Hypertension Management in PAD Patients

Optimal medical management.

BY JAMES A.M. SMITH, DO

Hypertension (HTN) can be defined as persistent elevation in blood pressure exceeding the ideal of 130/90 mm Hg (130/85 in diabetics). There are, however, many scenarios in which it is less than clear whether a patient with HTN needs to be treated. Each of us has encountered the patient who says, "My pressure is always high when I come to the doctor's office. At home, my pressure is fine." That person requires evaluation and follow-up to determine if there is a blood pressure (BP) problem that needs treatment.

HTN is one of the major risk factors for cardiovascular disease and poses a risk in other vascular territories; therefore, it is critical to evaluate the patient from a broad perspective regarding cardiovascular risk. Genetic predisposition to vascular disease is especially important when compounded with other risk factors: HTN, smoking, elevated lipids, insulin resistance, sedentary behavior, or previous vascular territory insult, such as myocardial infarction (MI), congestive heart failure (CHF), stroke, hypertensive retinopathy, left ventricular hypertrophy, and peripheral artery disease (PAD). It should be emphasized that BP control is a key element in minimizing the likelihood of cardiovascular death and morbidity in these patients. Interestingly, Wong et al reported that 75% of patients with systolic HTN had inadequate control. More importantly, although 89% of patients with strokes were treated for HTN, only 35% of those patients had their BP controlled to adequate levels (≤140/90 mm Hg), and subsequently, there was a one in six chance for recurrent stroke.[1]

HTN AND ITS CAUSES

In patients who insist that their BP is never high unless they are in the doctor's office, an echocardiogram is very useful to predict target-organ effects of sustained HTN. Because negative remodeling of the heart (ie, left ventricular hypertrophy and mitral regurgitation) is easily assessed by this noninvasive test, it is a very compelling argument that patients require more aggressive treatment of their BP. When coronary artery disease, PAD, or bruits are discovered or identified in any vascular territory, the issue of BP must be addressed because HTN accelerates the atherosclerotic process.

Although secondary causes of HTN are present in <10% of patients, the first step in treating essential HTN has been the restriction of dietary sodium because excess salt results in volume retention, which may exacerbate HTN in many individuals. This requires considerable education regarding dietary sodium because the diet in Western societies is very high in sodium content, much of which is "hidden" and unknown to the consumer. It is well known that canned soups and fast food (increasingly consumed by the older population), as well as many restaurant meals, snack foods, and luncheon meats, are very heavily salted, yet few of our patients take time to analyze what they eat on a daily basis.

Diastolic HTN frequently occurs in the obese population and is multifactor, including high sodium consumption, volume expansion, diastolic cardiac dysfunction in insulin resistance syndrome, and sedentary behavior. This group also includes individuals with obstructive sleep apnea, an ever-increasing number in Western society. These people may present with systolic HTN, diastolic HTN, or they may be in "sympathetic overdrive," which is HTN with resting tachycardia.

Systolic HTN is prevalent in older populations due to a decrease in large vessel compliance, salt and fluid retention, and left ventricular dysfunction. In certain individuals, sympathetic overdrive—resting tachycardia with increased systemic vascular resistance—can result in HTN, which accelerates the potential for cardiovascular morbidity, especially MI, stroke, and kidney failure.

HTN in patients with cardiac or renal disease invariably has a combination of risk factors. Idiopathic (essential) HTN is by far the common denominator in the population at risk for cardiovascular disease. However, these patients may progress to require the addition of multiple medications for BP control. When this happens, a physician may suspect that other factors, such as renal artery stenosis (RAS) or decreased large-vessel compliance, may be contributing.

RAS is predominantly due to atherosclerotic (macroarterial) disease, although in younger individuals (<35 years), a separate etiology, fibromuscular dysplasia of the renal arteries, should be considered. The groups of patients with intrinsic renal disease, glomerulonephritis, interstitial nephritis, and vasculitis represent a smaller proportion of the hypertensive population. Because these hypertensive patients are less common, this discussion focuses primarily on individuals in the risk pool for systemic atherosclerosis, patients >50 years with multiple cardiovascular risk factors.

HTN TREATMENT IN THE PAD PATIENT

PAD represents atherosclerosis of the lower extremities, and HTN is often a common denominator in these patients. Because HTN is a risk factor for MI, stroke, limb claudication, and renal failure, treatment of HTN is an essential element for treating any of these conditions.

Current therapy in patients with a history of MI includes beta blockade, angiotensin receptor blockade with or without angiotensin-converting enzyme inhibition, diuretics, and antiplatelet regimens. Calcium channel blockers have both antiarrhythmic and antihypertensive effects as well, and the majority of these patients are on some combination of these medications. Central alpha-adrenergic inhibitors may also be used. Thus, we treat these patients with volume (sodium) depletion, diuretics, renin inhibition, sympathetic inhibition, and calcium blockade while attempting to slow the progression of their cardiovascular disease.

In patients with resistant HTN who do not have RAS, hyperaldosteronism is recognized as the most common etiology. In this setting, a plasma aldosterone-to-renin ratio should be measured even if the serum potassium level is normal. A ratio >20 has sufficient sensitivity and specificity to serve as an effective screening test for hyperaldosteronism. Confirmation with a 24-hour urine test for aldosterone excretion confirms the diagnosis. Values of urinary aldosterone exceeding 12 mg/24 hours with urinary sodium >200 mEq/24 hours reflect primary aldosteronism.[2]

Medical therapy with mineralocorticoid receptor antagonists, such as spironolactone and eplerenone, offers a first line of therapy in these patients, especially when they are not good surgical candidates. Laparoscopic adrenalectomy should be considered in patients with a unilateral adenoma whose BP cannot be controlled adequately.[3]

Frequently lacking in these medical regimens are patients taking ownership of their condition. They often fail to make adequate lifestyle modifications to help control their disease process. As many of these patients are >50 years old, their lifestyles are ingrained such that they find it nearly impossible to exercise, lose weight, eat a healthy diet, and favorably influence their disease. A common argument is genetics, "My dad was big, my uncles, aunts, and mother had diabetes, etc." Thus, the patient has the foregone conclusion that, "There is nothing I can do about the cards I was dealt." This attitude permeates our society, and unless we as physicians intervene earlier, the idea of inevitability continues to become an insurmountable obstacle resulting in cardiovascular crisis intervention.

One startling trend in the US is the ever-increasing prevalence of diabetes, which correlates with obesity in our population.[4] Patients who claim that, "My HgA1c is good" tend to ignore the fact that any diagnosis of insulin resistance (prediabetes, type II diabetes) correlates with the presence of cardiovascular disease. Thus, cardiovascular disease can manifest as a macroarterial insult (MI, stroke, symptomatic PAD, RAS with renal insufficiency, HTN) or as a microvascular complication, such as retinopathy, nephropathy, diastolic dysfunction, peripheral neuropathy, lacunar stroke, claudication, and potential limb loss. Diabetes accelerates vascular disease, and once the diagnosis is made, the patient must understand the seriousness of potential cardiovascular complications.

Factors to Consider When Selecting a Treatment Plan

Key points in the assessment of HTN are the presence of target organ damage, such as left ventricular hypertrophy, stroke, and proteinuria. Any finding that suggests the presence of PAD, such as claudication and carotid or abdominal bruits, should heighten the acuity of the clinician's need to treat the patient's HTN and other risk factors. Pohl et al found that atherosclerotic renal artery disease progressed in 44% (37/85) of patients; 16% (14/85) of patients progressed to total occlusions at 1 year.[5]

We see patients over a wide spectrum of disease processes. One patient may present with an acute MI as the first symptom of cardiovascular disease, whereas another individual who had an MI 4 years before is seen for a routine physical. The common denominator is systemic atherosclerosis, and we as clinicians know that there are factors that favor progression and others that tend to slow the progression of the disease process. Although we physicians are not always model patients ourselves, it behooves us to set a good example by our lifestyles, appropriate exercise, and dietary behavior with judicious counseling. It is also critical that we use the resources available to us and provide this information to our patients to permit them to make

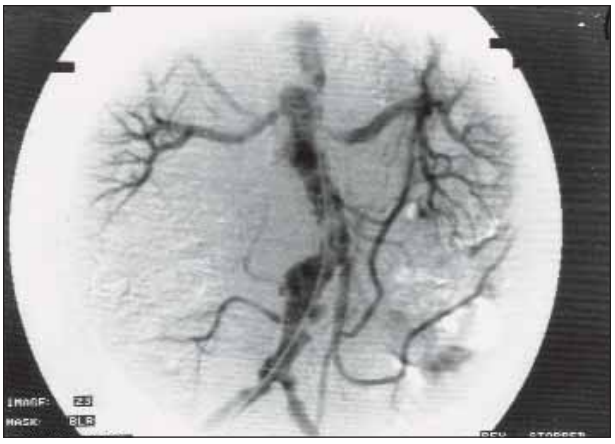

Figure 1. This 79-year-old patient with bilateral RAS had a hostile aorta and severe multidrug-resistant HTN. Because of insulin-dependent diabetes mellitus and severe CAD, she was not a candidate for surgical revascularization. She had two hospitalizations for "flash" pulmonary edema in the preceding 3 months and ultimately underwent bilateral renal artery percutaneous transluminal angioplasty with stents. She lived 4 additional years with no subsequent admissions for CHF and did not require dialysis.

healthy decisions. The psychology of medicine is an enormous part of our daily practice, and our relationship with patients is critical to modifying the natural history of systemic atherosclerosis. We are fortunate to have excellent pharmacology available, with the potential for even better drugs on the horizon.[6] However, unless we can convince patients to take ownership of their disease, make changes in lifestyles, and reinforce good behavior, we will continue to expend a very large amount of our health care resources on putting out fires and crisis intervention in cardiovascular care. Of those issues that may be successfully treated, our justification may be for the prevention of stroke, MI, renal failure, or lowered mortality rates. The prevention of renal failure usually is accomplished by interventional means in patients with severe bilateral RAS or unilateral disease to a solitary functioning kidney (Figure 1).

HOW OFTEN DO NEPHROLOGISTS REFER RAS PATIENTS?

On a monthly basis, I teach a course on angiography and peripheral vascular intervention. The students include cardiologists, radiologists, vascular specialists, and, increasingly, cardiovascular surgeons and general surgeons who are learning peripheral vascular intervention techniques. I ask them, "Do nephrologists refer patients for RAS?" Invariably, the answer is either "never" or "very seldom." These responses raise the question as to why this is the case. As I see it, there are a few possible answers.

Potential Reasons for Nonreferral

First, some nephrologists may not believe that percutaneous transluminal angioplasty with or without stents has been beneficial. The indications for percutaneous transluminal angioplasty with stenting have not been well defined. Current indications include difficult-to-control BP in patients with >70% unilateral or bilateral stenosis, azotemia caused by significant RAS, uncompensated CHF or flash pulmonary edema in patients with bilateral RAS, or decreasing renal mass (atrophy) caused by unilateral or bilateral RAS that has been assessed by serial imaging.

In the DRASTIC study, Van Jaasveld et al studied 106 patients with RAS exceeding 50% and a serum creatinine level of 2.3 micrograms per deciliter or less. These patients were also required to have a diastolic BP of ≥95 mm Hg despite treatment with two antihypertensive medications or a serum creatinine level increase of >0.2 micrograms per deciliter during treatment with an angiotensin-converting enzyme (ACE) inhibitor. The patients were monitored for 12 months, and the investigators found no significant differences in systolic and diastolic BP, daily drug doses, or renal function between the angioplasty without stents group and the drug therapy group. They concluded that in the treatment of patients with HTN and RAS >50%, angioplasty had little advantage over antihypertensive therapy. Patients were excluded from the DRASTIC study if they had proven secondary HTN from other causes (cancer, CHF, unstable CAD). Only two patients in the angioplasty group received renal artery stents, while two additional patients underwent surgical revascularization for failed angioplasty and in one patient whose HTN persisted (diastolic BP ≥95 mm) after 3 months. At 12 months, 48% (23/48) of the angioplasty patients had at least 50% stenosis of the treated artery, but none had total occlusion. In the drug therapy randomized group, 86% (43/50) underwent angiography at 12 months. Seventy-two percent (31/43) of these patients had stenosis ≥50%, and the stenosis had progressed to total occlusion in 9% (4/43). This study raised even more questions regarding the treatment of RAS, and the data were significantly flawed by the fact that stents (the current standard of care) were not used. The patients who underwent surgical revascularization confound not only the data but also suggest that the premise of endovascular therapy for preservation of renal size (mass) is correct. Although there was no significant benefit in BP control between the two groups, a selection bias against patients with CHF who were not included in the study may have actually favored intervention with angioplasty and stents had they been included.[7]

Second, some nephrologists may not pursue the diagnosis with fervor. Some HTN experts may claim that the

gold standard, the renal duplex scan, is "not that accurate" or is "technically difficult." Although it is true that the technical difficulty is an issue in large patients and sometimes requires a bowel preparation, it is widely viewed as the most accurate test with absolutely no potentially adverse biologic effects. In the proper hands, it is the gold standard (short of angiography) in diagnosing RAS. The duplex scan combines real-time imaging of the kidney with pulsed Doppler interrogation of the renal arteries. Thus, it provides information about kidney size, contour, and drainage, while also providing physiologic data about renal artery flow and resistance.

This raises other questions: "With an exam such as the renal duplex scan available, why is it not more widely available, and why do not vascular specialists, and especially nephrologists, insist upon excellence when providing this test?" The fact remains that the renal duplex scan, when performed by a registered vascular technologist, is the most specific, cost-effective test available to our patients with HTN who are in a high-risk category for atherosclerotic disease. Otherwise, the clinician is forced to rely on contrast imaging with computed tomography or magnetic resonance angiography, or a standard contrast angiogram. Knowing the value of this completely noninvasive test, it behooves all vascular laboratory directors to insist that their registered vascular technologists are proficient in performing a renal duplex scan.

Third, nephrologists believe that medical therapy is just as good or better than intervention. This argument may reflect local expertise or lack thereof or the false assumption that we are doing a better job of controlling HTN than we actually are. (See the National Health and Nutrition Exam Survey.)[1]

Furthermore, if the only alternative were progression to the need for dialysis, why would one not aggressively find and treat these patients with percutaneous transluminal angioplasty and stents? One might draw the conclusion on the behalf of the patient that a dialysis lifestyle is tolerable. However, the time commitment, comorbidities, cost of transportation, inconvenience to family members and patients, and burden of chronic illness must be considered. No one wants to be on dialysis unless every potential alternative has been exhausted.

Fourth, nephrologists may be afraid of losing control of their patients after referral to the vascular specialist. This argument is sound in that most of us as physicians believe that we can do as good a job at treating BP as another specialist or even the primary care physician. In fact, the National Health and Nutrition Exam Survey suggests that this mentality may have credibility because only 35% of patients who had strokes were subsequently treated with adequate BP control.

CONCLUSIONS AND PROVOCATIONS

The treatment of HTN in the cardiovascular patient population remains a significant clinical challenge. In fact, it needs to be one of the highest priorities in preventing the progression of cardiovascular disease in previously diagnosed target organs or undiagnosed other vascular territories. Because the treatment of HTN often requires a multidrug regimen, the physician must factor in a number of concerns—such as the frequency of dose administration, cost, and side effects—that weigh heavily on the clinical decision-making process. In addition, and perhaps just as important, is the fact that the patient has systemic atherosclerosis, a potentially terminal disease, and medication is only a part of the overall management of this condition. The patient must take ownership of his condition while the physician provides counseling, encouragement, and the psychological support necessary to help him make significant lifestyle changes.

Whether we are doing a good job in treating HTN remains in question, and recent data suggest that we can do much better.[1] Various types of physicians treat cardiovascular patients, and it is important to use the available resources to aggressively pursue a target BP of <140/90 mm Hg and to monitor disease progression. In some cases, endovascular intervention provides at least a palliative solution, but results need to be monitored. This includes monitoring of the BP and patient lifestyle, periodic assessment of glomerular filtration rate and serum creatinine, renal duplex surveillance after an intervention, and even more proactive evaluations of hypertensive patients with this highly effective technology. ■

James A.M. Smith, DO, is the Founder and Director of the River City Cardiac and Vascular Institute, in Wichita, Kansas. He is board certified by the American Board of Vascular Medicine, Intervention. Dr. Smith may be reached at (316) 462-1070; smithjams@cox.net.

1. Wong N, Lopez V, L'Italien G, et al. Inadequate control of hypertension in US adults with cardiovascular disease comorbidities in 2003-2004. Arch Intern Med. 2007;167:2431-2436.
2. Nishizaka MK, Pratt-Ubunama M, Zaman MA, et al. Validity of plasma aldosterone-to-renin activity ratio in African American and white subjects with resistant hypertension. Am J Hypertens. 2005;18:805-812.
3. Pimenta E, Gaddam KK, Oparil S. Mechanisms and treatment of resistant hypertension. J Clin Hypertens. 2008;10:239-244.
4. Celik T, Iyisoy A, Kursaklioglu H, et al. Comparative effects of nebivolol and metoprolol on oxidative stress, insulin resistance, plasma adiponectin and soluble P-selectin levels in hypertensive patients. J Hypertens. 2006;24:591-596.
5. Pohl MA, Novick AC. Natural history of atherosclerotic and fibrous renal artery disease: clinical implications. Am J Kidney Dis. 1985;4:A120-130.
6. Weber MA, Bakris GL, Giles TD, et al. Beta-blockers in the treatment of hypertension: new data, new directions. J Clin Hypertens. 2008;10:234-238.
7. Van Jaarsveld BC, Krijinen P, Pieterman H, et al. The effect of balloon angioplasty on hypertension in atherosclerotic renal artery stenosis. NEJM. 2000;342:1007-1014.