Renovascular Hypertension in Blacks
Osemwegie E. Emoven, Paul E. Klotman, N. Reed Dunnick, Saadoon Kadir, and Laura P. Svetkey

To define the clinical characteristics of renovascular hypertension (RVH) and determine the clinical usefulness of captopril stimulated peripheral renin and postcaptopril renography in blacks at risk for RVH, 79 clinically selected hypertensive blacks were evaluated. Unstimulated (U-PRA), captopril stimulated (S-PRA) peripheral renin, and postcaptopril renography (PC-RENO) were obtained. All subjects underwent conventional renal arteriography. Renal artery stenosis (RAS) was present in 14 of 79 (18%) patients. Renovascular hypertension (RVH) was present in 7 of 79 (9%) patients. S-PRA had a sensitivity and specificity of 38% and 86% respectively to detect RAS; and a sensitivity and a specificity of 17% and 85% respectively to detect RVH. PC-RENO had a sensitivity and a specificity of 64% and 88% respectively to detect RAS; and a sensitivity and a specificity of 67% and 88% respectively to detect RVH. This study suggests that RAS occurs in 18% of clinically selected hypertensive blacks. RVH was present in 9% of this population. Captopril stimulated peripheral renin and postcaptopril renography are not useful as screening tools for the diagnosis of renovascular disease in blacks. Blacks at high risk should be evaluated with angiography. Am J Hypertens 1996;9:18-23

KEY WORDS: Renovascular hypertension, noninvasive diagnostic tests, blacks, minority ethnic groups, renal artery stenosis, peripheral renin, renography.

It is frequently stated that renovascular hypertension (RVH) is uncommon in blacks. However, a review of these low prevalence studies suggests that this conclusion most likely represents an underestimate. We found no difference in the prevalence of RVH in a selected population of hypertensive blacks and whites. Of 167 (41% blacks) patients evaluated, 24% had renal artery stenosis (RAS) and 14% had RVH. RVH was diagnosed in 1 of 97 (18%) whites and 6 of 67 (9%) blacks (P = .25). These data suggest that RVH is common in clinically selected hypertensive blacks, posing an important question in the diagnostic surveillance of RVH in this population. What proportion of hypertensive blacks have high risk clinical characteristics for RVH? There is no immediate answer to this question, however, the clinical characteristics we and others have shown to be useful in selecting high risk patients appear to be present in a significant number of hypertensive blacks. For example, the percentages of blacks with severe hypertension (defined as diastolic blood pressure in excess of 115 mm Hg) based on the data from the second National Health and Nutrition Survey, translate to a rough estimate of 782,000 American blacks who have this one criterion for RVH. Further, clinical experience suggests that hypertension in blacks is frequently refractory, another suggestive clue for RVH. It is reasonable to speculate that blacks who have one or more of the suggestive high risk clinical characteristics for RVH may constitute a significant proportion of the hypertensive black population. Therefore, among blacks with these clinical characteristics, how do we identify those with RVH?

The purpose of this article is 1) to define the clinical characteristics of RVH in blacks; and 2) to determine
the sensitivity, specificity and clinical usefulness of non-invasive diagnostic tests for RVH in this population.

**METHODS**

Ambulatory hypertensive black patients were recruited from the Duke Hypertension Center (DHC) and the Durham Veterans Affairs Medical Center (DVA) Hypertension Clinics. The presence of one or more of the following clinical characteristics were required for entry into this study. These were: 1) severe hypertension (history of systolic blood pressure (SBP) >200 mm Hg or diastolic blood pressure (DBP) >115 mm Hg at any time, history of malignant hypertension or hypertensive encephalopathy, or grade III hypertensive retinopathy); 2) refractory hypertension (SBP >160 mm Hg or DBP >95 mm Hg on maximum tolerated doses of three hypertensive drugs); 3) recent onset of hypertension (within 2 years); 4) onset of hypertension before the age of 25 years or after the age of 45 years; 5) progressive hypertension (15% increase in SBP or DBP, unexplained by changes in medication, occurring within the previous 6 months); 6) abdominal bruit; and 7) previous urogram suggestive of RAS. Exclusion criteria included any of the following: myocardial infarction or cerebrovascular accident within the previous 3 months, secondary hypertension, renal insufficiency (serum creatinine >2 mg/dL), severe contrast allergy, and the presence of significant co-morbid diseases.

This study was approved by the institutional review boards and the human use committees of Duke University Medical Center and DVA. Informed consent was obtained from each study subject, and when feasible antihypertensive medications were discontinued for at least 2 weeks prior to evaluation. When this could not be safely done, blood pressure (BP) was controlled with hydralazine or a diuretic for at least 2 weeks. Diuretics were discontinued for at least 48 h prior to evaluation, and no dietary changes were recommended. Upon admission to Duke Clinical Research Unit or to the DVA, a peripheral blood specimen was obtained for measurement of unstimulated peripheral renin. Subjects then took a single oral dose of captopril (25 mg). Glomerular filtration rate (GFR) for each kidney was estimated by an Anger-type scintillation camera (General Electric MaxiCamera II, General Electric Company, Milwaukee, WI) after each subject had received an intravenous injection of 3 mCi 99mTc-DTPA, using a modification of the method developed by Gates. Background activity was defined in an area adjacent to the pole of each kidney. Differential function was calculated based on tracer activity within each kidney 2 to 3 min after injection. The postcaptopril renography data were analyzed as a differential GFR in each kidney, defined as a percent GFR in the right minus the percent GFR in the left kidney (absolute value). Renography was considered abnormal if differential renal function was more than 6%. This threshold was determined by ROC analysis, which is a statistical method that simultaneously maximizes both sensitivity and specificity. Other investigators have used a differential of 10% as a criteria for asymmetric renal function. Predictably, applying this more stringent criterion to our data results in higher sensitivity at the expense of lower specificity.

All subjects underwent conventional renal arteriography. Luminal narrowing of a main renal artery of 50% or greater was considered significant. Treatment decisions were based solely on the results of the arteriogram. Patients with > 50% luminal narrowing were offered percutaneous transluminal angioplasty. Subjects with complete occlusion of a main renal artery were advised to undergo surgical revascularization if the kidney was functional or nephrectomy if the kidney was nonfunctional (based on 201Tl-DTPA renography). If BP did not change after angioplasty, a repeat arteriogram was performed to confirm patency of the treated artery. A second angioplasty was performed if there was restenosis. If stenosis persisted after two technically successful angioplasties, surgical revascularization was recommended. In subjects with bilateral disease, the more stenotic lesion was treated first. In the absence of a decrease in BP, and patency of the treated renal artery confirmed on repeat arteriography, angioplasty or surgery was performed on the contralateral artery. All subjects were examined by an investigator 2 weeks after the initial evaluation, and those who were treated with angioplasty or surgery were examined at monthly intervals thereafter. RVH was diagnosed based on criteria established by the Cooperative Study on Renovascular Hypertension. A cure was defined as BP < 110/90 mm Hg on no antihypertensive medications. Significant improvement was defined as a 15% decrease in BP without change in medication or if less medication was required to maintain normal pressure. RVH was ruled out if there was no stenosis or if there was no BP response after angioplasty or revascularization.
response was determined by comparing BP at baseline to the BP obtained at least one month after intervention.

Proportions were compared by chi-square statistic using the Fischer's exact test when the expected number of observations was less than five. Group means were compared using the unpaired t test.

RESULTS

Data on 79 hypertensive blacks were analyzed. The mean age was 49 ± 13 years, 51% were females. RAS was found in 14 of 79 (18%) patients. Of these, 10 had atheroma, two had fibromuscular dysplasia, and the type of lesion could not be specified with certainty in two patients. Seven of 79 (9%) patients had RVH, based on previously defined criteria. Four patients with stenosis were classified as indeterminate for RVH for the following reasons: three were not candidates for intervention (one had a malignant neoplasm, one had severe coronary artery disease, and one developed severe nephrotoxicity precluding further contrast studies), and one patient with bilateral stenosis had angina on only one renal artery without definitive BP response.

The clinical characteristics of the study population and a comparison between patients with and without RAS is shown in Table 1. Compared to those without stenosis, patients with stenosis were older (mean age, 56 ± 11 years vs 48 ± 13 years; \( P = .05 \)). A higher proportion of patients with LVH was detected in 43% of patients with stenosis; and in 6% without stenosis (\( P = .04 \)). In both groups, the proportion of smokers and patients with a history of diabetes mellitus or coronary artery disease were similar. An abdominal bruit was present in 43% of patients with stenosis; and in 6% without stenosis (\( P = 0.02 \)). Although the mean serum creatinine was higher in the stenosis group, the difference was not statistically significant (1.4 ± 0.5 mg/dL versus 1.1 ± 0.4 mg/dL; \( P = .06 \)). Alternatively, when RVH (i.e., BP response to intervention) was considered, there were no differences between those with RVH and all others (including those with stenosis and no BP response) with respect to age and the proportion of patients with LVH. However, those with RVH tended to be smokers (67% vs 33%), consistent with other reports, but the difference was not statistically significant (\( P = .18 \)).

Table 2 displays the results of captopril-stimulated peripheral renin and postcaptopril renography in the study population and a comparison between those with and without stenosis. Similar to hypertensive blacks in general, these patients tended to have low or normal nonstimulated peripheral renin. Although captopril-stimulated peripheral renin was higher in those with stenosis, the difference was not statistically significant (31.2 ± 97 ng/mL/h vs 3.0 ± 6.9 ng/mL/h; \( P = .12 \)). The means are numerically different because of an outlier in the stenosis group (captopril-stimulated peripheral renin; 354 ng/mL/h). Without this outlier, the mean captopril-stimulated peripheral renin in those with stenosis was similar to those without stenosis (4.3 ± 7.5 ng/mL/h vs 3.0 ± 6.9 ng/mL/h; \( P = .2 \)). The proportion of patients with captopril-stimulated peripheral renin > 4 ng/mL/h in both groups was similar. With respect to postcaptopril renography, the proportion of patients with an abnormal test in both groups was similar (46% vs 42%; \( P = .3 \)).

Alternatively, when RVH was considered, the only difference between those with RVH and all others (including those with stenosis and no BP response), was

<p>| TABLE 2. STIMULATED PERIPHERAL RENIN ACTIVITY AND POSTCAPTOPRIL RENOGRAPHY IN THE STUDY POPULATION AND A COMPARISON BY RAS STATUS |</p>
<table>
<thead>
<tr>
<th>Variable</th>
<th>All Blacks</th>
<th>RAS</th>
<th>Without RAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>U-PRA ng/mL/h ( \pm SD )</td>
<td>2.1 ± 3.5</td>
<td>2.4 ± 2.6</td>
<td>2.1 ± 3.6</td>
</tr>
<tr>
<td>S-PRA ng/mL/h ( \pm SD )</td>
<td>8.8 ± 45</td>
<td>31.2 ± 97</td>
<td>3.0 ± 6.9</td>
</tr>
<tr>
<td>S-PRA &gt; 4 ng/mL/h ( n(%) )</td>
<td>12 (19)</td>
<td>5 (38)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>Renogram ( n(%) ) abnormal</td>
<td>25 (46)</td>
<td>7 (64)</td>
<td>18 (42)</td>
</tr>
</tbody>
</table>

RAS = renal artery stenosis; U-PRA = unstimulated peripheral renin activity; S-PRA = stimulated peripheral renin activity (obtained in 63 patients); PC-RENQ = postcaptopril renography (obtained in 54 patients).

**TABLE 1. CLINICAL CHARACTERISTICS IN THE STUDY POPULATION AND A COMPARISON BY RAS STATUS**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Blacks ( n = 79 )</th>
<th>RAS ( n = 14 )</th>
<th>Without RAS ( n = 65 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ( \pm SD ))</td>
<td>49 ± 13</td>
<td>56 ± 11</td>
<td>48 ± 13*</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>51</td>
<td>57</td>
<td>49</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>53</td>
<td>79</td>
<td>46**</td>
</tr>
<tr>
<td>DM (%)</td>
<td>37</td>
<td>46</td>
<td>35</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>14</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>ARB (%)</td>
<td>9</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Severity (%)</td>
<td>13</td>
<td>43</td>
<td>6**</td>
</tr>
<tr>
<td>Refractory (%)</td>
<td>81</td>
<td>71</td>
<td>83</td>
</tr>
<tr>
<td>Serum creatinine mg/dL (mean ( \pm SD ))</td>
<td>1.2 ± 0.4</td>
<td>1.4 ± 0.5</td>
<td>1.1 ± 0.4</td>
</tr>
</tbody>
</table>

*RAS = renal artery stenosis; LVH = left ventricular hypertrophy; CAD = coronary artery disease; DM = diabetes mellitus; Severity = SBP > 300 mm Hg or DBP > 115 mm Hg; history of malignant hypertension or hypertensive encephalopathy, or grade III hypertensive retinopathy. Refractory = SBP > 180 mm Hg or DBP > 95 mm Hg on maximum tolerated doses of 3 hypertensive drugs.

**P = .02 RAS v without RAS.**

**P = .002 RAS v without RAS.**
in the captopril-stimulated peripheral renin. In contrast to the comparison between those with and without stenosis, when comparing those with and without RVH, captopril-stimulated peripheral renin was lower in the RVH group (1.5 ± 1.7 ng/mL/h vs. 3.0 ± 7 ng/mL/h; P = 0.03).

Table 3 displays the sensitivities, specificities, and predictive values of captopril-stimulated peripheral renin and postcaptopril renography for the diagnosis of RAS and RVH. (Not all subjects underwent both tests, therefore, total number of patients differs from Table 1.) Five of 13 patients with stenosis had captopril-stimulated peripheral renin >4 ng/mL/h (sensitivity 38%). Forty-three of 50 patients without stenosis had captopril-stimulated peripheral renin <4 ng/mL/h (specificity 86%). One of 6 patients with RVH had captopril-stimulated peripheral renin >4 ng/mL/h (sensitivity 17%). Forty-five of 53 patients without RVH had captopril-stimulated peripheral renin <4 ng/mL/h (specificity 85%). The positive and negative predictive values of captopril-stimulated peripheral renin were 42% and 84%, respectively, for the diagnosis of stenosis, and 10% and 91%, respectively, for the diagnosis of RVH.

Seven of 11 patients with stenosis had an abnormal postcaptopril renogram (sensitivity 64%). Twenty-five of 43 patients without stenosis had a normal postcaptopril renogram (specificity 58%). Four of 6 patients with RVH had an abnormal postcaptopril renogram (sensitivity 66%). Twenty-six of 45 patients without stenosis had a normal postcaptopril renogram (specificity 57%). The positive and negative predictive values of postcaptopril renography were 28% and 86%, respectively, for the diagnosis of stenosis, and 14% and 96%, respectively, for the diagnosis of RVH.

**DISCUSSION**

Although it is frequently stated that RVH is uncommon in blacks, a review of these low prevalence studies suggest that this conclusion most likely represent an underestimate of the true prevalence of RVH in this population. For example, Seidat and Reddy evaluated a population of 500 consecutive hypertensive blacks attending an outpatient facility in South Africa and reported RAS in one patient. In another study that included 7,200 hypertensive blacks, less than 1% were found to have RVH. These studies failed to perform the gold standard test (ie, arteriography and documentation of DP response to angioplasty or revascularization) on all study subjects.

In contrast, there is evidence to support our findings that when hypertensive blacks are carefully selected and thoroughly evaluated, RVH is common. Thomas et al performed renal arteriography on 100 hypertensive blacks, most of whom had DBP in excess of 120 mm Hg. Sixteen patients (16%) had significant RAS. Although the BP response to intervention was not reported, the prevalence of stenosis is similar to what we have observed. In another study, Foster et al found RAS in 13 of 81 hypertensive blacks. Six percent of the population were judged to have hemo-dynamically significant lesions. Finally, 14 of 112 (13%) blacks in the Cooperative Study on Renovascular Hypertension were found to have RVH. In aggregate, these studies suggest that RVH is common blacks, with an estimated prevalence of 6% to 13% in a clinically selected population. Given the high prevalence of hypertension in blacks, a misdiagnosis of essential hypertension in patients with RVH will probably translate into an impressive number of blacks who could have benefitted from a cure of hypertension. Thus, identification of RVH in this population could contribute to a reduction in hypertension-related cardiovascular complications and avoid the expense and potential morbidity of lifelong pharmacological therapy for hypertension. In addition, accumulating data suggest that successful revascularization may preserve renal function, an issue that is particularly important in blacks, who are disproportionately represented among patients with end stage renal disease attributed to hypertension.

The vast majority of patients enrolled in this study had either severe or refractory hypertension, two frequently encountered clinical characteristics in hypertensive blacks. The difficulty in distinguishing patients with RVH from the remainder of the population was evident in this cohort. However, our data reaffirmed the value of careful auscultation for an abdominal bruit. This has been shown to be the most cost-effective strategy for initiating diagnostic evaluation for RVH. In this study, however, all bruits were systolic.

**TABLE 3. SENSITIVITY, SPECIFICITY, AND PREDICTIVE VALUE OF STIMULATED PERIPHERAL RENIN ACTIVITY AND POSTCAPTOPRIL RENOGRAPHY FOR RAS AND RVH**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PV+</th>
<th>PV-</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-PRA</td>
<td>38</td>
<td>86</td>
<td>42</td>
<td>84</td>
</tr>
<tr>
<td>PC-Reno</td>
<td>60</td>
<td>58</td>
<td>28</td>
<td>86</td>
</tr>
</tbody>
</table>

**S-PRA = stimulated peripheral renin activity >4 ng/mL/h; PC-Reno = Abnormal postcaptopril renography; PV+ = positive predictive value; PV- = negative predictive value.**
Renal arteriography remains the gold standard for identifying renovascular disease. However, it is not routinely recommended because of cost and the potential for complications. Peripheral renin measurements before or after captopril administration and post-captopril renography have been widely used and extensively studied as screening tools for renovascular disease. However, no previous study has systematically analyzed the value of these tests in blacks.

In this article, we report the results of a single measurement of peripheral renin after captopril administration. This test had a sensitivity of 17% in correctly diagnosing RVH, with positive and negative predictive values of 10% and 91%, respectively. That is, this test had no bearing on predicting the likelihood of RVH. In white subjects, other investigators have reported a wide range of sensitivities and specificities using this test as a screening tool for RVH (Table 4).

The diagnostic accuracy of this test in studies of white patients is uniformly superior to our results. Postma et al. studied 149 hypertensive patients and found stenosis, defined as greater than 50% luminal narrowing, in 44 of 149 (29.5%) of these patients. Fourteen patients either had surgery or angioplasty, five of whom were cured. All had elevated captopril-stimulated renin. The five patients who were judged to be failures had captopril-stimulated peripheral renin below the threshold level, probably representing true negatives. Two patients had false negative and another two had false positive tests. Therefore, the actual sensitivity of this test might be much higher than what was reported.

The population reported in this paper is a subset of a larger, mixed-race population that we have studied. The diagnostic accuracy of captopril-stimulated peripheral renin was superior in the 121 white subjects selected and evaluated in an identical manner (sensitivity 75% and specificity 61%). It is unclear why blacks with RVH have a more sluggish response to captopril than whites with RVH (reflected in the lower sensitivity among blacks). These data may reflect underlying physiologic or pathophysiologic differences between blacks and whites. Regardless of race, captopril-stimulated peripheral renin is not an ideal test. It is possible that additional stimulation by upright posture would improve the performance of this test, but it is difficult to speculate that the racial difference in test performance would be affected by this maneuver. Our data suggest that this test is less useful in blacks and should not be used as a screening tool for RVH in this population.

Similarly, post-captopril renography did not perform well in diagnosing RAS and RVH in blacks. Sensitivity and specificity in diagnosing RAS were 64% and 58%, respectively, with similarly low performance in diagnosing RVH. It must be emphasized that our estimates of sensitivity are based on a small number of subjects with RAS (11) or RVH (6). We can have little confidence in these sensitivities until they are confirmed in a larger sample. In contrast to our results, other investigators have reported a relatively high diagnostic accuracy of captopril renography. This discrepancy could be due to methodologic differences in the performance and/or interpretation of the test. We suspect, however, that the relatively poor results of post-captopril renography in our population are due to differences in test performance between blacks and whites since most subjects in other reports have been of white background. In support of this hypothesis, renography performed better in white subjects who were selected and evaluated by an identical protocol at our institution. Among 121 whites, captopril renography had a sensitivity of 78% for RAS, and 83% for RVH, compared to a sensitivity of 64% for RAS and 67% for RVH among blacks. The high prevalence of abnormal captopril renography in blacks without RVH (i.e., the low specificity of this test in our population) may reflect the low differential criterion for considering the test abnormal, supported perhaps by the fact that specificity was almost as low in whites (58% vs. 61%). On the other hand, if the specificity is truly lower in blacks, this may reflect higher rates of undetected renal parenchymal disease in blacks, which would lead to abnormal renograms. Our results may also have been influenced by the dose of captopril (25 mg) we administered. It is conceivable that captopril renography might have performed better if we had administered a higher dose.

In addition to the differences in the operating characteristics of captopril-stimulated peripheral renin determination and post-captopril renography which we observed between black and white subjects evaluated...
at our institution, there were notable differences in response to treatment (angioplasty or surgery). A total of 70% of blacks with stenosis were found to have RVH, compared to 95% of whites (P = .003). This observation may reflect black/white differences in the pathophysiology of renal vascular disease. More likely, the observation reflects a delay in the diagnosis of RVH in blacks, such that, among other physiologic alterations, hypertension-induced structural changes in the vascular wall may have resulted in the maintenance of the hypertensive state.24

The ideal noninvasive test for RVH is not yet available, and the data presented in this paper demonstrate the unique diagnostic challenge in hypertensive blacks. While a population of blacks at risk for RVH exists, there is no effective means of identifying this subset of patients from the high risk hypertensive population without incurring significant expense and exposing a sizeable number of patients to invasive diagnostic tests. Therefore, the decision to proceed with diagnostic evaluation for RVH should rest on careful clinical judgment. Nonetheless, we believe that blacks at high risk for RVH should be evaluated with angiography. The common and false perception that renovascular disease is rare in blacks has undoubtedly led to underdiagnosis of curable hypertension in blacks. Recognition that the prevalence of renovascular disease is similar in clinically selected blacks and whites may not be helpful in blacks. Clearly, further research is needed to improve our ability to make this diagnosis in blacks.

REFERENCES