Captopril renography and duplex Doppler sonography in the diagnosis of renovascular hypertension

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Abstract

Background. The purpose of this prospective study was to determine the clinical usefulness of captopril renal scintigraphy and duplex Doppler sonography in detecting haemodynamically significant renal artery stenosis (≥60%) and predicting cure or improvement of hypertension following revascularisation.

Methods. Twenty-eight patients with moderate or high index of clinical suspicion of renovascular hypertension underwent both captopril renal scintigraphy and duplex Doppler sonography before undergoing renal angiography. Patients with angiographically proved (≥60%) RAS were treated by percutaneous transluminal renal angioplasty unless it was contraindicated.

Results. The results of captopril renal scintigraphy and duplex Doppler sonography were compared by renal angiography of 45 renal arteries in 28 patients. Eleven renal arteries were excluded from further comparison, because no accurate Doppler signal could be obtained. The sensitivity and specificity of captopril renal scintigraphy in the identification of RAS (≥60%) was 78% and 81% respectively. The sensitivity of duplex Doppler sonography was 83% and the specificity was 81%. Positive predictive values of both tests for blood pressure cure or improvement after PTRA were 86% for CRS and 85% for DDS.

Conclusions. Captopril renal scintigraphy and duplex Doppler sonography are comparable tests for detection of patients with haemodynamically significant renal artery stenosis (≥60%). Positive predictive values of both tests for cure or improvement of hypertension after percutaneous transluminal renal angioplasty are good and comparable.

Key words: captopril renal scintigraphy; duplex Doppler sonography; renovascular hypertension

Introduction

Renovascular diseases which narrow the lumen of the renal arteries or their branches may lead to renovascular hypertension (RH), which is the most common potentially curable cause of hypertension and ischaemic renal disease [1]. In the light of the reported good therapeutic results (cure or improvement of hypertension and preservation of renal function) from percutaneous transluminal renal angioplasty (PTRA) and surgical revascularization, it is important to detect haemodynamically significant renal artery stenosis (RAS) early enough so that patients can benefit from treatment [2,3].

The diagnosis of RH is complicated because of the absence of a specific clinical picture and the fact that RAS occurs in normotensives as well as in patients with essential hypertension [4]. In spite of intensive research, an ideal screening test for RH has not been determined and diagnostic approaches to patients with clinical suspicion of RH vary. Recent studies show that captopril renal scintigraphy (CRS) is a good functional test providing a prognosis regarding revascularization therapy [5,6]. Duplex Doppler sonography (DDS), which combines direct visualization of the renal artery with Doppler measurement of renal artery blood flow velocity, provides both anatomical and functional assessment [7,8].

The purpose of our study was to determine and compare (a) sensitivity and specificity of CRS and DDS in detecting RAS ≥60%, experimentally determined as haemodynamically significant, and (b) positive predictive values of both tests for cure or improvement of hypertension after revascularization with PTRA.

Subjects and methods

We prospectively analysed 28 patients (17 women and 11 men, mean age 50 years, range 32–68) who were referred to our Department of Nephrology between January 1993 and December 1995 for evaluation of hypertension. Patients were selected for this study on the basis of the present clinical criteria of high or moderate possibility of RH as described by Mann and Pickering [9]. The most common clinical criterion was severe hypertension refractory to multiple antihypertensive drug therapy 16/28 (57%) patients were taking three or more antihypertensive drugs at the time of admission to the hospital; the mean baseline systolic blood pressure...
was 175 mmHg and the mean diastolic blood pressure was 106 mmHg). Hypertension with recent elevation of serum creatinine (>120 \( \mu \text{mol/L} \)) was found in 10 patients (36%). The suggestive abdominal bruit was present in 11 patients (39%).

All the patients underwent CRS and DDS before undergoing renal angiography or mostly IDSA. The findings of both screening tests were compared with the results of renal angiography which is the standard morphological method. The patients with angiographically proved \( \geq 60\% \) RAS in whom at least one of both non-invasive tests was positive, were treated by PTRA unless it was contraindicated.

Captopril renal scintigraphy

Renography with 99mTc mercaptoacetyltriglycine (MAG3) was performed in the supine position according to the following protocol. Antihypertensive medication was generally not altered prior to scanning with the exception of diuretics, which were excluded from therapy at least 48 h before investigation. All the patients were given 500 ml water for proper hydration 30 min before the study. The first postcaptopril renal scintigraphy was carried out 1 h after oral administration of 25 mg of captopril. If the result was positive, the basal scan without captopril was done. In patients who were receiving angiotensin-converting enzyme inhibitors (ACEI) for control of hypertension, scanning was performed initially on their normal medication and then after withdrawing therapy with ACEI for at least 14 days. The results of CRS and renal scintigraphy at basal conditions were compared.

Criteria suggestive of haemodynamically significant RAS \( \geq 60\% \) were: (a) a 5% or greater decline in MAG3 uptake of more than 120 mmHg/the aortic arch and/or (b) prolongation of mean parenchymal transit time (longer than 300 s) after captopril administration compared to renography under basal conditions [10,11].

Duplex Doppler sonography

Examinations were performed by three clinical nephrologists experienced in the technique. Colour duplex scanner with a 3.5-MHz transducer (Acuson X P/10, USA) was used. The patients were prepared for examination receiving a light diet for 1–2 days before following by fasting for 12 h and purgatives to reduce bowel gas artefacts. The presence, localization, and haemodynamic significance of RAS were determined. Criteria suggestive of RAS \( \geq 60\% \) were: (a) peak systolic renal artery velocity >180 cm/s and (b) renal artery aortic ratio (RAR) above 3.5 [8,13]. Other signs were poststenotic reduction of blood flow velocity, turbulence and reduced kidney length (<8 cm). A diagnosis of occlusion was made if the vessel was visualized, but no Doppler signal was obtained. If one or both renal arteries were insufficiently visualized to obtain Doppler signals, the procedure was considered a failure in that patient.

Renal angiography

The patients underwent either conventional abdominal aortography or mostly IDSA. The presence, localization, degree, aetiology and haemodynamic significance of RAS were determined. The localization of the stenosis was assessed by the same principle as for DDS. The degree of the stenosis was evaluated visually and by measurement of the diameters of the narrowed segment and the nearest normal part of the renal artery. The degree of the stenosis was expressed as the percentage of narrowing. Following other studies [8,22] we classified renal arteries according to the presence and the degree of stenosis into three categories: 0–59%, 60–99%, and occlusion. Radiographic criteria used for assessment of haemodynamic significance of the RAS were: RAS \( \geq 60\% \), collateral circulation, and poststenotic dilatation of the renal artery [14].

In order to evaluate the agreement between the results of DDS and CRS with renal angiography in detecting \( \geq 60\% \) RAS, sensitivity, specificity, positive and negative predictive values, and accuracy of both tests were calculated (Table 1b and 2b).

PTRA

The patients with angiographically proved RAS \( \geq 60\% \) were treated by PTRA. All the procedures were performed according to the standard technique [15]. The criterion for technically successful dilatation of the stenosis was residual stenosis <30%. In cases where residual stenosis exceeded 30%, the renal artery was stented. The blood pressure response to the intervention, which was the basic criterion of clinical success rate, was assessed at an average of 15 months after the procedure.

According to the US co-operative study for RH criteria [16] we have divided our patients in the following groups:

- **Cured.** Patients with diastolic blood pressure (DBP) 90 mmHg or less without medication and with at least 10 mmHg decrease from the preinterventional level.
- **Improved.** Patients with a minimum of 15% decrease in DBP, and whose DBP was greater than 90 mmHg but less than 110 mmHg.
- **Failure.** Patients with less than a 15% decrease in DBP and whose DBP was more than 110 mmHg.

The cured and improved patients were considered as successfully treated.

Results

Renal angiography

In 28 patients that we studied, 56 main renal arteries were angiographically investigated. In 24/28 patients (85.7%) renal angiography revealed RAS which was unilateral in 15 cases and bilateral in nine. Thirty-three of 56 renal arteries were found to be affected by renovascular disease (58.9%). RAS \( \geq 60\% \) was detected in 24/33 affected arteries (72.7%); one of those renal arteries was occluded, while RAS <60% was identified in 9/33 (27.3%). Twenty-three renal arteries were angiographically normal (41.1%). The aetiology of stenosis as assessed by arteriography was atherosclerosis in 20 patients (83.3%) and fibromuscular dysplasia in four (16.7%). The mean age of the patients with atherosclerosis and fibromuscular dysplasia was 53 years (range 36–68) and 42.5 years (range 32–56) respectively.

The results of CRS and DDS were compared with the results of renal angiography for 45 renal arteries successfully investigated with both screening tests. Eleven renal arteries were excluded from further comparison because they could not be visualized with DDS (Tables 1 and 2).
Table 1(a). Comparison of captopril renal scintigraphy with renal angiography in 45 renal arteries

<table>
<thead>
<tr>
<th>Status of the renal artery</th>
<th>Renal angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>No stenosis</td>
<td>&lt;60%</td>
</tr>
<tr>
<td>No stenosis</td>
<td>15</td>
</tr>
<tr>
<td>&lt;60%</td>
<td>0</td>
</tr>
<tr>
<td>≥60%</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
</tr>
</tbody>
</table>

CRS, captopril renal scintigraphy

Table 1(b). Detection of renal artery stenosis ≥60% with captopril renal scintigraphy

<table>
<thead>
<tr>
<th>Percentage stenosis</th>
<th>Renal angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60%</td>
<td>(a) 14</td>
</tr>
<tr>
<td>0–59%</td>
<td>(b) 4</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
</tr>
</tbody>
</table>

CRS, captopril renal scintigraphy; sensitivity, a/(a + b) = 78%; specificity, d/(c + d) = 81%; positive predictive value, a/(a + c) = 74%; negative predictive value, d/(b + d) = 85%.

Table 2(a). Comparison of duplex Doppler sonography with renal angiography in 45 renal arteries

<table>
<thead>
<tr>
<th>Status of the renal artery</th>
<th>Renal angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>No stenosis</td>
<td>&lt;60%</td>
</tr>
<tr>
<td>No stenosis</td>
<td>17</td>
</tr>
<tr>
<td>&lt;60%</td>
<td>0</td>
</tr>
<tr>
<td>≥60%</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
</tr>
</tbody>
</table>

DDS, duplex Doppler sonography

Table 2(b). Detection of renal artery stenosis ≥60% with duplex Doppler sonography

<table>
<thead>
<tr>
<th>Percentage stenosis</th>
<th>Renal angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60%</td>
<td>(a) 15</td>
</tr>
<tr>
<td>0–59%</td>
<td>(b) 3</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
</tr>
</tbody>
</table>

DDS, duplex Doppler sonography; sensitivity, a/(a + b) = 83%; specificity, d/(c + d) = 81%; positive predictive value, a/(a + c) = 75%; negative predictive value, d/(b + d) = 88%.

CRS

CRS revealed RAS regardless of the percentage of occlusion in 16/27 affected renal arteries (59%) with 11 false negative cases. RAS ≥60% was correctly identified in 14/18 renal arteries (sensitivity for detecting RAS ≥60% was 78%). With this method we could not identify any of RAS <60%. In two cases the stenosis was assessed as haemodynamically significant and the result of CRS was normal in seven cases. Of 27 angiographically normal or <60% narrowed renal arteries, the result of CRS was correctly negative in 22 cases and false positive in five (specificity for detecting RAS ≥60% was 81%).

DDS

In 8/28 patients (28.5%) the procedure was considered to be technically inadequate (in 4 of them RAS was bilateral). Visualization of 11/56 renal arteries was not possible (19.6%). Five of those arteries were angiographically normal and six were narrowed 60% or more. DDS identified RAS in 26 of 27 affected renal arteries (96%). The result was false negative in only one case. RAS ≥60% was correctly detected in 15/18 renal arteries (sensitivity for detecting RAS ≥60% was 83%), while RAS <60% was correctly identified in 5/9 cases (56%). Of the 27 renal arteries angiographically normal or narrowed <60%, the result of DDS was correctly negative in 22 cases and false positive in five (specificity for detecting RAS ≥60% was 81%).

Sensitivity, specificity, positive and negative predictive, and accuracy of DDS and CRS in detecting different degrees of RAS are presented in Table 3.

Table 3. The results of captopril renal scintigraphy and duplex Doppler sonography versus renal arteriography

<table>
<thead>
<tr>
<th>Detection of renal artery stenosis</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60%</td>
<td>78% (14/18)</td>
<td>81% (22/27)</td>
<td>74%</td>
<td>85%</td>
<td>80%</td>
</tr>
<tr>
<td>All stenoses</td>
<td>59% (16/27)</td>
<td>83% (15/18)</td>
<td>84%</td>
<td>58%</td>
<td>69%</td>
</tr>
</tbody>
</table>

CRS, captopril renal scintigraphy; DDS, duplex Doppler sonography.

Revascularization by PTRA

Sixteen patients were treated with PTRA, in three patients the intervention was bilateral. The procedure was technically successful in 14/16 patients (88%). Two renal arteries (in 2 pts) were stented. According to the blood pressure response to the intervention, the treatment was clinically successful in 11 of 13 patients with positive DDS and in 12 of 14 patients with a positive CRS result.

Table 4 shows the prediction of cure or improvement of hypertension after PTRA on the basis of DDS and CRS changes.
Table 4. Positive predictive values of captopril renal scintigraphy and duplex Doppler sonography for cure or improvement of hypertension after treatment with percutaneous transluminal renal angioplasty

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Cured or improved</th>
<th>Not improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS changes present</td>
<td>12/14 (86%)</td>
<td>2</td>
</tr>
<tr>
<td>DDS changes present</td>
<td>11/13 (85%)</td>
<td>2</td>
</tr>
</tbody>
</table>

Discussion

Numerous diagnostic tests have been proposed to detect patients with RH, but none of them has achieved a widespread clinical acceptance, and to date the ideal screening test is still not available. The ideal screening test for RH should not only determine the presence of RAS, but also define its localization, assess haemodynamic significance, and predict cure or improvement of hypertension after revascularization. The important problem in the diagnosis of RH is low prevalence of the disease in the hypertensive population and resultant low predictive value of any screening test. Accordingly, we analysed only patients with moderate [11] or high [17] index of clinical suspicion for RH. The resultant high prevalence of the renovascular disease in our group of patients (86%) confirms the value of clinical suspicion in deciding on a diagnostic plan.

Renal-vein renin activity, one of the first tests for recognition of curable form of RH has many disadvantages. Various studies confirmed that the positive predictive value of the test is high, but the negative result does not exclude the possibility of successful treatment [17]. Although many authorities consider standard arteriography as the first diagnostic intervention in most patients, it is an invasive procedure, which can only establish the presence of RAS, but not its functionality, so the method cannot reliably differentiate between anatomical stenosis and RH [9]. The only accurate criterion for diagnosing RH remains blood pressure response to the revascularization procedure. Accordingly, we have compared the results of both non-invasive tests, DDS and CRS, with blood pressure response after PTRA.

In recent years several groups have reported that CRS is a sensitive screening procedure for identification of haemodynamically significant RAS and a strong predictor of improvement of blood pressure control with revascularization [5,6,10]. Because the diagnostic criteria suggested by the committee for diagnostic measures for RH [18] are too complex to be followed in clinical practice, we have used the criteria that are most reliable and are the easiest to assess. All the procedures were performed with radiotracer 99mTc–MAG3, which has a comparable diagnostic accuracy with other tubular or glomerular agents and is most suitable in patients with renal function impairment [10,19]. The results of our study correlate well with studies published by Fommei et al. (SE 89%, SP 90%) [6] and Maher et al. (SE 85%, SP 72%) [11]. The slightly worse results in comparison with some other studies [5,6] can be due to the relatively high percentage of our patients with renal insufficiency (36% patients had serum creatinine ≥ 120 µmol/l).

Since duplex Doppler has become widely available, many investigators propose DDS as a screening technique for RH. The important advantage of DDS over other screening tests is that this method enables detection of haemodynamically insignificant RAS, which is important because of the progressive course of renovascular disease. Difficulties in accurate identification of the renal arteries and resultant high percentage of technical failure of DDS is an important limiting factor in this method. In our study examinations were performed by clinical nephrologists experienced in this technique. The percentage of technical failure was comparable with other studies [20], but relatively high, especially if we consider the percentage of unsuccessfully examined patients. The main reasons for unsuccessful examinations were obesity and bowel gas despite the specific instructions regarding diet and use of purgatives before examination. Using the same diagnostic criteria, sensitivity of DDS correlates best with studies published by Taylor et al. (SE 84%, SP 97%) [21] and Miralles et al. (SE 89.5%, SP 90.7%) [22].

We have confirmed the conclusions of Dondi et al. [23] that DDS and CRS are effective and comparable methods for the detection of haemodynamically significant RAS. The sensitivity of the two tests differed significantly based on the degree of stenosis. With CRS we could not identify any haemodynamically insignificant stenosis, which reflects the functional principle of this test. It enables identification of RAS on the basis of its haemodynamic significance, resultant hypoperfusion of the kidney and pharmacological blockade of activated renin–angiotensin system. On the contrary, the principle of DDS is based on change in blood flow velocity, which increases linearly with reduction in the diameter of the renal artery, enabling identification of lesser degrees of stenosis which are haemodynamically insignificant [23]. An important finding of our study is that DDS is capable of predicting success or failure of therapeutic intervention. Its accuracy is satisfactory and comparable with CRS.

In conclusion CRS and DDS are comparable tests for assessing renovascular hypertension in patients with moderate and high clinical criteria for RH. The selection of the screening test in patients with clinical suspicion for RH must be individual, depending on patient characteristics, availability of, and performer’s experiences in individual centres.

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