Hypertension Grand Rounds

Management of Prehypertension

Laura P. Svetkey

A 58-year-old woman is evaluated by her primary care physician, her gynecologist, or at employee health. On 2 separate occasions, duplicate seated blood pressure (BP) measurements average 132/84 mm Hg. She is informed that she has “prehypertension.” At her last check-up in 2002, she had a similar reading but was told she had normal BP.

The BP category “prehypertension” was first introduced by the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC-7) in 2003, replacing former categories of “high-normal” and “above-optimal” BP. The rationale for redefining this category was to emphasize the excess risk associated with BP in this range and to focus increased clinical and public health attention on prevention.

Management of prehypertension by lowering BP into a more optimal range can be expected to lower risk. The risks associated with prehypertension are in part related to the tendency of BP to increase with age in industrialized societies. Thus, prehypertension is a precursor of clinical hypertension and consequently of the cardiovascular disease (CVD) and renal risks associated with elevated BP (ie, SBP ≥140 or DBP ≥90 mm Hg). In addition, the relationship between BP and CVD risk is continuous over the whole range of BP, and therefore, prehypertension itself is associated with BP-related morbidity and mortality. Thus, the goals of treating prehypertension are to prevent hypertension and to reduce the excess CVD risk associated with BP in this preclinical range.

Although treatment of prehypertension is primarily nonpharmacological lifestyle change, redefining this range of BP also serves to emphasize the role of health care providers in its management. The terms “high-normal” or “above-optimal” BP in previous JNC reports might have implied in the past that appropriate action should originate in the public health or the lay public sectors, but the label “prehypertension” clearly calls for the attention of the physician. The management of prehypertension is an appropriate goal for clinicians in a wide range of practice settings.

This review will discuss the epidemiology and risk of prehypertension, the evidence underlying treatment recommendations, clinical and public health implications of prehypertension and its management, and issues concerning implementation of treatment recommendations.

Definitions and Epidemiology

“Prehypertension” is defined as systolic BP (SBP) 120 to 139 or diastolic BP (DBP) 80 to 89 mm Hg, based on “2 or more properly measured seated BP readings on each of 2 or more office visits.” If SBP and DBP fall into different categories, the category associated with the higher of the 2 pressures is applied. Prehypertension replaces former categories “high-normal” (130 to 139/85 to 89 mm Hg) and “above-optimal” (120 to 129/80 to 84 mm Hg) BP. The term “borderline hypertension” was imprecisely and inconsistently defined, and therefore should not be used. “Normal” (formerly “optimal”) BP is defined as SBP <120 and DBP <80 mm Hg.

Based on the third National Health and Nutrition Examination Survey (NHANES-III; 1999 to 2000), the prevalence of prehypertension is 31%, with no apparent difference by race/ethnicity. Women are less likely to have prehypertension than men (23% versus 40%). Prehypertension is associated with overweight/obesity, suggesting that prevalence of this condition will increase over time if the obesity epidemic continues to grow. Individuals aged ≥60 years of age are less likely to have prehypertension than younger individuals (24% versus 34%), probably because the majority of individuals in the older age group (65%) have progressed to clinical hypertension. Like hypertension, prehypertension tends to cluster with other CVD risk factors such as dyslipidemia and obesity. The proportion of prehypertensive individuals with ≥1 other risk factor is >85% (adjusted relative risk, 1.65 for prehypertension compared with normal).

Also like hypertension, prehypertension tends to increase in severity over time. Thus, prehypertension progresses to clinical hypertension at a rate of 19% over 4 years. Progression depends on the level of BP and age. The 4-year incidence of hypertension in individuals with higher levels of prehypertension (previously defined as “high-normal”; SBP 130 to 139 mm Hg and DBP 85 to 89 mm Hg) is 43% compared with 20% in those with lower levels of prehypertension (previously defined as “normal”; SBP 120 to 129 mm Hg and DBP 80 to 84 mm Hg), and 10% in those with SBP <120 and DBP <80 mm Hg. The 4-year incidence of hypertension in individuals with prehypertension who are ≥65 years of age is 42% compared with 27% in those 35 to 64 years of age. The presumption might be that prehypertension leads only to stage 1 hypertension, but 17% of those with higher levels of prehypertension develop stage 2 hypertension over 4 years. These data support current recommendations for yearly measurement of BP in patients with prehypertension to detect and treat hypertension as early as possible.

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<table>
<thead>
<tr>
<th>Strategy*</th>
<th>Recommendation</th>
<th>SBP Effect in Prehypertension</th>
<th>Effect on Incidence or Prevalence of Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>DASH dietary pattern</td>
<td>4–5 fruits/day</td>
<td>3.5 mm Hg</td>
<td>decreased by 62% (prevalence)</td>
</tr>
<tr>
<td></td>
<td>4–5 vegetables/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2–3 low-fat dairy/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>Effective BP lowering even without attaining normal BMI</td>
<td>1 mm Hg/kg weight loss</td>
<td>decreased by 42% (incidence)</td>
</tr>
<tr>
<td>Reduced sodium intake</td>
<td>&lt;2400 mg/day</td>
<td>2 mm Hg per 76 mmol/L per day decrease</td>
<td>decreased by 38% (incidence)</td>
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<tr>
<td>Physical activity</td>
<td>Moderate exercise ≧30 minutes most days</td>
<td>3–4 mm Hg</td>
<td>N/A</td>
</tr>
<tr>
<td>Moderation of alcohol intake</td>
<td>≦2 oz/day (men); ≦1 oz/day (women)</td>
<td>3.5 mm Hg</td>
<td>N/A</td>
</tr>
</tbody>
</table>

N/A indicates not available.
*Additional information for health care providers can be found at www.nhlbi.nih.gov. Information for patients concerning the DASH eating pattern can be found at www.nhlbi.nih.gov/health/public/heart/hbp/dash.

Excess Risk Associated With Prehypertension

The risk of CVD increases progressively throughout the range of BP, including ranges previously considered normal. For example, the risk of coronary heart and stroke death associated with SBP of 135 mm Hg is double that associated with SBP of 115 mm Hg. Compared with normal BP, prehypertension is associated with a 27% increase in all-cause and 66% increase in CVD mortality.

Given this excess risk in a very large population, an estimated 32% of BP-related deaths occur in individuals with SBP between 110 and 139 mm Hg. Although the absolute event rates associated with prehypertension are relatively low, morbidity, mortality, and health care costs attributable to prehypertension are substantial. In a simulation based on >20 years of follow-up of the NHANES-I cohort, an estimated 3.4% of hospitalizations, 6.5% of nursing home stays, and 9.1% of deaths could be attributed to prehypertension.

The mechanism of excess risk from prehypertension is presumed to be the same as that from hypertension. It is known that prehypertension is associated with subclinical atherosclerosis, including increased coronary atherosclerosis and increased carotid and brachial intima-media thickness. In addition, prehypertension is associated with elevated C-reactive protein (CRP), tumor necrosis factor-α, homocysteine, oxidized LDL, and other inflammatory markers.

Treatment of Prehypertension

The excess risk associated with prehypertension can presumably be prevented by reducing BP. Therefore, the goal of managing prehypertension is to lower BP into the normal range, prevent a rise in BP with age, and prevent BP-related CVD events. Although there is extensive evidence that prehypertension can be treated effectively, the impact of treatment on outcomes is largely unknown.

Management for most patients consists of nonpharmacologic interventions that lower BP. In patients with diabetes mellitus (DM) or chronic kidney disease (CKD), pharmacological treatment must also be considered.

Nonpharmacological Interventions

JNC-7 recommends 5 nonpharmacological treatments for prehypertension (Table). Each treatment has been proven in clinical trials to significantly lower BP, and most have been shown to prevent the development of hypertension.

Dietary Approaches to Stop Hypertension Dietary Pattern

The Dietary Approaches to Stop Hypertension (DASH) dietary pattern was designed in response to epidemiologic and limited clinical trial data implicating particular micronutrients and macronutrients in BP regulation. Consequently, the DASH dietary pattern is rich in potassium (from fruits and vegetables) and calcium (from dairy), reduced in total and saturated fat, and contains limited amounts of meats and sweets. The DASH study was specifically designed to test interventions other than weight loss and reduced sodium intake, which were already known to lower BP (see below). The impact of this dietary pattern on BP was tested in a randomized, controlled feeding study in 459 individuals with DBP 80 to 95 mm Hg and SBP <160 mm Hg. Thus, the trial included individuals with prehypertension (71%) as well as those with stage 1 hypertension (29%).

Compared with a typical American control diet, the DASH dietary pattern reduced SBP by 5.5 mm Hg and DBP by 3.0 mm Hg overall (each P<0.001). In the participants with prehypertension, corresponding reductions were 3.5 mm Hg (P=0.001) and 2.1 mm Hg (P=0.003). The DASH dietary pattern is efficacious in treating prehypertension in a diverse population: men and women, old and young, and black and nonblack individuals experienced a significant reduction in BP, and it was particularly efficacious in blacks. The BP-lowering effect of DASH in prehypertension was confirmed in the DASH sodium trial and the PREMIER trial.

Overall, prehypertension was reduced to normal BP in 62% of study participants eating the DASH dietary pattern.

Weight Loss

Extensive clinical trial data document a substantial and significant BP-lowering effect of weight loss. Reductions in BP occur even without attainment of normal body mass index (BMI). In a meta-analysis of 25 randomized, controlled trials, weight loss of 1 kg was associated with an 1 mm Hg reduction in SBP and DBP in individuals with prehypertension. The largest of the trials included in this analysis, Trials of
Hypertension Prevention (TOHP), demonstrated a larger effect. In that trial, a behavioral weight loss intervention in adults with prehypertension led to an average reduction in body weight of 2 kg at 6 months, associated with an average reduction in SBP of 3.7 mm Hg and DBP of 2.7 mm Hg. This weight loss intervention was associated with a 42% reduction in incident hypertension. Although point estimates of this effect vary, evidence of an effect of weight loss on BP is strong and consistent.

Reduced Sodium Intake
Epidemiologic surveys show a consistent direct correlation between sodium intake and BP, and numerous human trials indicate that reducing sodium intake leads to reductions in BP. In a comprehensive overview of randomized clinical trials, an average reduction of sodium intake of 76 mmol/L per day was associated with a 1.9/1.1 mm Hg reduction in BP in patients with prehypertension. Although the effect appears modest, a treatment arm in TOHP-1 that provided a behavioral intervention for lowering sodium intake demonstrated a similar BP reduction with only a 44 mmol/L reduction in sodium intake, with a 38% reduction in hypertension incidence. Although reduced sodium intake is difficult to implement in the general public, attributable largely to food manufacturing practices, lifestyle trials generally indicate that reduced sodium intake, once achieved, tends to be well maintained.

Regular Physical Activity
Numerous studies have found a negative correlation between habitual physical activity and the development of hypertension. This relationship has been observed in both sexes, all age groups, and in blacks and whites. In addition, a number of clinical trials demonstrate that increased physical activity can lower BP independent of any effect on body weight, although this finding is not universal. However, 2 meta-analyses conclude that physical activity independently lowers BP. In one of these meta-analyses, 27 of 50 studies reported results in a nonhypertensive subgroup, which presumably includes a large proportion of participants with prehypertension. In the other meta-analysis, the average baseline BP was <140/90 in 8 of 12 studies, and a ninth study included a nonhypertensive subgroup. Therefore, the results of meta-analysis indicating that exercise leads to a reduction in SBP of 3 to 4 mm Hg can be interpreted to apply to prehypertensives. Moderate-intensity activity appears to be sufficient.

Moderation of Alcohol Intake
The relationship between high alcohol intake and elevated BP has been reported in observational studies, but results from clinical trials have been inconsistent, and the largest trial showed no significant effect on BP of reducing alcohol intake by 1.3 drinks per day. Nonetheless, some well-done trials demonstrate benefit, and a meta-analysis suggests that moderation of alcohol intake, independent of other effects such as associated weight loss, lowers SBP. Almost half of the studies in this meta-analysis included nonhypertensive participants, with SBP reduction of >3.5 mm Hg in this subgroup. Overall, the evidence favors moderation of alcohol intake to currently recommended limits (2 ounces per day for men and 1 ounce per day for women) in the management of prehypertension.

On the basis of the evidence reviewed above, each of these nonpharmacologic strategies for lowering BP is currently recommended for adults with prehypertension. As noted above, this target population is extremely large. However, there is no indication that any of these interventions, implemented in moderation, is unsafe, and most have been proven to be effective in men and women, blacks and whites, and older and younger individuals, all of which suggests that broad recommendations are appropriate. Combining several of these strategies simultaneously leads to further reduction in BP and a potential reduction in the incidence of hypertension of ~50%.

Pharmacological Intervention
The JNC-7 report recommends drug treatment “if a trial of lifestyle modification fails to reduce . . . BP to 130/80 mm Hg or less” in patients with either DM or CKD, implying that prehypertension in these clinical subgroups should be treated pharmacologically. These recommendations are based on evidence from clinical trials that suggest that the goal of BP treatment should be lower in this population once hypertension develops. However, the benefits of pharmacological therapy in prehypertensive patients with diabetes or CKD are not well established, especially compared with lifestyle modification. Nonetheless, given the high risk of adverse outcomes in this population and the evidence to date, use of medication in this subgroup is reasonable. However, continued emphasis on nonpharmacologic therapy is an important component of care.

Drug therapy for other patients with prehypertension cannot be justified at this time. Drug therapy in >30% of the adult population would be prohibitively expensive, would potentially cause side effects and adverse biochemical changes that would counteract any beneficial effects of BP lowering, and perhaps most important, would not address the underlying modifiable causes of elevated BP, namely suboptimal dietary habits, overweight/obesity, and low levels of physical activity.

Clinical and Public Health Implications
The potential impact of managing prehypertension is speculative because direct evidence that treatment of BP in this range leads to reduced CVD events is lacking. An outcome trial in the general population with prehypertension that has the power to demonstrate beneficial effects of BP lowering in this range would need to be prohibitively large. However, given the clustering of risk factors with prehypertension, an outcome trial in high-risk prehypertensives is potentially feasible. Indeed, there is already 1 such trial: patients with coronary artery disease and prehypertension treated with 2 different classes of antihypertensive agents experienced BP lowering and reduction in CVD events compared with a control group. The fact that there was equivalent reduction in CVD outcomes with different classes of antihypertensive agents in this trial and others suggests that the benefit can be
attributed to the BP lowering itself, and therefore can be expected with nonpharmacological interventions with similar efficacy. Ongoing trials may offer an opportunity to study the impact of long-term lifestyle change on CVD outcomes.

In the absence of direct evidence, the effect of nonpharmacologic therapy on surrogate markers of CVD (in addition to BP) suggests the likelihood of benefit. For example, DASH and weight loss are associated with reductions in total and LDL cholesterol and inflammatory mediators such as CRP, and weight loss is associated with reductions in blood sugar and insulin resistance.

**Implementation**

The current model for implementing lifestyle recommendations involves public health and clinical strategies. Dietary guidelines for lowering BP (and other health benefits) are developed by a consensus panel, incorporated into national goals, promoted by national organizations, and publicized through various media. Encouragement to implement these recommendations comes from the media and the personal physician. The physician’s role primarily involves offering advice and, in some cases, referral to a dietician. An important obstacle to the success of this strategy is the lack of time and training that physicians have for providing behavior change counseling. However, a physician using brief motivational counseling techniques can be an effective stimulus for change.

An additional obstacle is that this strategy is based on individual intervention that is infrequent and passive from the patient’s point of view. Significant behavior change is most likely if there is prolonged frequent contact with a trained counselor provided in a group intervention and using active participation and behavioral cognitive theory. Either approach (physician counseling or group behavioral intervention) is hampered by the fact that most health care insurers do not cover physician counseling or behavioral interventions for the prevention and treatment of hypertension.

**Case Discussion**

An otherwise healthy middle-aged woman is diagnosed with prehypertension according to current guidelines. The probability that she will develop hypertension over the next 4 years is close to 40%. Her lifetime risk of eventually developing hypertension is estimated to be ≥80%. Her current BP puts her at increased risk for CVD events compared with BP in the normal range (<120/80 mm Hg). The challenge for the patient and the physician is to implement therapy purely for prevention. The clinician should explain to the patient that guidelines have been revised to emphasize the need to prevent hypertension by getting BP to more optimal levels. She should be counseled to adopt the DASH dietary pattern, to lose weight if her BMI is ≥25 kg/m², to reduce sodium intake to 2400 mg per day or less, to increase moderate physical activity to 30 minutes most days, and not to drink >1 ounce of alcohol per day. Using brief motivational counseling techniques, the clinician should assess her readiness to change, help her set short- and long-term goals, and identify sources of additional assistance such as behavior change counseling. If she is able to adopt some or all of these recommendations, the probability is high that BP will decrease, and the development of hypertension will be prevented or delayed.

**Perspectives**

The establishment of a “prehypertension” category draws attention to a preclinical range of BP that has clinical and public health significance. Prehypertension is common and likely to increase in prevalence if the obesity epidemic continues to grow. This condition is associated with excess CVD risk and frequently progresses to clinical hypertension. Treatment strategies emphasize nonpharmacological lifestyle interventions in all patients, with the addition of antihypertensive medication in some high-risk subgroups (ie, DM and CKD). These treatments effectively lower BP and prevent hypertension. Implementation of a management strategy for prehypertension requires attention from patients, public health organizations, clinicians, industry, and health insurers. Successful management can reasonably be expected to reduce CVD morbidity and mortality.

**References**


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