Similar Prevalence of Renovascular Hypertension in Selected Blacks and Whites

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Renovascular hypertension is a potentially curable form of high blood pressure that is thought to be extremely rare among blacks. We demonstrate, however, that in a clinically selected population, the prevalence of renovascular hypertension is similar in blacks and whites. We prospectively evaluated 167 hypertensive subjects who had one or more clinical features known to be associated with renovascular hypertension. All subjects had captopril-stimulated peripheral renin measurements and conventional renal arteriography. All significant renal artery stenoses (greater than 50% luminal narrowing) were treated with percutaneous transluminal angioplasty or surgery. Renovascular hypertension was diagnosed if there was a blood pressure response to interventional therapy, according to the criteria established by the Cooperative Study of Renovascular Hypertension. Of the total group evaluated, 24% (39 of 167) had renal artery stenosis and 14% (23 of 167) had renovascular hypertension. Renal artery stenosis or occlusion was found in 27% (26 of 97) of whites and 19% (13 of 67) of blacks (p=0.27). Renovascular hypertension was diagnosed in 18% (17 of 97) of whites and 9% (6 of 67) of blacks evaluated (p=0.25). Renovascular hypertension was associated with severe or refractory hypertension and with smoking, but there were no racial differences in these associations. Blacks with renovascular hypertension tended to have low captopril-stimulated peripheral renin activity. We conclude that blacks with clinical features suggestive of renovascular hypertension should be evaluated with angiography. Captopril-stimulated plasma renin may not be useful in detecting blacks with renovascular hypertension, but this and other potential screening tests require further evaluation. (Hypertension 1991;17:678–683)

Renovascular hypertension is a potentially curable form of high blood pressure that is thought to be extremely rare among blacks. There is a clear association, however, between renovascular hypertension and extreme elevations in blood pressure. The high prevalence of severe hypertension among blacks suggests that this subgroup may have a high prevalence of reversible hypertension. In addition, other clinical features found to be associated with renovascular disease in whites have not been adequately evaluated in blacks. There is no previous report of racial differences in renovascular hypertension in which the diagnosis was made or excluded conclusively based on angiography and response to interventional treatment. We demonstrate that in a clinically selected population, the prevalence of renovascular hypertension is similar in blacks and whites.

Methods

Ambulatory hypertensive adults were recruited from the Duke Hypertension Center and the Durham Veterans Affairs Medical Center Hypertension Clinic. Blacks comprise 40% of the combined populations of these two clinics. The diagnosis of hypertension was confirmed if untreated systolic blood pressure was greater than 145 mm Hg or diastolic blood pressure was greater than 90 mm Hg on two separate occasions. Patients were eligible to enter the study if one or more of the following clinical features, suggesting the diagnosis of renovascular hypertension, was present: 1) severe hypertension (history of diastolic blood pressure greater than 115 mm Hg or systolic blood pressure greater than 200 mm Hg at any time, history of malignant hypertension or hypertensive encephalopathy, or physical examination revealing grade III hypertensive retin-
opathy); 2) refractory hypertension (systolic blood pressure greater than 160 mm Hg or diastolic blood pressure greater than 95 mm Hg on maximum tolerated doses of three antihypertensive drugs); 3) onset of hypertension within the previous 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 systolic or diastolic blood pressure, unexplained by changes in medication, occurring within the previous 6 months); 6) abdominal or flank bruit; 7) previous hypertensive urogram suggestive of renal artery stenosis; 8) acute renal failure with administration of angiotensin converting enzyme inhibitor.

Subjects were excluded from entry if they had experienced a myocardial infarction or cerebrovascular accident within the previous 3 months, or if there was evidence on history, physical examination, or routine laboratory evaluation of other secondary forms of hypertension. Subjects were also excluded if renal insufficiency (serum creatinine greater than 2 mg/dl) or severe contrast allergy precluded multiple contrast studies. Subjects who were not considered to be operative candidates due to severe comorbid disease were excluded because of the possibility of a complication of angiography or angioplasty that might require emergency surgery.

This study was approved by the institutional review boards and the human use committees of Duke University Medical Center and the Durham Veterans Affairs Medical Center. Written informed consent was obtained from each subject. Two weeks before evaluation, all blood pressure medication was discontinued if possible. In some patients, safety issues prevented discontinuation of all antihypertensive medication. In these circumstances blood pressure was controlled with hydralazine for at least 2 weeks, and diuretics were discontinued for at least 48 hours before evaluation. No changes in diet were prescribed.

Subjects were asked to obtain a 24-hour urine collection that was initiated on the morning before admission. On admission to the Duke Clinical Research Unit or to the medical service of the Durham Veterans Administration Hospital, an oral dose of captopril (25 mg crushed and dissolved in drinking water) was administered. Subjects remained seated for 60 minutes, after which a captopril-stimulated peripheral renin specimen was obtained. In a subset of patients, a peripheral venous blood sample was also obtained before the captopril dose for measurement of unstimulated plasma renin activity. Plasma renin activity was measured by radioimmunoassay.

All subjects then had conventional renal arteriography. Subjects were pretreated with atropine, meperidine, and local anesthetic. A 5F pigtail catheter was passed percutaneously via the femoral artery into the abdominal aorta. Conventional intravascular contrast material (Renografin 60, Squibb Diagnostics, New Brunswick, N.J.) was injected at 25 ml/sec for 2 seconds, for a total infusion of 50 ml contrast material. Roentgenograms were obtained in the anteroposterior projection at 3 frames/sec. If the main renal arteries were not clearly seen, additional views were obtained in oblique projections. Occasionally, selective renal artery injections were required for adequate visualization. In such cases, a preformed end-hold catheter was used, and the injection rate varied with the size of the renal artery. Luminal narrowing of a main renal artery of 50% or more was considered significant renal artery stenosis.

Treatment decisions were based solely on the results of conventional renal arteriography. (Captopril-stimulated selective renal vein renin was measured, as previously reported, but the results of these and peripheral renin measurements were not known until after interventional treatment had occurred.) Subjects without significant renal artery stenosis on arteriography were treated with antihypertensive medication. Patients with 50% or greater luminal narrowing of a main renal artery were advised to have percutaneous transluminal angioplasty. Subjects with complete occlusion of a main renal artery were advised to undergo surgical revascularization if the kidney was functional (based on technetium-99m–diethylenetriamine pentaacetic acid renography) or nephrectomy if the kidney was small and nonfunctional. If blood pressure did not change after angioplasty or surgery, repeat angiography was performed to confirm patency of the treated artery. If the treated artery had restenosed, a second angioplasty was performed. After two technically unsuccessful angioplasty treatments, revascularization surgery was recommended. In subjects with bilateral renal vascular disease, the more severe stenosis was treated first. If there was no subsequent decrease in blood pressure and if repeat angiography revealed that the treated artery was patent, angioplasty or surgery was then performed on the contralateral artery. Stenosis or occlusion of a branch renal artery was treated medically.

Regardless of treatment (medical, angioplasty, or surgery), each patient was examined by an investigator (L.P.S., S.R.S., C.B.D., or M.L.) 2 weeks after evaluation. Subjects with renal artery stenosis or occlusion were examined again 1 month after interventional therapy. At that time, renovascular hypertension was diagnosed if correction of a renal artery stenosis by percutaneous transluminal angioplasty, surgical revascularization, or nephrectomy resulted in cure or improvement in the patient's hypertension, based on criteria established by the Cooperative Study of Renovascular Hypertension. "Cure" was defined as blood pressure less than or equal to 140/90 mm Hg on no antihypertensive medication. "Significant improvement" was defined as a 15% decrease in blood pressure without change in medication regimen or if less medication was required to maintain normal blood pressure. Renovascular hypertension was ruled out if there was no significant stenosis of a main renal artery or if successful correction of a renal vascular lesion (proven by repeat angiography) did not result in a decrease in blood pressure.
TABLE 1. Baseline Characteristics of Total Study Population and by Race

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All subjects</th>
<th>Whites</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>167</td>
<td>97 (59)</td>
<td>67 (41)</td>
</tr>
<tr>
<td>Age (yr±SD)</td>
<td>49±14</td>
<td>50±15</td>
<td>49±13</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>35</td>
<td>28</td>
<td>46</td>
</tr>
<tr>
<td>Blood pressure (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>164±29</td>
<td>162±29</td>
<td>168±30</td>
</tr>
<tr>
<td>Diastolic</td>
<td>100±15</td>
<td>98±12</td>
<td>104±17</td>
</tr>
<tr>
<td>Mean arterial</td>
<td>121±17</td>
<td>119±15</td>
<td>125±18</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl±SD)</td>
<td>1.2±0.4</td>
<td>1.1±0.3</td>
<td>1.2±0.4</td>
</tr>
</tbody>
</table>

All subjects category includes three subjects who were neither white nor black and who were not included in subsequent analysis.

Proportions were compared by $\chi^2$ statistics, using Fisher's Exact Test when the expected number of observations per cell was less than five. Means were compared by unpaired $t$ test. The associations of both race and smoking with renovascular hypertension were also evaluated (separately) by age-adjusted logistic regression models.

**Results**

Baseline characteristics of the total group and by race are shown in Table 1. One hundred sixty-seven subjects were evaluated. Ninety-seven (59%) were white and 67 (41%) were black. Three subjects were nonwhite of ethnic origin other than black and were not included in subsequent analysis. Mean age for the total group was 49±14 years (range 18–79 years) and did not differ by race. Thirty-five percent of the total group, 28% of whites and 46% of blacks, were women. Mean blood pressure on entry into the study was 164±29/100±15 mm Hg and was similar in both races. In most patients, baseline blood pressure represented measurements obtained while the patient was taking antihypertensive medication. There was no difference between whites and blacks in baseline serum creatinine (mean 1.2±0.4 mg/dl).

Table 2 displays the prevalence of renal vascular disease and renovascular hypertension overall and by race. Of the total group evaluated, 24% (39 of 167) had significant stenosis or occlusion of a main renal artery; bilateral disease was found in 15 patients (9% of total, 38% of those with renal artery stenosis). Fourteen percent (23 of 167) of the total group had renovascular hypertension, as defined by blood pressure response to interventional treatment. These data confirm that the clinical inclusion criteria used in this study effectively selected a population with relatively high prevalence of renovascular hypertension. To diagnose renovascular hypertension in subjects with renal artery stenosis, we compared baseline blood pressure to postintervention blood pressure 1 month after angioplasty or surgery. It is possible that a longer follow-up time would provide additional information about the hemodynamic significance of a renal artery stenosis. For instance, in some patients, blood pressure may decrease over a longer period of time. In other patients, intervention may cause a short-term decrease in blood pressure that does not persist. To address these possibilities, we also evaluated follow-up blood pressure in 26 subjects with renal artery stenosis at 2 to 12 months after interventional therapy (blood pressure data within this time interval were not available for 13 subjects with renal artery stenosis). The original (1 month) assessment of whether these subjects had renovascular hypertension was confirmed at this later time in 21 subjects. Four subjects were not on antihypertensive regimens comparable with the regimen before interventional therapy, so that any comparison of blood pressures before and 2–12 months after intervention was not reliable. One additional subject originally believed to have renovascular hypertension would not have been so diagnosed if the 3-month follow-up blood pressure was compared with blood pressure before angioplasty. In this subject, however, restenosis was not adequately excluded.

Contrary to our a priori expectation, Table 2 also demonstrates that there was no significant difference between the proportion of whites with renal vascular disease and renovascular hypertension and the proportion of blacks with these conditions. Renal artery stenosis or occlusion was found in 26 whites (27%) and 13 blacks (19%). Vascular lesions were due to atherosclerotic disease in 72% of whites and 75% of blacks. Bilateral renal artery stenosis was found in 14 whites and one black. Renovascular hypertension was diagnosed in 17 whites (18%) and six blacks (9%). $\chi^2$ tests for differences in these proportions were not significant ($\chi^2=1.2$, $p=0.27$ for renal vascular disease and $\chi^2=2.7$, $p=0.25$ for renovascular hypertension). The numerical difference in prevalence of renovascular hypertension (18% versus 9%) might conceivably reach statistical significance if confirmed in a larger sample. Nonetheless, these data strongly suggest that renovascular hypertension is not rare in clinically selected black hypertensive patients. In addition, when these data are analyzed in an age-adjusted logistic regression model, race does not significantly affect the likelihood of having renovascular hypertension ($p=0.14$).

Having established which subjects had renovascular hypertension by the gold standard of diagnosis (angiography and blood pressure response to interventional therapy), we then compared blacks and whites with respect to putative risk factors for reno-
vascular hypertension (Table 3). In the subset of 74 subjects in whom we measured unstimulated plasma renin activity (32 blacks and 42 whites), there were no significant differences by race or diagnosis. Stimulated plasma renin activity, however, measured 60 minutes after captopril stimulation, was higher in whites than in blacks (16±46 ng/ml/hr versus 3±7 ng/ml/hr, *p=0.02), consistent with previous observations that blacks tend to have low renin hypertension.8 Surprisingly, renin activity tended to be low even in the blacks with renovascular hypertension. Mean captopril-stimulated plasma renin activity in whites with renovascular hypertension was 19±26 ng/ml/hr, compared with a mean of 1.7±2 ng/ml/hr in blacks with renovascular hypertension (*p=0.03). The proportion of blacks with elevated captopril-stimulated plasma renin was also lower than whites both in the total group and in those with renovascular hypertension. We used receiver operating characteristic analysis in this patient population to establish the optimal threshold between “normal” and “elevated” captopril-stimulated plasma renin activity.9,10 Based on the results of this analysis, we considered a captopril-stimulated renin greater than 4 ng/ml/hr to be elevated. Defined in this way, this test had a sensitivity of 48% overall, but sensitivity was only 17% among blacks. Specificity was 89% overall and 86% among blacks. A subset of 69 subjects also had an unstimulated renin measurement, allowing us to apply the “captopril test” criteria established by Muller et al.10 Sensitivity of the captopril test was only 17% overall, without a significant race effect, confirming numerous other investigations suggesting that the criteria for the captopril test do not validate well.11-13

The majority of patients entered this study because of severe hypertension, as defined in the Methods section (many met more than one of these entry criteria). Blacks who entered the study were more likely to have severe hypertension than whites (57% of whites versus 85% of blacks, *χ²=14.4, p<0.001), but blacks and whites ultimately found to have renovascular hypertension were equally likely to have severe disease. A similar relation was seen for refractory hypertension. Patients with renovascular hypertension were more likely to smoke than those with essential hypertension (*χ²=9.5, p=0.002), but there was no significant difference in smoking rates between blacks and whites with renovascular hypertension. The association between smoking and renovascular hypertension, reported previously,14,15 was confirmed by an age-adjusted logistic regression model (*χ²=8.5, p=0.004).

Table 3. Racial Differences in Potential Predictors of Renovascular Hypertension

<table>
<thead>
<tr>
<th>Predictor</th>
<th>All whites</th>
<th>All blacks</th>
<th>Whites with RVH</th>
<th>Blacks with RVH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstimulated PRA (ng/ml/hr±SD)</td>
<td>2.8±2.9</td>
<td>2.17±3.6</td>
<td>3.4±4</td>
<td>0.14*</td>
</tr>
<tr>
<td>Post-captopril PRA (ng/ml/hr)</td>
<td>16±46</td>
<td>3±7†</td>
<td>19±26</td>
<td>1.7±2‡</td>
</tr>
<tr>
<td>Post-captopril PRA (&gt;4 ng/ml/hr) (%)</td>
<td>39</td>
<td>16†</td>
<td>48</td>
<td>17</td>
</tr>
<tr>
<td>Severe hypertension (%)</td>
<td>57</td>
<td>85†</td>
<td>71</td>
<td>83</td>
</tr>
<tr>
<td>Refractory hypertension (%)</td>
<td>16</td>
<td>49†</td>
<td>24</td>
<td>33</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>41</td>
<td>40</td>
<td>65</td>
<td>80</td>
</tr>
</tbody>
</table>

RVH, renovascular hypertension; PRA, plasma renin activity.
*Data available for one patient only.
†p<0.05 compared with all whites.
‡p<0.05 compared with whites with RVH.

Discussion

Many medical textbooks state that renovascular hypertension occurs in less than 1% of blacks with high blood pressure. The data generally cited to support this statement come from a survey in which 7,200 black adults were referred to a tertiary care hypertension clinic for evaluation.3 In this group, only 47 individuals were found to have renal artery stenosis and 20 were found to have renovascular hypertension, as defined by a decrease in blood pressure after surgical correction of a main renal artery stenosis. This careful and thoughtful investigation characterized renovascular hypertension in blacks, demonstrating that treatment results were similar to those in whites. The very low prevalence of renovascular hypertension in this population (0.2%), however, is very likely an underestimate. Of the 7,200 patients referred for evaluation, only 238 had angiography. Forty-seven of these 238 patients had renal artery stenosis (19.7%), and 20 (8%) had surgically proven renovascular hypertension. These rates correspond closely to ours (18% and 9%, respectively).

Two other studies suggest that renovascular hypertension is not rare in clinically selected blacks. Thomas et al16 performed renal arteriography in 100 “fairly unselected” black hypertensive patients and found renal artery stenosis in 16% of these patients. Unfortunately, the blood pressure response to intervention was not reported, and it is unclear what clinical features distinguish the 100 subjects evaluated from the general population of blacks with hypertension. In the Cooperative Study of Renovascular Hypertension, the authors reported that 30% of the study population but only 8% of those with renovascular hypertension were black.4 These data suggest that renovascular hypertension is less common in blacks than in whites. But the Cooperative Study data also suggest that renovascular hypertension is not rare in
clinically selected blacks. Among this study population, selected and evaluated in a manner similar to the present study, there were 112 black subjects; 14 of these (12.5%) had renovascular hypertension.

Our present study, in which both anatomic and clinical diagnosis was made by gold standard (conventional renal arteriography and blood pressure response to a corrective intervention), suggests that clinical selection criteria can be used to define a population of blacks likely to have renovascular hypertension and that this strategy will be as successful in blacks as it is in whites. These results raise two important questions. First, what proportion of black hypertensive individuals meet our selection criteria? Data from the second National Health and Nutrition Evaluation Survey (NHANES II) indicate that 2.2% of the black male population and 0.8% of the black female population have severe hypertension (defined as diastolic blood pressure of 115 mm Hg or higher). These percents translate into approximately 582,000 blacks who would meet this single criterion. Furthermore, clinical experience suggests that hypertension in blacks is frequently difficult to control. Severe and refractory hypertension are among the more predictive criteria for renovascular hypertension. It is also reasonable to speculate that many additional black hypertensive individuals would meet other selection criteria. It is unclear, however, whether our results, in a highly selected referral population, will apply to all blacks with severe or difficult to control hypertension. A truly population-based study is required to confirm the universality of our findings.

The second question is, what proportion of blacks with none of these selection criteria also have renal vascular disease? We do not yet have data in either race to answer this question, but it is clear that atherosclerosis of the renal arteries is often undetected in life. Renal angiography cannot be performed in every hypertensive; clearly there is a need for an accurate screening test. We evaluated one potential screening test, captopril-stimulated plasma renin activity. In our patient population, captopril-stimulated renin was not elevated in the majority of blacks with renovascular hypertension. Several investigations of the usefulness of this measurement and of comparisons between stimulated and unstimulated renin have resulted in widely varying test characteristics with sensitivities of the captopril test, for example, ranging from 17% to 100%. A subset of our study population also had the captopril test, with no indication that this approach to stimulated renins was superior to a single measurement after captopril stimulation. Thus, our data suggest that renin levels may be even less helpful in screening for renovascular hypertension in blacks than in whites. Dietary sodium and potassium may affect renin secretion and renin response to captopril. Therefore, racial differences in dietary intake of these nutrients could affect the diagnostic accuracy of plasma renin activity. We estimated dietary intake based on urinary excretion of these elements. There were no significant differences in urinary excretion of sodium or potassium by race or by diagnosis (data not shown), perhaps due to the very large variation and potential inaccuracy of these measurements (urinary sodium excretion overall ranged from 4 to 478 meq/24 hr, and urinary potassium excretion overall ranged from 8 to 917 meq/24 hr).

Renal vascular disease is frequently treated medically unless blood pressure is difficult to control. The implication of this approach, however, is that many individuals will be exposed to the expense and risk of life-long antihypertensive medication unnecessarily. In addition, there is recent evidence that reperfusion of an ischemic kidney may preserve renal function. Given the propensity for development of renal disease in black hypertensive patients, the incentive to detect all cases of renovascular hypertension in blacks increases as these data accumulate.

We conclude that blacks with clinical features suggestive of renovascular hypertension should be evaluated with angiography. Captopril-stimulated plasma renin may not be useful in detecting blacks with renovascular hypertension, but this and other potential screening tests require further evaluation. Recognition of the high prevalence of renovascular hypertension in clinically selected blacks could result in significant reductions in hypertension-related morbidity and mortality in this population.

Acknowledgments

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References


**KEY WORDS** • renovascular hypertension • ethnic differences • renal artery stenosis • plasma renin activity
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