Evaluation of Patients with Renovascular Hypertension

MORTON H. MAXWELL AND ABRAHAM U. WAKS

RENOVASCULAR hypertension is the most prevalent form of surgically curable high blood pressure. Nevertheless, controversy surrounds the screening of patients and the choice of appropriate diagnostic workup.

In testing for renovascular hypertension, differences of opinion can be anticipated in view of several dilemmas. First, renovascular hypertension is a retrospective diagnosis. A technically acceptable renal arteriogram can establish the diagnosis and usually the etiology of renal artery stenosis. Whether the stenotic lesion is responsible for all or part of the elevated blood pressure is determined retrospectively by the blood pressure response to corrective surgery or to transluminal angioplasty (PTA). Other diagnostic tests are not specific for renal artery stenosis. Rather, they merely indicate nonspecific phenomena, such as turbulent blood flow in a large intraabdominal artery (abdominal bruit), disparity of kidney or endocrine function between the two kidneys (radionuclide studies, intravenous urogram, renal vein renins), or angiotensin-mediated hypertension (saralasin test). Each of these tests may be positive in disorders other than renovascular disease and has significant rates of false negativity. Thus, no test or combination of tests can reliably diagnose renovascular hypertension.

Second, renovascular hypertension is a "rare" disorder. Depending upon referral sources, estimates of the prevalence of renovascular hypertension range from 0.2% to 10% of the hypertensive population. This low prevalence compared to essential hypertension suggests cost and risk benefits of the tests for its diagnosis. Because of the low prevalence of renovascular hypertension, even a given diagnostic test of high sensitivity and specificity will have a low predictive value and will result in a large number of patients with essential hypertension being subjected to unnecessary procedures.

Third, renovascular hypertension responds to antihypertensive drug therapy. No prospective, randomized trials of medical vs operative therapy of renovascular hypertension have been published. Nevertheless, recent reports suggest that the elevated blood pressure can be controlled, particularly with the use of beta-blockers or captopril.

These dilemmas lead to the following questions. What are the indications for a diagnostic workup for renovascular hypertension? What strategy would achieve maximal diagnostic efficacy with minimal cost and risk? Should most patients who are suspect for renovascular hypertension receive treatment with antihypertensive drugs, which thus eliminates the need for most diagnostic studies?

The last question is the easiest to answer. Cure is preferable to amelioration of hypertension and eliminates probability of poor compliance, cost, side effects, the potential risk with lifetime drug therapy, and the danger of progressive renal failure due to advanced ischemia. The risk and cost of curative procedures have decreased dramatically with the introduction of PTA. This decrease justifies a diagnostic workup in higher risk patients. In the only long-term comparative follow-up published, operated patients had a lower mortality and better blood pressure control than did the drug-treated group.

Practical Strategies

The suggested strategy that follows is based upon our own decision making in clinical practice at present and reflects the practice of most colleagues we have questioned. It is based upon two premises. First, the low "prior probability" of renovascular hypertension precludes any valid estimate of "posterior probability" based upon the usual (p value) statistical analyses of the various diagnostic tests, so that decision making reverts back to clinical acumen and the physician's perception of benefit vs risk for a particular patient. Second, most patients with renovascular hypertension do not present with the prototypical history of sudden onset of severe hypertension at an inappropriate age, but are clinically indistinguishable from patients with essential hypertension.

The suggested strategy also takes into cognizance the markedly lower cost and morbidity of PTA than that of operation and thus expands the diagnostic base. This classification of patients and selection of diagnostic studies are not meant to be rigid or precise; there is overlapping of patient groups. This classification and selection represent our best clinical judgment at the present time.

Intervention with Possible Cure or Improvement of Hypertension

For some patients, intervention with possible cure or improvement of hypertension is preferable to long-term drug therapy. This group includes children, pa-

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tients with severe and accelerated hypertension, and patients with hypertension that cannot be controlled with antihypertensive drug therapy (e.g., with poor blood pressure response, adverse side effects, or lack of compliance). Patients in this category comprise about 10% of the hypertensive population.

The usual type of diagnostic workup for renovascular hypertension (plasma renin activity, radionuclide studies, intravenous urogram, digital subtraction angiography [DSA], renal vein renins, testing with angiotensin analogs or converting-enzyme inhibitors) is complicated, costly, nondiagnostic, and designed to determine the need for renal arteriography. In clinical practice, a negative or questionably positive screening test is often ignored, and a more complicated study is ordered because the need for intervention is so great in this type of patient. Usually, renal arteriography is eventually performed, regardless of prior test results. Therefore, why not proceed directly to renal arteriography?

Renal arteriography is diagnostic of the type, degree, and operability of renal artery stenosis. With further technological improvement, DSA may replace renal arteriography as the initial examination in this patient group. At present, however, DSA is not as dependable as standard arteriography in visualizing main renal artery lesions, and the renal arterial branches are seldom visualized at all. In our experience, even with a positive DSA surgeons will seldom operate without first requesting conventional arteriography.

Regardless of the type or degree of stenosis demonstrated arteriographically, PTA is attempted during the same procedure. Successful initial dilation by PTA is possible in 90% of main renal artery stenoses. If initial dilation is successful, as judged by radiologic appearance and confirmed by a decreased pressure gradient, then the short-term blood pressure response (days, weeks) offers the most accurate and practical diagnosis of renovascular hypertension; if the blood pressure falls significantly, the diagnosis of renovascular hypertension is established, even if the blood pressure should subsequently increase because of restenosis. Thus, PTA is used as a diagnostic test as well as a therapeutic modality. When PTA is not technically feasible or is initially unsuccessful in dilating a stenotic lesion, the usual diagnostic tests to ascertain its significance (renal vein renins, saralasin test) are employed.

This approach permits diagnosis and therapy during a brief hospital admission and reduces the costs and risk of the traditional approach.

Suspected Renovascular Hypertension

Clinical correlates of renovascular hypertension include inappropriate age of onset, sudden onset or abrupt worsening of preexisting hypertension, and systolic-diastolic epigastric bruits. The degree of blood pressure elevation in the group of patients with these correlates is irrelevant. Duration of hypertension has an inverse relationship to the operative cure rate in renovascular disease, and the possibility of cure should be offered prior to the long-term cardiovascular sequelae of high blood pressure. These patients should be screened for renovascular hypertension with DSA or with a rapid sequence intravenous urogram, with renal arteriography performed only if the screening test is positive. A rapid sequence urogram has a high exclusion value. Radionuclide studies and saralasin testing (utilizing both blood pressure and renin responses for interpretation) are useful if administration of radiocontrast material is contraindicated.

Mild and Moderate Hypertension

Diagnostic workup is most controversial for patients with mild and moderate hypertension that is not suspect for renovascular disease, a group that comprises over 75% of the hypertensive population. Most patients with renovascular disease do not have distinctive clinical features and simulate patients with essential hypertension. The decision to test further is based upon clinical judgment (patient compliance, target organ damage, family history, drug side effects) and the desires of the individual patient.

We use the blood pressure response to diuretics as a gross screening test. Over 60% of these patients will exhibit a significant reduction in blood pressure following a brief period of thiazide therapy or will exhibit this reduction the morning after a single oral dose of furosemide (1 mg/kg body wt) that has been administered the evening before. This responsive group is not studied further for renovascular hypertension (volume-mediated hypertension?). Patients whose blood pressure fails to respond to a diuretic are more likely to have renin-dependent hypertension. Moderate sodium depletion following thiazide or furosemide administration improves the predictive value of the saralasin test, especially when postsaralasin PRA, as well as blood pressure response, is used to evaluate test results. Thus, when there is no vasodepressor response to diuretic administration, the natriuresis will have served to prepare the patient for a saralasin bolus test. Only those with a positive saralasin test are considered for further studies in renovascular hypertension. This sequence is cost-effective and avoids unnecessary invasive procedures.

Conclusions

The strategies above are based upon particular clinical circumstances and risks, as well as upon the likelihood of renovascular disease, rather than upon a prefixed set of diagnostic tests for all patients. They are not intended to be exclusive or categorical. When the patient is at high cardiovascular risk or when the likelihood of renovascular disease is great, renal arteriography is used to rule out this disorder or to delineate the renal artery lesion. The early blood pressure response to PTA determines its significance. When the likelihood of renovascular disease is lower, then standard tests are used. Obviously, further technical improvements in DSA could change these strategies.
have some reservations about the preceding recommendations of Maxwell and Waks (see pp 589-591). First, the major premise that transluminal angioplasty (PTA) has greatly reduced the risks and costs of treating renal artery stenosis is not based on long-term follow-up of formal cost analysis. The references (9 to 11) cited are some of the earliest reports and had an average follow-up time of only 6 months. Indeed, our data suggest that the chances of long-term reduction of arterial pressure in most patients with atherosclerotic stenosis are so poor that I have some reservations about using PTA for treating atherosclerotic ostial lesions.2 3 A recent review4 of 214 published cases of PTA and 903 surgical cases of atherosclerotic disease that were followed-up for at least 6 months reports a cure rate of only 15% with PTA, but a rate of 37% with operation. Furthermore, the failure rate was 42% with PTA. The results were better for fibromuscular dysplasia. The possibility of a different therapeutic approach for patients with atherosclerotic disease and with fibromuscular dysplasia should be considered.

The second premise that “cure” is preferable to amelioration is not based on firm data and rests primarily on the Mayo Clinic study which was done before the availability of our more powerful antihypertensive agents such as beta-blockers, minoxidil, captopril, and now calcium slow-channel blockers. Indeed, the likelihood of cure in patients with atherosclerotic lesions, even with surgery, is again extremely low; at more than 2 years of follow-up, most patients are back on some type of antihypertensive drug therapy. Thus, if one takes the Maxwell and Waks approach of PTA for all atherosclerotic lesions, in only 15% of the patients will the probability of poor compliance, cost, side effects, potential risk of lifetime drug therapy, and the danger of progressive renal failure due to advanced ischemia be eliminated for more than perhaps 2 years.

Although PTA may have reduced cost more than 10 times, the cost of the approach recommended by the authors will likely be at least $3000 for the average patient so treated. These costs are:

<table>
<thead>
<tr>
<th>Cost ($)</th>
<th>Description</th>
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<tbody>
<tr>
<td>$800-$1000</td>
<td>average 4 days in the hospital</td>
</tr>
<tr>
<td>$200/day</td>
<td>@ $200/day</td>
</tr>
<tr>
<td>$400-$1000</td>
<td>arteriogram</td>
</tr>
<tr>
<td>$600-$1000</td>
<td>dilation cost</td>
</tr>
<tr>
<td>$400-$1000</td>
<td>follow-up studies</td>
</tr>
<tr>
<td>$2200-$4000</td>
<td>(arteriogram, isotope, etc.)</td>
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This averages out to about $3000. One can purchase a lot of medications for $3000. This does not appear to be cost-effective, especially since only a small number of patients with atherosclerotic stenosis will benefit in the long run. An additional concern with their approach is the possibility of increased risk of arteriography and angioplasty at the same time. Certainly, twice as much contrast material is required. In the older, high-risk patient with atherosclerotic stenosis, the risk of renal failure is real, although probably low. If only one patient (age 60) develops renal failure and requires long-term hemodialysis at $30,000 per year for, say, 7 years, then the cost is increased by...
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