure

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Abstract

Background. The pulsatility index (PI) and the resistive index (RI) are used as pulsed-wave Doppler measurements of downstream renal artery resistance. PI and RI have been found to correlate with renal vascular resistance, filtration fraction and effective renal plasma flow in chronic renal failure. The aim of the present study was to evaluate the potential relationship between these indices and the rate of decline in renal function, as reflected by changes in different parameters of renal function in patients with chronic renal failure.

Methods. Twenty-one patients (8 females, 13 males, mean age 58 years (range 36–75)) with chronic renal failure were enrolled in the study. Doppler examinations were performed in the segmental arteries by an Acuson 128XP. The PI and the RI was calculated from the blood flow velocities. Parameters of renal function were measured every 3 months, and all patients were followed for 18–21 months. Progression of renal dysfunction was estimated by linear regression of parameters of renal function versus time.

Results. In a multiple regression analysis both PI and RI correlated significantly to the rate of decline in reciprocal serum creatinine (PI: \(r = -0.48, P = 0.03\); RI: \(r = -0.52, P = 0.02\)). Furthermore, when separating the patients in two groups by the median RI value, there was a significant difference between the groups in rate of decline in reciprocal serum creatinine (\(P = 0.02\)). For PI this distinction was also present (\(P = 0.04\)).

Conclusion. PI and RI correlated to the severity of the renal disease, as reflected by the rate of decline in reciprocal serum creatinine during antihypertensive treatment. The median RI or PI value could separate the patients into groups one of slow and another of fast progression.

Key words: duplex scanning; doppler measurements; progression of renal failure; renal artery; renal function; renal haemodynamics

Introduction

The pulsatility index (PI) and the resistive index (RI) are different indices calculated from the blood flow velocities in vessels during the cardiac cycle. PI and RI are used as pulsed-wave Doppler measurements of downstream resistance in arteries. Originally both PI and RI were introduced to detect peripheral vascular diseases [1,2], but are rarely used in these conditions. However, if the indices are measured in renal arteries they are reported as reliable measurements of downstream renal resistance [3–5]. Furthermore, PI has been reported to increase while increasing renal vascular resistance by angiotensin II infusion [6,7]. An increasing amount of information is available about the usefulness of PI and RI in the investigation and monitoring of renal artery stenosis [8–12] and kidney graft rejection [13–15], but only little information is available about their usefulness in chronic renal failure. RI has been reported to correlate to the level of serum creatinine in chronic renal failure [16], but also to be normal in patients with renal diseases limited to the glomeruli [17]. We have previously reported that both PI and RI correlate significantly to the effective renal plasma flow (ERPF), the renal vascular resistance (RVR) and the filtration fraction (FF) in patients with chronic renal failure [5]. In that study an abnormally high PI or RI was associated with a low ERPF, a high RVR and a high FF. This points to the possibility that the indices may be used to monitor the severity of the renal disease.

Therefore the purpose of this study was to examine possible correlations between PI and RI measured at baseline and different measurements of long-term progression in patients with chronic renal failure.

Subjects and methods

Patients

Twenty-one patients, (8 females and 13 males, mean age 58 years (range 36–75)), with chronic renal failure were enrolled in the study. Renal insufficiency was caused by glomerulo-
nephritis in two patients, diabetic nephropathy in five, nephrosclerosis in nine, polycystic kidney disease in three, and contracted kidneys in two patients. All patients were hypertensive and received as antihypertensive medication either isradipine or spirapril, or a combination of the two. The patients were recruited from a longitudinal trial evaluating the influence of the above-mentioned antihypertensive drugs on the progression in chronic renal failure (the IS study). Before entering this Doppler study the antihypertensive treatment had been kept constant for at least 3 months. The antihypertensive medication was kept constant during the study, allowing only changes in diuretics during the study. The patients received either 5 mg of isradipine, 6 mg of spirapril, or a combination of the two periods. The patients were followed for 18–21 months. All patients underwent 99mTc-DTPA (diethylene-triaminepentaacetic acid) renography and ultrasonic examination of the kidneys before entry to the study to exclude subjects with renal artery stenosis or postrenal obstructive disease [18]. The pulsed-wave Doppler examinations were performed by an Acuson 128XP, using a 3.5 MHz transducer during a duplex scan. The Doppler frequency was 5 MHz. The patients were examined in the supine position at least 30 min of rest during the period of constant infusion of 51Cr-EDTA. The kidneys were examined by ultrasonic from a lateral lumbar window. Measurements were performed at the level of the segmental arteries in the hilus area. At least three measurements were done in different segmental arteries in each kidney. The PI and the RI were calculated by the Acuson software. The PI and the RI were calculated as:

\[ PI = \frac{(PSV-MDV)}{MV} \]

and

\[ RI = \frac{(PSV-MDV)}{PSV} \]

where PSV = peak systolic velocity, MDV = minimum diastolic velocity, and MV = mean velocity (time averaged velocity). Doppler measurements were performed at baseline of the study after at least 3 months of constant antihypertensive treatment.

GFR was calculated from the clearance rate of 51Cr-EDTA during constant infusion:

\[ GFR = 1.1 \times \left( \frac{U_{EDTA} \times V_u}{P_{EDTA} \times t} \right) \]

where \( U_{EDTA} \) = 51Cr-EDTA concentration in the urine, \( V_u = \) urine volume, \( P_{EDTA} = 51\text{Cr-EDTA} \) concentration in the plasma, and t = time of the clearance period. The factor 1.1 compensates for the underestimation of GFR by the EDTA clearance method [19]. GFR was always measured at the same time in the morning, as this parameter has a high degree of diurnal variation [20,21].

Effective renal plasma flow (ERPF) was calculated from the clearance rate of paraaminohippuric acid (PAH) during constant infusion:

\[ ERPF = \left( \frac{U_{PAH} \times V_u}{P_{PAH} \times t} \right) \]

where \( U_{PAH} = \) PAH concentration in the urine, \( V_u = \) urine volume, \( P_{PAH} = \) PAH concentration in the plasma, and t = time of the clearance period.

For both measurements, the first h of infusion was used to reach a steady state followed by two 30 min clearance periods. The patients were in a resting supine position during infusion. Urine was collected by free voiding.

The renal blood flow (RBF) and the filtration fraction (FF) were calculated as:

\[ RBF = \frac{ERPF}{(1-HCT)} \]

and

\[ FF = \frac{GFR}{ERPF} \]

where HCT = haematocrit.

Renal vascular resistance (RVR) was calculated as:

\[ RVR = \frac{79680 \times (MAP-12\text{ mmHg})}{RBF} \]

where 79680 is a factor for converting mmHg to dyn/cm², and ml/min to cm²/s, MAP = mean arterial blood pressure. A constant renal venous pressure of 12 mmHg was assumed. Serum and urine level of creatinine and urea were measured by an autoanalyser (Technicon SMAC 3, Tarrytown, NY, USA).

Clearance of creatinine (Ccr) and urea (Ccr) were calculated as:

\[ \frac{C_{cr}}{} = \left( \frac{U_{cr} \times V_u}{S_{cr} \times t} \right) \]

and

\[ \frac{C_{ur}}{} = \left( \frac{U_{ur} \times V_u}{S_{ur} \times t} \right) \]

where \( U_{cr} = \) concentration of creatinine in the urine, \( V_u = \) urine volume, \( S_{cr} = \) serum creatinine, t = 24 h, \( U_{ur} = \) concentration of urea in the urine, and \( S_{ur} = \) serum urea.

All parameters of renal function were measured every 3½ months. All patients were followed for 18–21 months. Progression of renal disease was estimated by linear regression with a GFR estimate as the dependent variable and time as the independent variable. Furthermore, progression was also estimated by linear regression of reciprocal serum creatinine versus time.

All parameters of renal function and haemodynamics were corrected to a standard surface area of 1.73 m².

Statistics

Covariation was expressed by a multiple regression analysis by the least-squares method. Statistical comparisons between groups were made with a two-sample t test. A two-sided 5% level of significance was used. Results are given by the mean values and ranges.

Results

Doppler measurements were successful in all patients except one in whom only RI was possible to calculate. None of the patients suffered from cardiac arrhythmias that could influence the Doppler flow velocity measurements. The mean heart rate was 74 beats per minute (range 60–90).

The mean baseline PI was 1.57 (median 1.55; range 1.02–2.15) and mean baseline RI was 0.76 (median 0.75; range 0.64–0.87).

Progression of renal failure was estimated by the rate of decline in GFR, creatinine clearance, urea
clearance and reciprocal serum creatinine. Covariation between the Doppler indices and the different measures of progression in renal failure was expressed in a multiple regression analysis. In this analysis only progression estimated by reciprocal serum creatinine was significantly correlated to PI and RI (PI: \( r = -0.48; \ P = 0.03 \) and RI: \( r = -0.52; \ P = 0.02 \)) (Figure 1). RI was significantly correlated to the age of the patients (\( r = 0.49; \ P = 0.02 \)), but PI was not (\( r = 0.42; \ P = 0.07 \)). The age was not correlated to progression estimated by reciprocal serum creatinine (\( r = -0.09; \ P = 0.70 \)) or to progression estimated by other methods. In a new multiple regression analysis PI could by described from progression estimated by reciprocal serum creatinine (coefficient \(-2.990\)) and age (coefficient \(0.011\)) (\( r = 0.61; \ P = 0.02 \)). RI could also be describe in a multiple regression analysis by progression estimated by reciprocal serum creatinine (coefficient \(-0.619\)) and age (coefficient \(0.003\)) (\( r = 0.68; \ P = 0.004 \)).

Furthermore, the patients were separated in two groups by either the median baseline PI or RI. Diagnoses of the different subgroups are shown in Table 1. Baseline characteristics of the patients in the different subgroups are listed in Table 2. Patients with a high RI were older than patients with a low RI, only a trend was present regarding PI (Table 2). No difference was present in other baseline characteristics (Table 2). The patients with high baseline PI had a significantly faster progression measured by the rate of decline in reciprocal serum creatinine than the patients with PI lower than the median value (\(-0.065 \ l/(mmol \times 1.73 \ m^2 \times \text{month})\) versus \(-0.020 \ l/(mmol \times 1.73 \ m^2 \times \text{month})\), \( P = 0.02 \)). When separating the patients into two groups by the median baseline RI, patients with high baseline RI also had a significantly faster progression measured the reciprocal serum creatinine than patients with low RI (\(-0.065 \ l/(mmol \times 1.73 \ m^2 \times \text{month})\) versus \(-0.017 \ l/(mmol \times 1.73 \ m^2 \times \text{month})\), \( P = 0.02 \)) in patients with baseline RI lower than median value.

**Discussion**

Studying PI and RI in patients with chronic renal failure we found that a PI higher than 1.55 or a RI higher than 0.75 was associated with a faster decline in renal function evaluated by the reciprocal serum creatinine. Although patients with high indices tended to be older than patients with low indices, the faster progression could not be explained from difference in age as no significant covariation between age and progression was found. Furthermore, we found a significant correlation of PI and RI to the progression of renal failure evaluated by reciprocal serum creatinine. The indices also depended on the age of the patients, and in the multiple regression analysis both indices were significantly correlated to progression and age. To our knowledge similar results have not been demonstrated previously.

We have previously demonstrated correlations between renal haemodynamics and the Doppler indices, suggesting that PI and RI are associated with the severity of renal disease [5]. The indices are calculated from the blood flow velocity during systole and dia-

**Table 1. Diagnoses in the subgroups**

<table>
<thead>
<tr>
<th></th>
<th>PI &lt; 1.55</th>
<th>PI ≥ 1.55</th>
<th>RI &lt; 0.75</th>
<th>RI ≥ 0.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerulonephritis</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Nephrosclerosis</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Contracted kidneys</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

PI, pulsatility index; RI, resistive index.
stole, and a high index is associated with a high difference in velocity between the systole and the diastole. Differences in flow velocities reflect downstream resistance, which could at least in part depend on the degree of arterial stiffness. But also functional changes like angiotensin II infusion [6,7] or vasoconstriction due to hepatic failure [22] may raise the indices without a morphological pathology.

Other studies evaluating R1 in chronic renal failure have demonstrated a correlation of this index to the level of serum creatinine [16,17]. Furthermore, R1 has been found to be normal in renal disease limited to the glomeruli [17], which is not in concordance with the present study and a previous study from our group suggesting a relation between the indices and renal haemodynamics [5]. In patients with acute renal failure PI has been shown to be higher in oliguric patients than in non-oliguric patients [23]. This result also indicates a dependency of the indices upon the severity of the renal disease.

The Doppler derived indices have been used as a marker of acute changes in renal plasma flow and renal vascular resistance in patients with essential hypertension and in healthy volunteers [6–8]. These results underline that the indices also depend upon functional changes. To our knowledge the indices have not been used as markers of chronic changes in renal haemodynamics.

The rate of decline in chronic renal failure is normally monitored by repeated determinations of GFR or simply by the slope of the reciprocal value of serum creatinine. No single-standing parameter has been found useful as a marker of future progression in renal disease. Such a marker would be of great value, as therapy could be intensified before the renal function is lost.

The use of antihypertensive drugs could be a confounder in the present study, as ACE inhibition has been shown to reduce PI in normotensives [6], and to increase R1 in hypertensives [7]. The potential influence of other antihypertensive drugs including diuretics has not been reported. However, the antihypertensive treatment was kept constant during the investigation. Furthermore, the different renal diagnoses could confound the results.

PI and R1 are new parameters reflecting renal haemodynamics. Although the exact information given by these indices is still unknown, the indices in the present study correlated to the severity of the renal disease, measured as the rate of decline in reciprocal serum creatinine during antihypertensive treatment. Of great interest is the question of whether changes in progression will be reflected by similar changes in the Doppler indices. To answer this question further intervention studies are needed.

### Table 2. Patient characteristics (mean values) at baseline in the groups of high and low pulsatility index (PI) and resistive index (RI)

<table>
<thead>
<tr>
<th></th>
<th>PI&lt;1.55 n=10</th>
<th>PI≥1.55 n=10</th>
<th>P</th>
<th>RI&lt;0.75 n=10</th>
<th>RI≥0.75 n=11</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine (µmol/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>205</td>
<td>224</td>
<td>n.s.</td>
<td>213</td>
<td>241</td>
<td>n.s.</td>
</tr>
<tr>
<td>Albuminuria (µmol/24 h)</td>
<td>20.9</td>
<td>12.8</td>
<td>n.s.</td>
<td>21.1</td>
<td>19.6</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean arterial blood pressure (mmHg)</td>
<td>111</td>
<td>105</td>
<td>n.s.</td>
<td>112</td>
<td>107</td>
<td>n.s.</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>76</td>
<td>72</td>
<td>n.s.</td>
<td>76</td>
<td>71</td>
<td>n.s.</td>
</tr>
<tr>
<td>GFR (ml/min*1.73 m²)</td>
<td>32</td>
<td>28</td>
<td>n.s.</td>
<td>29</td>
<td>29</td>
<td>n.s.</td>
</tr>
<tr>
<td>ERPF (ml/min*1.73 m²)</td>
<td>297</td>
<td>250</td>
<td>n.s.</td>
<td>284</td>
<td>247</td>
<td>n.s.</td>
</tr>
<tr>
<td>Filtration fraction (%)</td>
<td>14</td>
<td>12</td>
<td>n.s.</td>
<td>14</td>
<td>13</td>
<td>n.s.</td>
</tr>
<tr>
<td>RVR (dyn<em>s</em>cm⁻⁵)</td>
<td>29951</td>
<td>27108</td>
<td>n.s.</td>
<td>32325</td>
<td>30501</td>
<td>n.s.</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54</td>
<td>63</td>
<td>0.08</td>
<td>53</td>
<td>63</td>
<td>0.04</td>
</tr>
</tbody>
</table>

GFR, glomerular filtration rate; ERPF, effective renal plasma flow; RVR, renal vascular resistance.

### References


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