Renovascular Hypertension in Black Patients

THOMAS A. KEITH, III, M.D.

SUMMARY In a 10-year period, 7200 of 19,000 black hypertensive adults in the University of Cincinnati Medical Center were referred to the Hypertension Service. In selected patients, intravenous urograms (1038) and renal arteriograms (238) were performed; 47 cases of renovascular hypertension (0.65% of the referred group and 0.25% of the entire sample) were identified. Atherosclerosis (32 patients) and fibromuscular dysplasia (11) were the most common causes of renal artery obstruction. Other lesions included traumatic thrombosis (2), Leriche syndrome (1), and postrenal transplant anastomotic thrombosis (1). Twenty-four patients were operated on (6 cured, 14 improved, 4 dead) and 23 treated medically (18 improved, 2 unimproved, 3 dead). Surgical mortality was 0. Follow-up exceeded 5 years in 25 patients. Extrarenal vascular lesions were found in 30 patients and accounted for six of seven deaths. Renal vein renin ratios ≤ 1.5:1 (affected to unaffected side) predicted successful surgery in 14 patients, but eight of nine operated patients with ratios < 1.5:1 also had favorable results. Factors in addition to renin assay were weighed before surgery was recommended. Since renovascular hypertension is rare in adult blacks, identification of curable forms deserves emphasis. While demographic surveys describe prevalence and disease course, they do not define the number of adult hypertensive blacks with a demonstrable specific cause.

Predominantly white hypertensive groups referred to treatment centers included 4% and 16% with renovascular disease. A previously unscreened series of white men (aged 47 to 54 years) yielded 1% with renovascular hypertension (RVH). Sixteen of 100 "fairly unselected" black hypertensive patients in one center had angiographic evidence of renal artery stenosis; but the degree of obstruction, differential renal function, or renal vein renin assay, and the results of treatment, were not specified.

We analyzed a 10-year sample of hypertensive black patients in our center to determine the incidence of RVH. We anticipated a lower incidence in blacks than in whites and sought quantitative support of our premise. By emphasizing techniques of evaluation, renal artery anatomy, differential renal vein renin secretion, choice and results of treatment, and coincidence of advanced extrarenal arterial disease, we attempt to portray the spectrum of RVH in the study population. With increasing emphasis on cost-containment in medical care, efficient triage of hypertensive patients is paramount. Knowledge of the incidence and clinical behavior of secondary hypertension in discrete population segments promotes economy, without sacrificing accuracy in diagnosis and treatment. The following discussion focuses on the small subset of hypertensive blacks with clinically significant renal artery stenosis.

KEY WORDS • atherosclerosis • fibromuscular hyperplasia • associated diffuse vascular disease
Methods

Patient Sources

Between September 1, 1969, and September 1, 1979, approximately 19,000 black hypertensive (diastolic blood pressure \( \geq 95 \) mm Hg) adults (aged \( \geq 16 \) years) were treated in the emergency rooms, clinics, and wards of the Cincinnati General and Veterans Administration Hospitals. Hypertension was seldom the presenting complaint in the overall sample. Patients with accelerated or malignant hypertension, a hypertension-related vascular catastrophe, preliminary evidence of a specific cause, or those refractory to antihypertensive medication were referred to the Hypertension Service. In the 10-year study period, we examined 7200 black patients.

Patterns of Investigation

Minimum laboratory studies included urinalysis; clean-voided urine culture; serum sodium, potassium, chloride, bicarbonate, uric acid and creatinine; 2-hour postprandial blood glucose; blood urea nitrogen; fasting lipid profile (cholesterol, triglycerides, high- and low-density lipoprotein cholesterol); white blood count with differential and hematocrit; 12-lead scalar electrocardiogram; and a posteroanterior chest radiogram.

Rapid sequence intravenous urography (IVU) and/or isotope renography and scan were performed in patients with: 1) a history of recurrent upper urinary tract infection; 2) a family history of polycystic renal disease or premature deaths from renal failure; 3) onset of hypertension at under age 18 or over 50 years; 4) accelerated or malignant hypertension (diastolic blood pressure \( \geq 110 \) mm Hg and \( \leq 50 \) years); 5) abdominal bruits consistent with renal artery narrowing were present in patients responding poorly to antihypertensive drugs, regardless of the results of IVU; 3) recurrent episodes of accelerated hypertension occurred despite appropriate medical treatment, regardless of findings on IVU; or 4) when angiography performed for reasons (e.g., iliofemoral insufficiency) other than suspected renal artery stenosis demonstrated advanced renal artery occlusion. Such patients were required to have diastolic pressures \( \geq 100 \) mm Hg.

Extrarenal arterial lesions were demonstrated by angiography, computerized axial tomography, surgery, or autopsy. Coronary insufficiency included patients with myocardial infarction or angina pectoris. Myocardial infarction was diagnosed by scalar electrocardiography, enzymatic changes, radioisotope imaging, or autopsy. Angina was documented by symptomatology, graded treadmill exercise, ST segment and T wave changes on scalar electrocardiograms, coronary angiography, or autopsy.

Treatment Decisions and Classification of Results

Recommendations for treatment of RVH were made by the Hypertension Service after consultation with the radiologist and the vascular surgeon. In patients with cerebrovascular disease, the neurologist participated in management decisions. Preoperative planning incorporated the anesthesiologist and the nephrologist (for patients with bilateral parenchymal renal disease). Follow-up was conducted by the Hypertension Service, regardless of attendance at other medical facilities. Assessment of treatment results began at the first postoperative clinic visit for surgical patients and 6 weeks from initial treatment for medical patients. Patient status was reassessed at 6- to 12-week intervals.

The term "cure" is applied to patients with recumbent and standing blood pressure \( \leq 90 \) mm Hg without antihypertensive medication. "Improved" patients are those whose pretreatment diastolic pressure was reduced \( \geq 20\% \) by medication, by surgery, or by both. In postoperative subjects requiring medication, the dosage had to be reduced \( \geq 50\% \) from preoperative levels. "Unimproved" individuals sustained less than 20% reduction in diastolic pressure during the posttreatment period.

Results

Incidence and Etiology

There were 1038 individuals who had IVU, either prior to our initial evaluation or ordered according to the criteria above. Renal artery stenosis was suspected in 112 of these studies. Isotope renography (IR) was utilized primarily not to complement IVU but in patients who either refused the latter examinations or who had a history of allergy to iodine-containing substances or a history of multiple allergies. We ordered 84 IRs, two of which suggested unilateral impairment in renal blood flow. Renal arteriography and renal vein renin assay were accomplished in 238 patients. We became more conservative in ordering all of the three above studies as the number of negative studies accrued.

Of the 7200 referred patients, 47 (0.65%) had a diastolic blood pressure \( \geq 100 \) mm Hg (recumbent or standing, measured on 3 separate days) and \( \geq 50\% \) cross sectional narrowing of a main renal artery or one of its primary branches demonstrated by transfemoral angiography. With four exceptions, the obstruction was produced by fibromuscular dysplasia (FMD) or by atheroma (table 1). Women outnum-
TABLE 1. Etiology and Sex of Patients with Renovascular Hypertension

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Men</th>
<th>Women</th>
<th>Etiology</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atherosclerosis</td>
<td>10</td>
<td>22</td>
<td>Fibromuscular dysplasia</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>2</td>
<td>1</td>
<td>Traumatic</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Leriche syndrome†</td>
<td>1</td>
<td>1</td>
<td>Post-renal transplant; anastomotic occlusion</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total no.</td>
<td>47</td>
<td>32</td>
<td>Total no.</td>
<td>47</td>
<td>32</td>
</tr>
<tr>
<td>Age (yrs)*</td>
<td>38-60</td>
<td>52-55</td>
<td>Age (yrs)*</td>
<td>35-71</td>
<td>27-53</td>
</tr>
</tbody>
</table>

*Mean age given in parentheses.
†Thrombosis of the left main renal artery suggested by aortography and observed at the time of surgery.

Surgery was recommended for 24 subjects with favorable preoperative profiles or with life-threatening, drug-refractory hypertension. Aortorenal bypass was performed in 18 patients (bilateral in six), three of whom later required nephrectomy because of torsion or thrombosis of the shunt(s). Three individuals had primary nephrectomy for an infarcted kidney producing excessive renin. Endarterectomy was employed in two patients. In one case, the surgeon found more extensive involvement than shown by angiography, and no repair was attempted. There were no intraoperative or early (within 4 weeks) postoperative deaths.

Six of 47 patients were "cured," 32 "improved," and two "unimproved" (figs 1 and 2). Mortality for the series was 15% (three in the medical and four in the surgical group). Survival ranged from 6 weeks (one patient) to 6 years (three patients); the remaining three patients lived for 2½ years (one) and 4 years (two). All seven deaths occurred in subjects with atheromatous renal artery occlusion; six patients died suddenly from cardiovascular events, the seventh from nephrosclerosis and chronic left ventricular failure. Follow-up exceeded 5 years in 25 patients, who had favorable results except for three deaths. Five subjects were lost to follow-up (from 6 weeks to 2 years following initial treatment by our service).

Renal Vein Renin Activity

A unilateral increment in renal vein renin activity > 1.5:1 was present in 11 surgically-treated patients with unilateral stenosis (contralateral renin suppression in nine) and in three with bilateral obstruction. Operation significantly lowered blood pressure in all 14 subjects, four of whom died after varying periods of improvement (fig. 2). Nine operated patients had renal vein renin ratios < 1.5:1, and results were favorable in all but one. The renal vein and inferior caval renin ratio...
assays were lost in a single patient, who benefited from aortorenal bypass.

Fourteen medically treated patients had renal vein renin ratios < 1.5:1 and four ≥ 1.5:1 (contralateral renin suppression in three). The angiographer omitted sampling of renal venous blood in five patients whose complex renal arterial lesions precluded surgery. Otherwise we would have obtained renal vein and inferior caval renin assays on a subsequent day.

Extrarenal Vascular Disease

A variety of nonrenal cardiovascular abnormalities complicated our patients' courses (table 2): 79 were found in 30 individuals, four of whom had FMD. The abnormalities included iliofemoral insufficiency (18 patients), cerebral large-artery stenosis (17 patients), left ventricular failure (17 patients), symptomatic coronary-artery involvement (11 patients), ≥ 50% angiographic narrowing of celiac and/or mesenteric arteries (5 patients), and abdominal angina, relieved by superior mesenteric bypass (one patient). Bruits associated with visceral artery stenosis were indistinguishable from those reflecting renal artery lesions. Six of seven deaths resulted from these extrarenal vascular events.

Symptomatic extrarenal vascular disease preceded documentation of renal artery stenosis in 10 individuals, was discovered simultaneously in five, and followed treatment of RVH in 15 patients. Sudden death occurred in four patients, in whom extrarenal complications were not discovered until autopsy. Protracted follow-up revealed increasing evidence of generalized arterial occlusive disease which, in many instances, was amenable to surgical correction before catastrophic target-organ events.

TABLE 2. Coexisting Cardiovascular Lesions (79 Lesions in 30 Patients)

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>No. of patients*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iliofemoral insufficiency</td>
<td>18</td>
</tr>
<tr>
<td>Carotid and/or basovertebral insufficiency</td>
<td>17</td>
</tr>
<tr>
<td>Left ventricular failure</td>
<td>17</td>
</tr>
<tr>
<td>Coronary insufficiency</td>
<td>11</td>
</tr>
<tr>
<td>Celiac and/or mesenteric stenosis (≥ 50%)</td>
<td>5</td>
</tr>
<tr>
<td>Abdominal angina I</td>
<td></td>
</tr>
<tr>
<td>Abdominal aortic aneurysm</td>
<td>4</td>
</tr>
<tr>
<td>Berry aneurysm</td>
<td>3</td>
</tr>
<tr>
<td>Acute bacterial endocarditis (S aureus, aortic</td>
<td>1</td>
</tr>
<tr>
<td>valve) following nephrectomy</td>
<td></td>
</tr>
<tr>
<td>Aortic dissection, Type III</td>
<td>1</td>
</tr>
<tr>
<td>Coarctation of thoracic aorta</td>
<td>1</td>
</tr>
<tr>
<td>Thoracic aortic aneurysm 13 years after coarct-</td>
<td>1</td>
</tr>
<tr>
<td>ation repair</td>
<td></td>
</tr>
<tr>
<td>n = 79</td>
<td></td>
</tr>
</tbody>
</table>

Incidence

The paucity of RVH in blacks is implied by a number of observers. Foster and his associates at Vanderbilt recorded a lower incidence of advanced renal artery stenosis in black than in white women and no instance of RVH in 28 black men, compared with a 30% incidence in 68 white men. Early experience with RVH at Baylor University included two blacks in a series of 200 patients. Simon et al., analyzing the Cooperative Study of Renovascular Hypertension, found that 8% of all patients with renal artery stenosis were black, although blacks comprised 30% of the study sample (2442 patients). Of 113 subjects operated on for FMD at the University of Michigan, one was black. A South African clinic recorded a single case of renal artery stenosis in 500 black hypertensive patients. On the other hand, one of the earliest reports (1938) of successful surgery for FMD was recorded in a 5½-year-old black child. Our investigation of 7200 black hypertensive adults revealed only 47 (0.65%) with RVH and reinforces Foster's impression that blacks have a lower incidence of the disease than their white cohorts. While we did not submit all of our subjects to IVU and/or to angiography, our yield of positive results in these studies support the conclusion of other investigations in which these examinations were uniformly procured.

Diagnosis and Choice of Treatment

Three categories of evidence characterize hypertension caused by renal artery stenosis: 1) suggestive, including history (accelerated disease, trauma, age at onset of under age 18 or over age 50), characteristic abdominal bruits, hypokalemia in the absence of diuretic therapy; 2) presumptive, including IVU, isotope renography and scan, elevated peripheral renin activity (PRA), and a marked fall in blood pressure following administration of saralasin or angiotensin I and II converting enzyme inhibitor; and 3) definitive, renal arteriography combined with differential renal vein renin production. Strictly defined, RVH implies a fall in systemic blood pressure following repair of the renal artery defect or removal of the involved kidney. Patients treated medically cannot meet this criterion, but not all subjects with definitive clinical studies are surgical candidates.

Marks et al. reported 90% success in renal artery repair when the renal vein renin ratio was ≥ 2:1 and 83% in patients with ratios of < 2:1. For optimum surgical results, the clinician must weigh all preoperative data; ≥ 50% renal artery narrowing accompanied by augmented renin secretion is the most accurate, but not absolute, prognostic factor.

Significance of Renin Assay

Successful surgery for RVH without increased renin production by the involved kidney(s) prompts speculation regarding pathogenesis. Errors in sampling tech-
niques and renin assay undoubtedly occur, but can be
minimized by stringent quality control and repeat
testing.

Preparation for renal vein renin sampling is not uni-
form in large series of RVH. All investigators agree
that sodium restriction and elimination of renin-
suppressing drugs are critical for accurate results.
Ideally, 24-hour urinary sodium excretion should
verify restriction in sodium intake. In our patients, we
eliminated all medication except diuretics and
restricted sodium intake to 500 mg daily for 72 hours.
In patients with advanced renal artery stenosis (≥
50%) and a renal vein renin ratio of < 1.5 to 1, we
resampled renal vein and inferior caval blood for renin
activity at least once.

Black patients with essential hypertension have a
higher percentage of low PRA than whites, even
after stimulation with furosemide. Furthermore, the
proportion of low-renin hypertensive blacks increases
with age, as does the incidence of RVH. Failure of
preoperative renal vein renin assay to uniformly
predict surgical results may reflect a genetic difference
in renin production, even when renal perfusion is
markedly diminished. The effect of altered prostag-
landin and of kallikrein-kinin secretion in
hypertensive blacks has been investigated. Routine
measurement of these substances may eventually sub-
stantiate their role in the genesis of essential and of
renovascular hypertension with hyporeninemia.

Dynamics of Renal and Extrarenal Vascular Lesions

We monitor myocardial function, critical vascular
beds (cerebral, coronary, renal, iliofemoral), and the
aorta in hypertensive patients treated for occlusive
arterial disease in any area. Generalized athero-
matous occlusive disease reduces the success rate of
surgery for RVH, and mandates careful periodic (at
least every 3 months) examination in the posttreat-
ment period. Holley et al. found atheromatous
occlusion of the renal arteries at autopsy in hyper-
tensive and normotensive subjects; degenerative
changes began in the fourth decade and advanced with
age. Wollenweber et al. correlated progressive renal
artery stenosis by serial angiography with the clinical
course in hypertensive patients whose longevity was
increased by blood pressure control. The incidence of
nonfatal cardiovascular events was not diminished by
treatment.

The preponderance of women (22 of 32 subjects)
with atherosclerotic RVH in our series is partially ex-
plained by the proportion of women (57%) in our
group of 7200 patients. Foster et al. found five of 53
black hypertensive women, subjected to renal
arteriography and split renal function studies, to have
"significant renal artery stenosis" and none of 28
hypertensive black men. Comparable values in white
subjects were 19 of 59 females and 20 of 68 males.

Fibromuscular dysplasia in adults is usually con-
fined to the renal arteries and exhibits three anatomic
patterns: intimal, medial, and adventitial. Stewart
et al. attached prognostic significance to these vari-
ants; Kincaid et al. and Sheps et al. found angio-
graphic evidence of progressive narrowing regardless
of the anatomic pattern. Four of our 11 black pa-
tients with FMD displayed extrarenal narrowing, and
one patient displayed transient right hemiparesis as
the initial symptom. In this latter patient, who also
had inoperable, bilateral renal FMD, surgical dilata-
tion of the left internal carotid artery prevented
further episodes during a 5-year postoperative period;
her hypertension responded favorably to medication.
In our series of 150 white adult patients with RVH,
three of 35 with FMD presented with extrarenal
vascular events. A fourth individual had autopsy-
proven subintimal hyperplasia in the renal, coronary,
cerebral, and iliofemoral arteries. Two white women
in our series had FMD and atherosclerosis-producing
bilateral renal arterial narrowing. We agree with Hunt
and Strong that surgical treatment of RVH does not
permanently alleviate but modifies the course of a pro-
gressive degenerative process. In our experience, renal
artery stenosis often signifies disseminated arterial
disease, particularly when atherosclerosis is the pri-
mary lesion.

Conclusions and Recommendations

From our study of RVH in a black hypertensive
population, we conclude that:

1. Clinically significant renal artery stenosis is
uncommon in adult black hypertensives, who
should not be subjected to intensive investiga-
tion without specific suggestive findings.
2. Results of medical and surgical treatment for
RVH in blacks are similar to those in whites.
3. In blacks with FMD, the ratio of women to
men (5 to 1) was the same as in whites.
4. Atherosclerotic or, occasionally, fibrodys-
plastic renal artery occlusion may signify
lesions in other vascular beds, which can evoke
symptoms years after detection of the renal
abnormality, and, conversely, patients with
stroke, claudication, coronary insufficiency, or
aortic aneurysm may later develop RVH.
5. Differential renal vein renin assay does not
necessarily predict surgical success in any
series of patients with renal artery stenosis and
hypertension. We are most cautious in recom-
mending surgery to patients without renin
step-up after repeated sampling. Such opera-
tive candidates are told that their statistical
chance for improvement is less than if a
significant renal vein renin ratio exists.
Increasing knowledge of prostaglandin and kinin
metabolism may clarify the pathogenesis of
low-renin RVH.
6. Methodical follow-up of all patients with
RVH (e.g., auscultation of the carotid
arteries, palpation of the abdominal aorta,
and of pulses in the lower extremities) can
detect complications in nonrenal arterial beds.
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