Renal Scintigraphic Captopril Test in the Diagnosis of Renovascular Hypertension

ENZA FOMMEI, SERGIO GHIONE, LINO PALLA, FRANCO MOSCA, MAURO FERRARI, CARLO PALOMBO, STEFANO GIACONI, PAOLO GAZZETTI, AND LUIGI DONATO

SUMMARY Angiotensin converting enzyme (ACE) inhibitor--induced renal failure has been reported in bilateral renal artery stenosis and in stenosis in solitary kidneys, but not in unilateral renal artery stenosis. In these patients, however, a functional impairment of the kidney ipsilateral to the stenosis can often be detected after ACE inhibition by scintigraphic techniques employing glomerular radionuclide tracers like 99mTc-diethylenetriamine pentaacetic acid (DTPA). Dynamic renal scintigraphy with 99mTc-DTPA before and 1 hour after administration of captopril, 25 mg (renal scintigraphic captopril test; RSCT), was performed in a selected series of 39 hypertensive subjects with suspected renovascular hypertension. Changes in glomerular filtration rate induced by captopril on the individual kidney were estimated by assessing the early (120-180 seconds) DTPA uptake by the kidney. Values were expressed as the ratio between the kidney with the lower uptake and the contralateral one in 34 patients and as the ratio of the kidney counts to the injected dose in five patients with solitary kidneys, aortic coarctation, or both. Compared with precaptopril values, postcaptopril uptake decreased markedly in 14 subjects (-62.42 ± 30.94 [SD]%: range, -25 to -100%) and decreased modestly or even increased in the other 25 (+0.57 ± 9.83%; range, +28 to +13%). Of the 14 subjects considered to be RSCT-positive diagnostic workup revealed either established (10) or strongly suspected (2) renal artery stenosis in 12 and aortic coarctation in 2 subjects. In another patient with established renovascular hypertension, results of the RSCT were negative when performed in the supine position but became positive when repeated in the sitting position. Nine patients underwent repair of stenosis by either operation or angioplasty, and a striking correspondence was observed between response to RSCT and success of intervention. Taken together these findings strongly suggest that renal scintigraphy after ACE inhibition represents a promising tool for diagnosis of renovascular hypertension and its follow-up after operation or angioplasty. (Hypertension 10: 212-220, 1987)

KEY WORDS • renovascular hypertension • angiotensin converting enzyme inhibition • renal scintigraphy

It is well known that suppression of the renin-angiotensin system by angiotensin converting enzyme (ACE) inhibition may induce reversible renal failure in hypertensive patients with bilateral renal artery stenosis or with renal artery stenosis and a single kidney because of a critical decrease of glomerular filtration rate (GFR).1-3 Perhaps not surprisingly, in patients with unilateral renal artery stenosis GFR also may be reduced in the kidney ipsilateral to the stenosis after inhibition of ACE. In these patients, however, functional renal impairment usually is not clinically detectable (because of the compensatory function of the intact contralateral kidney), but it can be demonstrated by scintigraphic techniques, as recently reported by several authors. To our knowledge, the first to report on this effect were Majd et al.,4 who observed that captopril induced a unilateral renal functional impairment on the affected side detectable by renal scintigraphy in four children with unilateral renal artery stenosis. These results were partially confirmed by Wenting et al.,5 who reported that, in seven of 14 patients with unilateral renal artery stenosis receiving short-term captopril treatment, the uptake by the affected kidney of the glomerular tracer 99mTc-diethylenetriamine pentaacetic acid (DTPA) was markedly decreased, indicating an almost complete suppression
of GFR on this side. Oei et al.\(^6\) reported similar results in five of seven patients with angiographically proven unilateral artery stenosis and severe hypertension who underwent percutaneous transluminal angioplasty. Interestingly, Oei et al.\(^5\) reported an association between the renographic abnormalities induced by captopril and the therapeutic success of percutaneous transluminal angioplasty, since only the five patients with abnormal renograms were cured by this procedure. The growing interest in this potentially diagnostic technique is apparent from the increasing number of papers reporting both clinical and experimental observations on this subject.\(^1\)-\(^10\)

In two preliminary accounts\(^1\),\(^12\) we also reported similar results. The present report details our comparison of 14 patients with abnormal postcaptopril DTPA renal scintigrams with a group of patients with normal scintigrams. Moreover, we compared the scintigraphic observations with the concomitant responses to captopril of blood pressure (BP) and plasma renin activity (PRA) and, in several patients, with the effects of vascular repair by operation or angioplasty.

**Subjects and Methods**

**Subjects**

This study retrospectively reports the data of 39 hypertensive patients who underwent renal scintigraphy before and after captopril administration as a diagnostic tool. Our series represents a mixed population, comprising both patients referred to us from other departments because of strong diagnostic suspicion of renovascular hypertension and unsel ected hypertensive patients attending our outpatient clinic. All patients had a diagnosis of arterial hypertension, although in some, who were not under antihypertensive treatment, BP was found to be in the normal range on the day of the test (after a period of quiet rest, in a supine position). All had normal serum creatinine levels at the time of scintigraphic evaluation, except for one with slightly increased levels (132 \(\mu\)mol/L). Informed consent was obtained from each patient. All antihypertensive medications were maintained, except for ACE inhibitors and diuretics, which were discontinued at least 3 days before the scintigraphic study. No drug was administered on the day of the test.

**Scintigraphic Protocol**

Each patient underwent two dynamic renal scintigraphic studies: one before and the other 1 hour after oral administration of captopril (25 mg). The second scintigraphic study was performed on the same day, 2 hours after the first study. \(^{99m}\)Tc-DTPA (7 mCi) was used as a tracer and injected intravenously. Immediately after injection, a sequence of kidney images was acquired by a large field-of-view gamma camera (Medusa 12B; Sepa, Turin, Italy), at a rate of one frame/20 seconds for 15 minutes, with the patient lying on his or her back over the collimator. Immediately before the injection of the second dose, a 20-second image was acquired, as representative of the residual renal activity after the first bolus, and subsequently was subtracted from each frame of the second scintigraphic study.

The third-minute summation image was displayed on a video screen, and two regions of interest were traced on each side, over the renal parenchyma and a background area surrounding the kidney. By subtracting the background activity–time curves from the renal ones, renographic curves were obtained (Figure 1). An estimate of the ratio of GFR between the two kidneys was obtained as the ratio of the corresponding kidney counts 120 to 180 seconds after tracer injection. Results of both studies were always expressed as the ratio of the uptake of the kidney with the lower uptake to the contralateral one, as observed in the first study, except for five patients with single scintigraphically detectable kidney, aortic coarctation, or both, in whom the ratio of kidney counts to the injected dose (acquired for 60 seconds) was calculated as an index of GFR\(^13\) and expressed as (kidney counts 120–180 seconds) \times 1000/dose.

The renograms of the two kidneys were also compared for the upslope of the first and second segments of the curves, reflecting mainly the perfusion and parenchymal accumulation phases, respectively.\(^14\),\(^15\) The presence of a reduced upslope of the first or second segment, or both, in one curve compared with the other was considered suggestive of a functional asymmetry. In the patients with a single kidney, in whom this comparison was impossible, the renogram was considered abnormal when the renographic curve was clearly delayed.

**Blood Pressure and PRA Measurements**

Immediately after the first scintigraphic study, patients remained supine in a quiet room and BP was measured for 15 minutes at 3-minute intervals by an automatic recorder (Dinamap 845 vital signs monitor; Critikon, Tampa, FL, USA). A blood sample was then taken for PRA determination (angiotensin I radioimmunoassay kit; Sorin Biomedica, Saluggia, Italy), and 25 mg of captopril was administered. BP measurements were continued for 1 hour, and then a second blood sample was taken. The average of the last two BP measurements before each blood sample was used in the evaluation of the results. All results are expressed as means \(\pm\) SD. The Student’s \(t\) test for paired data was used to compare within-groups changes.

**Results**

As shown in Figure 2A, captopril induced various changes in the renal DTPA uptake ratio in the patients studied. In 10 patients the DTPA uptake ratio decreased markedly, indicating a deterioration of GFR on the side where glomerular filtration was already reduced before administration of captopril, whereas in the remaining 24 it either decreased very slightly or increased. In the five subjects with a single kidney,
FIGURE 1. Scintigraphic images (third minute after injection) and activity-time curves, before (left side) and after (right side) captopril administration in one patient with right renal artery stenosis. Marked decrease of right kidney DTPA uptake occurred after captopril treatment. The right renogram had aspects of a blood disappearance curve.

FIGURE 2. Effect of captopril on renal DTPA uptake: absolute and percentage changes in the individual patients. A. Changes of the DTPA uptake ratio (UR) between the two kidneys in two-kidney patients (n = 34). B. Changes of the renal uptake as fraction of the injected dose in patients with a single kidney, aortic coarctation, or both (n = 5).
aortic coarctation, or both, in whom GFR was estimated as the ratio of the kidney counts to the injected dose (Figure 2B), a marked reduction of uptake was observed in four patients and only a modest one in the fifth.

When the postcaptopril results of both groups were expressed as percentage changes relative to precaptopril values, 25 patients had a variation of less than -15% (ranging from +28 to -13%) and 14, of more than -25% (ranging from -25 to -100%). Since the two groups appeared to be clearly distinct, the first was considered to have negative and the second positive renal scintigraphic captopril test (RSCT) results. The individual data of the clinical features, including medications and responses to captopril of PRA, BP, and DTPA uptake in the two groups, are reported in Tables 1 and 2, respectively.

### Patients with Negative Test Results

The RSCT-negative group contained 11 male and 14 female patients with a mean age of 43.88 years (age range, 15–73 years). Diagnostic workup for renovascular hypertension included evaluation of PRA before and after administration of captopril (in 23), rapid-sequence pyelography (in 18), renal vein PRA (in 5), and arteriography (in 10). Seven patients met examination criteria for unilateral renal dysfunction at baseline renographic evaluation, but only in two was unilateral renal artery stenosis found on arteriography (Patients 11 and 12). In one (Patient 11), the RSCT results were strongly positive when repeated in the sitting position; he underwent percutaneous transluminal angioplasty, and BP was normalized 3 months after intervention. The other patient remained hypertensive after operation, despite a well-functioning bypass.

### Table 1. Clinical Features, Diagnostic Criteria, and Responses to Captopril of BP, PRA, and DTPA Uptake in Patients with Negative Renal Scintigraphic Captopril Test Results

<table>
<thead>
<tr>
<th>Patient no., sex, age (yr)</th>
<th>Medication</th>
<th>Diagnostic tests for RHT</th>
<th>Arterial BP (mm Hg)</th>
<th>PRA (ng ANG I/ml/hr)</th>
<th>DTPA uptake*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IVP AG RVRR Renogr.</td>
<td>After Baseline</td>
<td>After Baseline</td>
<td></td>
</tr>
<tr>
<td><strong>PRA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>captopril</td>
<td>captopril</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1, M, 34</td>
<td>Nifedipine</td>
<td>- - -</td>
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<td>175/113</td>
<td>1.45 2.40</td>
</tr>
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<td></td>
<td>1.50 2.50</td>
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<td>125/64</td>
<td>1.30 1.70</td>
</tr>
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<td>156/109</td>
<td>135/96</td>
<td>1.13 1.13</td>
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<td>5, F, 39</td>
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<td>- - -</td>
<td>142/95</td>
<td>126/75</td>
<td>6.13 6.00</td>
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<tr>
<td>6, F, 35</td>
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<td>157/96</td>
<td></td>
<td>5.26 4.26</td>
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<tr>
<td>7, F, 35</td>
<td>Indapamide</td>
<td>- - -</td>
<td>132/78</td>
<td>121/78</td>
<td>1.80 2.10</td>
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<tr>
<td>8, F, 53</td>
<td>Atenolol</td>
<td>- - -</td>
<td>166/104</td>
<td>144/98</td>
<td>2.23 2.51</td>
</tr>
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<td>9, F, 73</td>
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<td>- - +</td>
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<td>180/86</td>
<td>0.96 1.84</td>
</tr>
<tr>
<td>10, M, 55</td>
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<td>- - -</td>
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<td>138/88</td>
<td>0.16 0.94</td>
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<tr>
<td>11, M, 15</td>
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<td>+ + -</td>
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<td>158/87</td>
<td>0.10 0.94</td>
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</tr>
<tr>
<td>13, F, 46</td>
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<td>0.96 1.31</td>
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<tr>
<td>14, M, 43</td>
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<td>134/65</td>
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<td>125/69</td>
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</tr>
<tr>
<td>17, M, 38</td>
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<td>- - -</td>
<td>153/102</td>
<td>149/100</td>
<td>1.30 2.60</td>
</tr>
<tr>
<td>18, M, 69</td>
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<td>- - -</td>
<td>200/102</td>
<td>177/77</td>
<td>1.80 0.60</td>
</tr>
<tr>
<td>19, F, 50</td>
<td>Atenolol</td>
<td>- - -</td>
<td>163/116</td>
<td>156/104</td>
<td>2.20 2.13</td>
</tr>
<tr>
<td>20, F, 47</td>
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<td>- - -</td>
<td>142/104</td>
<td>135/86</td>
<td>1.41 1.24</td>
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<td>- - -</td>
<td>142/104</td>
<td>192/115</td>
<td>1.00 0.40</td>
</tr>
<tr>
<td>22, F, 36</td>
<td>None</td>
<td>- - -</td>
<td>163/114</td>
<td>146/102</td>
<td>1.99 0.98</td>
</tr>
<tr>
<td>23, F, 50</td>
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<td>- - -</td>
<td>137/95</td>
<td>119/89</td>
<td>5.80 10.00</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>155 497.1</td>
<td>145 388.1</td>
<td>1.88 2.41</td>
</tr>
<tr>
<td>± SD</td>
<td></td>
<td></td>
<td>20 316.6</td>
<td>21 314.4</td>
<td>1.64 2.14†</td>
</tr>
</tbody>
</table>

* = abnormal results; - = normal results; RHT = renovascular hypertension; IVP = intravenous pyelography suggestive of RHT; AG = arteriographic finding of a stenosis of the renal artery; RVRR = renal vein renin ratio >1.5; Renogr. = unilateral renographic abnormalities suggestive of RHT (see also text); ANG I = angiotensin I.

*DTPA uptake was expressed for all patients as the uptake ratio between the two kidneys, except for Patient 7, who had a single kidney, in whom DTPA uptake was expressed as fraction of the injected dose x 1000, and who was excluded from statistical analysis (see also text). *tp<0.05, **tp<0.001, compared with pretreatment values.
curves after captopril administration were clearly normalized after intervention. The remaining two patients (Patients 30 and 34) had stenosis of the branch (Figure 3), and two had an aortic coarctation. Of these, nine patients had stenosis of the main renal artery, one had stenosis of a renal artery branch (Figure 3), and two had an aortic coarctation. The remaining two patients (Patients 30 and 34) had intravenous pyelographic (IVP) findings suggestive of renovascular hypertension but refused to undergo further investigation. Two other patients with positive RSCT results also had abnormal IVPs. All four patients, in whom renal vein PRA was determined had a significant laterization (PRA ratio > 1.5). Inspection of baseline renograms suggested unilateral renal dysfunction in eight patients. Surgical repair or angioplasty was performed in seven patients and was technically successful in six; in this latter group BP normalized after intervention.

On inspection, the activity-time (renographic) curves after captopril administration were clearly modified in 11 of the 14 patients with positive results; a typical example is shown in Figure 1. In four of these patients, after captopril treatment, the second and third phases of the renogram (which reflect, respectively, the parenchymal uptake and the excretion phase of the tracer) were absent and the curve closely resembled a blood disappearance (first-pass) curve. In the remaining seven patients, the second and third phases were visible but clearly delayed. The three patients without clear renographic modifications were represented by the two patients with aortic coarctation and by a patient with a single kidney and segmental renal artery stenosis (Patient 36). As shown in Table 2, after captopril treatment, on average, PRA increased and BP and DTPA uptake decreased.

An adverse effect to captopril was observed only in one patient (Patient 37, RSCT-positive, with renal artery stenosis and a single kidney) who exhibited symptoms of orthostatic hypotension at the end of the study and in whom creatinine levels increased from 132 to 352 µmol/L but returned to normal within 2 days.

Effect of Repair of the Stenosis
Nine patients underwent repair of the stenosis either by surgical revascularization or by angioplasty; in these patients the test was repeated at various intervals after intervention and revealed a good correspondence with the therapeutic success of revascularization (Table 3). In fact, the test results were negative in all five patients who were completely cured and remained positive in the two patients who had nonfunctioning

### Table 2. Clinical Features, Diagnostic Criteria, and Responses to Captopril of BP, PRA, and DTPA Uptake in Patients with Positive Renal Scintigraphic Captopril Test Results

<table>
<thead>
<tr>
<th>Patient no., sex, age (yr)</th>
<th>Medication</th>
<th>Disease</th>
<th>IVP</th>
<th>AG</th>
<th>RVRR</th>
<th>INT</th>
<th>Renogr.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with two kidneys</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>26, F, 25</td>
<td>None</td>
<td>FMD</td>
<td>+</td>
<td>RAS-R</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>27, F, 33</td>
<td>Clonidine</td>
<td>FMD</td>
<td>+</td>
<td>RAS-R</td>
<td>+</td>
<td>+</td>
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</tr>
<tr>
<td>28, M, 38</td>
<td>Nifedipine</td>
<td>FMD</td>
<td>RAS-R</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>29, M, 48</td>
<td>Nifedipine</td>
<td>ASO</td>
<td>RAS-L</td>
<td>+</td>
<td></td>
<td>-</td>
<td></td>
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<tr>
<td>30, F, 49</td>
<td>Atenolol</td>
<td>?</td>
<td>?</td>
<td></td>
<td></td>
<td>-</td>
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<tr>
<td>31, F, 57</td>
<td>None</td>
<td>ASO</td>
<td>RAS-R</td>
<td>+</td>
<td>+</td>
<td>-</td>
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<tr>
<td>32, M, 69</td>
<td>None</td>
<td>ASO</td>
<td>RAS-R</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
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<tr>
<td>33, M, 57</td>
<td>Nifedipine</td>
<td>ASO</td>
<td>RAS-L</td>
<td>-</td>
<td></td>
<td>-</td>
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<td>34, M, 64</td>
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<td>ASO</td>
<td>+</td>
<td>?</td>
<td>-</td>
<td>-</td>
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<tr>
<td>35, F, 31</td>
<td>Nifedipine</td>
<td>FMD</td>
<td>RAS-L</td>
<td>-</td>
<td></td>
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<td></td>
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<tr>
<td>Mean ± SD</td>
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</tr>
<tr>
<td>Patients with single kidney, aortic coarctation, or both</td>
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<tr>
<td>36, F, 15</td>
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<td>FMD</td>
<td>SS; SK</td>
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<td>-</td>
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</tr>
<tr>
<td>37, M, 66</td>
<td>Nifedipine</td>
<td>ASO</td>
<td>RAS; SK</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>38, M, 48</td>
<td>Atenolol</td>
<td>AC</td>
<td>AC; SK</td>
<td>+</td>
<td>+</td>
<td>-</td>
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</tr>
<tr>
<td>39, M, 31</td>
<td>None</td>
<td>AC</td>
<td>AC</td>
<td>-</td>
<td></td>
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</tr>
<tr>
<td>Mean ± SD</td>
<td>45.07</td>
<td>16.61</td>
<td></td>
<td></td>
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</tr>
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</table>

FMD = fibromuscular dysplasia; ASO = atherosclerosis obliterans; RAS = renal artery stenosis; R and L = right and left; SS = segmental stenosis; AC = aortic coarctation; SK = single kidney; INT = BP normalization after technically successful intervention of revascularization (see also text). See Table 1 for key to other abbreviations.

*DTPA uptake was expressed as the ratio between the two kidneys in the patients with two kidneys and as the fraction of the injected dose X 1000 in the patients with a single kidney, aortic coarctation, or both; the mean ± SD uptake values of this last group are indicated in parentheses.

†Values excluded from statistical computation. ‡p < 0.001; §p < 0.01, compared with pretreatment values.
bypass and persistent hypertension. In one patient (Patient 28) who underwent partial repair of multiple renal artery stenosis both test results and BP improved, whereas the patient (Patient 12) who remained hypertensive despite a well-functioning bypass, still had a negative scintigraphic response, as before operation.

**Discussion**

Our observations are in keeping with previous reports that inhibition of ACE may markedly reduce renal uptake of Tc-DTPA in renovascular hypertension. The uptake rate of this glomerular tracer by the kidney during the first minutes after intravenous injection (i.e., after plasma concentration equilibrium has been attained and before urinary excretion becomes significant) is proportional to GRF. Thus, our findings clearly point to a captopril-induced disturbance of GFR. In this study results were expressed in all subjects, except for those with a single kidney and with aortic coarctation, as the ratio of the uptake of the kidney with a lower uptake to the contralateral one rather than as individual uptake data from each kidney. Strictly speaking, the finding of a reduced uptake ratio after captopril in renovascular hypertension indicates an increased functional disparity between the two kidneys, which may represent the net effect of two responses: the reduction of GFR in the kidney ipsilateral to the stenosis and the increase in the contralateral kidney. This second aspect is important, since in experimental two-kidney, one clip hypertension, ACE inhibition has been shown to induce substantial increases of GFR of the intact kidney. However, the finding of clear renographic and morphological abnormalities suggestive of functional impairment in the kidney ipsilateral to the stenosis (i.e., flattening or disappearance of Phase 2 and 3 of the renal curve) in the majority of the patients with positive RSCT results seems to indicate, at least in our series, a predominant effect of captopril on the affected kidney. Similar observations were recently reported by Nally et al. in a canine model of two-kidney, one clip hypertension. Finally, the observation reported by Textor et al. of an average, significant reduction of overall GFR by 25% after short-term captopril administration in renovascular hypertension, would further suggest that, at least acutely, in this disease the negative effect on GFR of the stenosed kidney outweighs the positive effect on the contralateral kidney.

ACE inhibitors may impair GFR in renal artery stenosis by their systemic hypotensive action or by an intrarenal effect. Although a few reports suggest the importance of the first mechanism, most studies in animals provide evidence that inhibition of the renin-angiotensin system in states of reduced renal perfusion pressure impairs GFR predominantly by reducing angiotensin II–mediated postglomerular arteriolar vasoconstriction. In human renovascular hypertension, the importance of efferent arteriolar vasoconstriction caused by angiotensin II has been shown by Textor et al., who observed that, when compared with BP reduction due to nitroprusside administration, initial captopril therapy in patients with unilateral stenosis produced a selective decrease in glomerular filtration despite well-preserved renal blood flow. The dissociation in the kidney ipsilateral to the stenosis between the effect of captopril on renal blood flow (which was maintained) and that on GFR (which was suppressed) recently has been demonstrated by our group in one renovascular patient by comparing Tc-DTPA renal scintigraphy and scintigraphic images of the kidneys after injection of labeled microspheres during arterio-

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**Table 2. (continued)**

<table>
<thead>
<tr>
<th>Arterial BP (mm Hg)</th>
<th>PRA (ng ANG I/ml/hr)</th>
<th>DTPA uptake*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After captopril</td>
</tr>
<tr>
<td>171/122</td>
<td>151/90</td>
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</tr>
<tr>
<td>148/97</td>
<td>148/91</td>
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</tr>
<tr>
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<td>138/95</td>
<td>5.52</td>
</tr>
<tr>
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<td>148/84</td>
<td>4.63</td>
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<tr>
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<td>119/69</td>
<td>—</td>
</tr>
<tr>
<td>140/81</td>
<td>131/64</td>
<td>2.01</td>
</tr>
<tr>
<td>190/85</td>
<td>183/68</td>
<td>2.06</td>
</tr>
<tr>
<td>154/77</td>
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<td>—</td>
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<tr>
<td>161/112</td>
<td>127/89</td>
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</tr>
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<tr>
<td>136/93</td>
<td>112/47</td>
<td>&gt;257</td>
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<td>131/72</td>
<td>114/68</td>
<td>2.03</td>
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<td>159/76</td>
<td>156/73</td>
<td>—</td>
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<tr>
<td>162.4/97.7</td>
<td>142.6/79.6</td>
<td>4.14</td>
</tr>
<tr>
<td>22.7/23.3</td>
<td>21.4/18.7</td>
<td>3.36</td>
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</table>

* DTPA uptake measured in percentage of control uptake.
The recent report of Miyamori et al., of a selective decrease of GFR in the stenosed kidney despite an increase of plasma flow after 1 to 48 weeks of captopril treatment, adds further support to the idea that ACE inhibition induces an impairment of GFR autoregulation in the affected kidney. Compared with essential hypertensive patients, renovascular hypertensive patients not only had scintigraphically detectable effects on kidney function, but also had a more marked increase of peripheral PRA and decrease of arterial BP, a finding already reported by others. We found significant correlations in renovascular patients (but not in essential hypertensive patients) between changes reflecting renal function and those of BP and peripheral PRA. This observation seems to suggest a physiological link between the GFR autoregulatory mechanisms and the humoral and hemodynamic aspects in renovascular hypertension. In this context, it is interesting to note the positive response to captopril observed in the patients with aortic coarctation, a disease in which a renovascular component, responsive to treatment with ACE inhibitors, has been demonstrated. Since captopril not only inhibits the renin-angiotensin cascade but also potentiates the prostaglandin and the kallikrein-bradykinin systems, both important modulators of renal hemodynamic function, further studies are needed to ascertain the involvement of these systems in the scintigraphic effects described.

An important aspect of this study concerns the diagnostic implications of RSCT. As recently pointed out by the NHLBI Workshop on Renovascular Hypertension, attention is being shifted from making the diagnosis of renal artery stenosis to identifying patients who have a high likelihood of being cured or improved by surgical repair (or angioplasty). In this view this technique seems to be very promising, since it investigates a functional consequence of renal hypoperfusion that appears to be intimately linked to BP regulation (i.e., the critical dependence of GFR on activation of the renin-angiotensin system). Another important advantage of this technique is its noninvasiveness and relative simplicity compared with other techniques, such as digital subtraction angiography. However, captopril administration is not devoid of potential hazards, especially in sodium-depleted patients, patients with bilateral renal artery stenosis, and patients with a single kidney. Furthermore, since our series did not include any patients with bilateral renal artery stenosis, and patients with a single kidney, we cannot exclude the possibility that, especially in patients with equally severe stenoses, the assessment of the uptake ratio between the two kidneys could fail to detect this abnormality. In this situation, as in the case of single kidneys, individual uptake of each kidney should be assessed.

Although our series cannot be considered as representative of a hypertensive population and further studies on larger populations are needed to validate these preliminary observations, our data suggest the RSCT is a specific and sensitive technique for the detection of renovascular hypertension. In fact, an abnormal scintigraphic response to ACE inhibition would seem to be very specific for renovascular hypertension, as shown by the finding that in all patients of our series with abnormal renographic results this disease was diagnosed either before or after scintigraphy. This finding confirms the observations reported by Wenting et al. and Oei et al., who found abnormal responses only in patients affected by renal artery stenosis. The good correspondence observed between scintigraphic and angiographic data in our patient with segmental hypoperfusion of the kidney also suggests a particular use-
fullness of this technique in the detection of forms of renovascular hypertension that often present diagnostic difficulties.

An estimation of the sensitivity of captopril renography is affected by the well-known problems related to the diagnostic recognition of this disease. As recently pointed out by Maxwell and Waks, no test or combination of tests can reliably diagnose this disease, and renovascular hypertension is still a retrospective diagnosis based on the finding of normalization of blood pressure after correction of renal artery stenosis by surgery or angioplasty.

In our series, a close correspondence was found between the scintigraphic response to captopril and the results of operation or angioplasty. These findings are in agreement with the observations of Oei et al. On the other hand, Wenting et al. reported a normal scintigraphic response to captopril in seven of 14 hypertensive patients with angiographically proven unilateral renal artery stenosis. In that study the results of renal revascularization were not reported, and it is impossible to exclude the possibility that some of their patients may not have had true renovascular hypertension. It is well known that renal artery stenosis is observed in essential hypertensive and normotensive subjects and that, in a consistent proportion of patients with renal artery stenosis, surgical revascularization fails to normalize BP levels. However, it is difficult to believe that none of these patients had true renovascular hypertension. An alternative explanation might be that in some cases of renal artery stenosis the critical dependence of GFR on the renin-angiotensin system may not be a constant condition but rather a situation that could occur transiently under particular circumstances, when filtration pressure decreases, as a consequence, for instance, of a reduction of systemic BP or of an increase of preglomerular vascular resistances. The importance of renal vascular tone in determining the severity of renal artery stenosis has been demonstrated by Anderson et al. Activation of the sympathetic system might represent such a mechanism since it is a powerful stimulator of both glomerular vasoconstriction and PRA secretion, such a mechanism might be activated during physical and emotional stress, or simply on assuming the upright position. It is tempting to speculate that such a situation could have occurred in the only patient in our series with true renovascular hypertension (as proven by BP normalization after angioplasty) and a normal renal scintigraphic response to captopril (Patient 11), in whom the test results were clearly positive when repeated in the sitting position.

References


<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Type of intervention</th>
<th>RSCCT after intervention</th>
<th>BP after intervention</th>
<th>Outcome of vascular repair</th>
<th>Method of evaluation</th>
<th>Time after intervention (mo)</th>
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<tr>
<td>11</td>
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</tr>
</tbody>
</table>

RSCT = renal scintigraphic captopril test; Echo = echography.


Renal scintigraphic captopril test in the diagnosis of renovascular hypertension.
E Fommei, S Ghione, L Palla, F Mosca, M Ferrari, C Palombo, S Giaconi, P Gazzetti and L Donato

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