

Update on Hypertension

Number 70

July/August, 2002

Cardiovascular disease (CVD) is the number one cause of death in the US, and hypertension is the most common CVD risk factor.¹ Hypertension, one of the most common adult diseases in the US, is the most common reason for which Americans visit physicians. It is a well-established risk factor for fatal and non-fatal cardiovascular and cerebrovascular events, including stroke, coronary artery disease, heart failure, and renal disease.

Although its risks have been known for decades, hypertension remains inadequately diagnosed and treated. This *Heartbeat* update will provide an overview of the evaluation and management of hypertension and help in developing a management plan.

Evaluation

The obvious first step is to take a proper blood pressure (BP). Our assistants take patients' weight and BP, and document smoking history after transfer from the waiting room to the examining room. This is the only practical way, but we also know that, in addition to using proper cuff size, having patients resting quietly and comfortably for 5 min. before measurement is optimum. Simply repeat the BP if it is high (you know they have been waiting at least 5 min. before we get there).

Initial elevated readings should be confirmed on at least two subsequent visits over a few weeks. A value that is consistently $\geq 140/90$ mm Hg in healthy patients and $\geq 130/80$ mm Hg in patients with diabetes (DM), heart failure (HF) or renal

disease and proteinuria should be considered as high.

Initial evaluation of the hypertensive patient should focus on two things:

- (1) Target organ damage (TOD)—eyes, heart and kidneys.
- (2) Global risk assessment in order to establish an absolute CV-risk estimate (Framingham risk score). The primary goal of treating any CV risk factor is to improve outcomes.²

This evaluation should include a complete history and physical, along with laboratory check of lytes, sugar, lipid profile, renal function and urinalysis.³ The possibility of a secondary cause of hypertension should be considered in each patient. One's choice of medication and aggressiveness of treatment should be based on this evaluation, with the goal of improving outcomes and controlling BP in that patient.

BP Goals

Goal BP management is determined by the presence or absence of TOD, DM other CV risk factors and other co-morbidities (Table 1).

TABLE 1. Recommended Target BP Goals

Guideline	Uncomplicated Hypertension	No TOD or Clinical CV Disease; at Least 1 CV Risk Factor Excluding Diabetes	
		Diabetes*	Diabetes*
JNC VI	<140/90 mm Hg	<140/90 mm Hg	<130/85 mm Hg
NKF			$\leq 130/80$ mm Hg
ADA			$\leq 130/80$ mm Hg

NKF indicates National Kidney Foundation; ADA, American Diabetes Association.

*JNC VI BP goal also recommended for those with TOD or clinical CV disease.

** < 125/75 for patients with renal insufficiency and proteinuria >1gm/24hr or heart failure.

Optimal BP is < 120/80 mm Hg. Goal recommendations for BP are based on results of the randomized trials and recommendations from the guidelines committee (Table 1).

Barriers to achieving BP target

Physician under-aggressiveness is the primary reason for poor hypertension control. The majority of uncontrolled patients are older adults with isolated mild stage 1 systolic hypertension. A substantial portion of this dilemma can likely be attributed to the “single-pill myth” that most hypertension can be adequately managed with one medication. Several large randomized trials have demonstrated that it is more likely that 3-4 drugs will be needed and sometimes more. The advantage of combining antihypertensive drugs with different modes of action is that it will often allow smaller doses of drugs to be used to achieve control, thereby minimizing the potential for dose-dependent side effects. In the HOT (Hypertension Optimal Treatment) study an average of 3.6 medications were needed to achieve a diastolic BP of < 80 mm Hg.⁴ In the African-American Study of Kidney Disease (AASK), 3.8 drugs were needed to reach a goal mean arterial pressure of < 92 mm Hg.⁵

It is crucial that health care providers be aware of the large degree of effort necessary to achieve the BP goals of existing guidelines.

All BP parameters important

A new analysis from the large Multiple Risk Factor Intervention Trial (MRFIT) cohort confirms the importance of considering not just systolic or diastolic BP but both of these parameters together, since those with concordant elevations of both had the highest overall risk of CVD related death.⁶ In addition the results also showed that pulse pressure (PP)—the difference between the SBP and DBP readings representing a measure of large artery stiffness—is much more important than previously thought.

In the presence of arteriosclerosis and aortic stiffening (consequences of arterial hypertension), the pulse wave velocity is increased, causing the pulse waves to reflect more quickly off the arteriolar vessels during systole. This amplifies SBP. In the presence of normal vascular compliance, the reflected waves return during diastole and augment DBP. Consequently, arteriosclerosis (occurring much more frequently in older patients) tends to simultaneously increase SBP and decrease DBP, resulting in a widened PP.

Widened PP increases CV morbidity because elevated SBP is associated with greater left ventricular workload and oxygen demand, whereas a decreased DBP may decrease coronary perfusion, resulting in decreased myocardial oxygen supply and a greater risk for myocardial ischemia and injury. The findings in older people that higher CVD risk is associated with either elevated SBP and DSP or elevated SBP and low DBP warrants taking into consideration all BP components as predictors.

Management of hypertension: BP endpoint not the only goal

The primary goal of BP reduction is to reach optimal BP by the least intrusive means possible. The ultimate goal of improved outcomes involves choosing an antihypertensive agent (or agents) based on the ability of that agent to reduce morbidity and mortality, especially in the areas of CV and kidney disease—not just its ability to lower BP.

The life-saving results reported in recent hypertension trials have been large while the antihypertensive results have been small, suggesting that other effects of the particular specific drugs, beyond their antihypertensive effect, underlie results. In the absence of huge study enrollments and long follow-up, only studies (HOPE-ramipril⁷ and LIFE-losartan⁸) with very high-risk subjects are able to show differences among specific drug types. This is very important, since most hypertensives are

elderly and/or have a lot of other diseases (DM, renal insufficiency, or CVD), and CHD increases with age in all populations. Therefore, it is important to treat CHD along with HBP in these older and/or higher risk group—real-life hypertensives.

Selection of antihypertensive agents

There is now strong evidence that drugs that inhibit the renin-angiotensin system and provide vascular protection should be a prominent part of the antihypertensive regimen for those with DM and/or kidney disease or CVD. In non-diabetic kidney disease, ACE inhibitors have dramatically decreased proteinuria and reduced the risk of doubling of creatinine and progression to end stage renal disease (ESRD).⁹ Albuminuria is an independent risk factor for both CV and kidney disease.¹⁰

All diabetics (whether hypertensive or not), and all patients with hypertension should be screened for it. ACE inhibitors have been shown to prevent renal disease in type I DM, but only the use of an angiotensin-receptor blocker (ARB) has been proven to reduce the risk of developing ESRD or doubling of creatinine in type II DM.¹¹ Both have been shown to blunt increases in microalbuminuria and, in some cases, normalize it. *However, only ACE inhibitors have been shown to decrease CV events in diabetics, irrespective of whether microalbuminuria was present.* An algorithm to achieve BP goal in DM and renal insufficiency is presented in Figure 1.

We strongly favor angiotensin blockade—ACE inhibitors first (HOPE) and ARBs (LIFE) if ACEs can't be tolerated—as firstline therapy for all HBP. However, some prefer ARBs because of their better side effect profile. These agents are favored, obviously, because of their non-hypertensive benefits—vascular protection. Diuretics are usually the first add-on and will almost always have to be added to get BP to goal, especially in elderly or blacks.

Combination therapy with a fixed-dose combination of medication may be the first option. They frequently offer more rapid achievement of goal BP, improved tolerance, better compliance (less pills) and more “bang for the buck.” There is also a psychological impact—the less pills you take the better you feel, and the more pills you take, the sicker.

The same treatment algorithm for DM or renal insufficiency (Figure 1) is applicable for the elderly and blacks, except the goal BP would be \leq 140/90 for uncomplicated hypertension—no TOD or clinical CVD or DM).

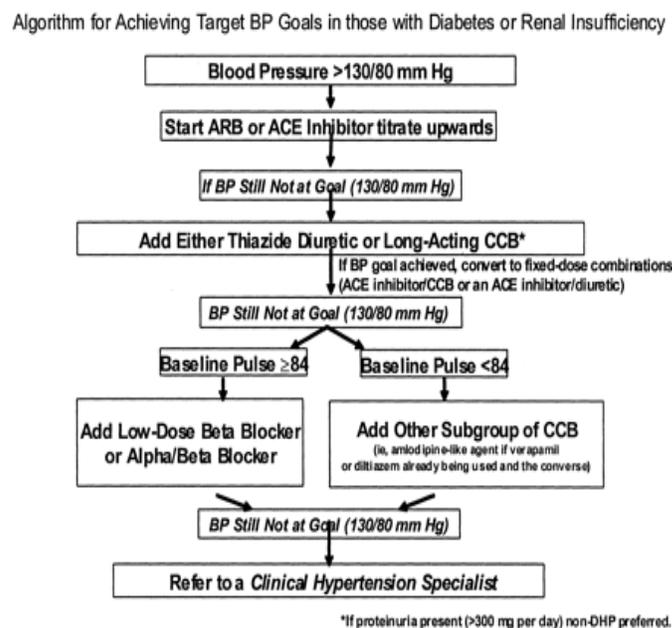


Figure 1. Algorithm for an approach to controlling hypertension in patients with DM or renal insufficiency.¹²

When selecting an agent, it is important to identify comorbidities, because these will impact what a patient’s goal BP should be (Table 1), as well as which antihypertensive agents should be used (Table 2).

Dihydropyridine calcium channel blockers (CCB) should not be used in the absence of an ACE inhibitor or an ARB for hypertension in those with Type II DM or kidney disease.^{13, 14}

Table 2. Treatment Hypertension 2002

Comorbid Condition	Indicated Drugs*
Heart failure	ACE inhibitors, diuretics, B-blockers**, ARBs
DM with or without proteinuria	ACE inhibitors, ARBs or possibly B-blockers – all with a diuretic (avoid dihydropyridine calcium antagonist alone)
Post-MI	B-blockers, ACE-inhibitors
Systolic hypertension (elderly)	Low dose ACE-inhibitor or ARB combined with a low dose diuretic (preferred), Alternative therapy: calcium channel blocker or B-blocker
Angina	B-blocker, calcium antagonist, ACE-inhibitor (not yet approved)
Pregnancy	Labetolol, methyldopa, calcium antagonists (ACEI contraindicated)
Prostatism	Alpha-blocker (not used alone)
Kidney insufficiency (non-diabetic)	ACE- inhibitor (ARB if ACEI not tolerated)

*Three or more medications often necessary to achieve BP goal

**Carvedilol is preferred for hypertension and has been shown to improve proteinuria. Only two B-blockers are approved for HF (carvedilol and metoprolol xl/cr).

Summary:

Hypertension is a complex widespread disease. It should be addressed with the urgency it demands. Decreasing vascular risk to improve outcomes is critical. We can no longer be content with elevated systolic or diastolic BP.

Mario L. Maiese, DO, FACC, FACOI

maiese@dnamail.com

Heartbeats can be found at www.sjhg.salu.net under Patient Education- From Your Physician.

¹ American Heart Association. 2001 Heart and Stroke Statistical Update. Dallas TX: American Heart Association 2000.

² Brook RD, et al. How to achieve control in managing hypertension? ACC Current Journal Review May/June 2002; 35-40

³ Joint National Committee. The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure. Arch Intn Med. 1997;157: 2413-46.

⁴ Hansson L, et al. Effects of intensive blood pressure lowering and low dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomized trial. Lancet. 1998; 351:1755-62.

⁵ Agodoa LY, et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. JAMA 2001; 285: 2719-28.

⁶ Domanski M, et al. Pulse Pressure and Cardiovascular Disease- Related Mortality: Follow-up Study of the Multiple Risk Factor Intervention Trial (MRFIT). JAMA 2002 May 22; 287: 2677-83.

⁷ Heart Outcomes Prevention Evaluation Study Investigators (HOPE). "Effects of angiotensin converting enzyme inhibitor, ramipril on cardiovascular events in high-risk patients." N Engl J Med 2000; 342: 145-53.

⁸ Dahlof B, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE). A randomized trial against atenolol. Lancet 2002; 359:995-1003

⁹ Jafar TH, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease: a meta-analysis of patient-level data. Ann Intern Med 2001; 135: 73-87.

¹⁰ Keane WF et al. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. Am J Kidney Dis 1999; 33: 1004-10.

¹¹ Maiese M et al. Optimizing cardiovascular and renal risk-reduction. Heartbeat #65 January 2002; www.SJHG.salu.net. Patient Education-From Your Physician.

¹² Garg J, et al. Evaluation and treatment of patients with hypertension. Circulation May 2002; 105:1458-61

¹³ Estacio RO, et al. The effect of nisoldipine as compared with enalapril on CV outcomes in patients with non-insulin-dependent DM and hypertension. N Engl J Med 1998; 338:645-52.

¹⁴ Agodoa LY, et al. Effect of ramipril vs amlodipine on renal outcomes in hypertensive nephrosclerosis: a randomized controlled trial. JAMA 2001; 285:2719-28.