

## 2004 Korean Hypertension Treatment Guideline and Its Perspective

Jeong Bae Park, MD, PhD

Department of Medicine, Cardiology, Cheil General Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

### ABSTRACT

The risk attributable to cardiovascular disease (CVD) that is induced by hypertension in the Korean population is 35% for stroke and 21% for ischemic heart disease. The prevalence of hypertension in persons older than 30 years is as high as 34.4% in men and 26.5% in women, and the prevalence of prehypertension is 39.4% in men and 30.6% in women. Therefore, the proportion of normotension is merely 28.4% in men and 47.3% in women. However, the current control rates (a systolic blood pressure (BP) <140 mmHg and a diastolic BP <90 mmHg), although improved, are still only 10%, which is far below those of western society. This situation urgently mandates a new guideline for making appropriate clinical decisions regarding the needs of individual patients and that this guideline can be applied with due regard to local circumstances and policies. Individuals with hypertension or prehypertension require health-promoting lifestyle modifications to prevent CVD. Drug treatment is recommended for most patients with uncomplicated hypertension that is persistently higher than 140/90 mmHg. The BP goal is less than 140/90 mmHg for most uncomplicated patients with hypertension, and less than 130/80 mmHg for the patients with diabetes or chronic kidney disease. In the absence of compelling indications, any kind of thiazidetype diuretics, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers,  $\beta$ -blockers or calcium channel blockers are recommended for initial use as antihypertensive drugs. If 2 or more drugs are needed to achieve the BP goal the committee recommends a treatment algorithm based on the AB/CD rule. Even though the committee had concerns on the guideline's accuracy due to the paucity of data on Korean people, the Korean Hypertension Treatment Guideline should be implemented to educate and guide both patients and physicians. (Korean Circulation J 2006;36:405-410)

**KEY WORDS :** Hypertension ; Guideline.

### Introduction

The risk of cardiovascular disease (CVD) is increasing as our Korean society ages and becomes westernized. A lot of new evidence has emerged concerning the importance of blood pressure (BP) as a risk factor for cardiovascular disease,<sup>1)</sup> and also for the importance of controlling hypertension for the prevention of CVD, and particularly stroke, renal and heart disease.<sup>1)</sup> However, national surveys continue to show substantial under-diagnosis, under-treatment and poor control rates of hypertension in Korea, although this has somewhat improved as compared to the previous times.<sup>2-4)</sup> Although we do not have sufficient data for the Korean people, the committee recognizes the necessity of the Korean Hypertension Treatment Guideline to guide and educate

both patients and physicians to meet the following goals: 1) reducing the CV risk through lifestyle modification by increasing the awareness of hypertension among the public and by emphasizing the importance of prehypertension, and 2) improving the suboptimal control rates of hypertension by simplifying the doctor's prescription options. The Korean Society of Hypertension recommends a treatment algorithm based on the AB/CD rule as suggested by the British Hypertension Society.<sup>5)</sup> To meet this goal, a new category designated as prehypertension, which is defined as a systolic BP of 120 to 139 mmHg or a diastolic BP of 80 to 89 mmHg, was added in between normotension and hypertension. More than one third of general population shows the signs of prehypertension. The theoretical reason of designating prehypertension is based on the following 2 studies; 1) Framingham's study and our prospective study showed an increased risk for the progression to hypertension from prehypertension<sup>6)</sup> and for the development of CVD that starts from prehypertension,<sup>7,8)</sup> 2) for the middle age or older individuals, each increment of 20 mmHg in the

**Correspondence :** Jeong Bae Park, MD, PhD, Department of Medicine, Cardiology, Cheil General Hospital, Sungkyunkwan University School of Medicine, 1-19 Mukjung-dong, Jung-gu, Seoul 100-380, Korea  
Tel: 82-2-2000-7249, Fax: 82-2-2000-7152  
E-mail: parkjb@skku.edu

systolic BP (approximately equivalent to 10 mmHg diastolic BP) has demonstrated a doubled risk from all vascular death across the entire BP range from 115/75 to 185/115 mmHg.<sup>9)</sup> Therefore, because most management of BP and the risk of CVD take place in the primary care setting, the guidelines are intended for the general practitioners in hospital practice in Korea. In this review, the outline of the Korean Hypertension Treatment Guideline will be introduced and the distinctions from other guidelines and our current situation will be discussed.

## Guideline; Briefs

### Epidemiology

#### Classification of BP and its prevalence

The Korean Society of Hypertension's classifications of BP levels have changed to come in line with the recent Joint National Committee VII (JNC VII) guidelines in the USA (Table 1).<sup>10)</sup> In contrast with the classification provided in the recent 2003 European Society of Hypertension (ESH) guideline,<sup>11)</sup> the 2003 World Health Organization/International Society of Hypertension (WHO/ISH) guideline,<sup>12)</sup> or the 2004 British Hypertension Society (BHS) guideline,<sup>13)</sup> the Korean classification is divided by 4 categories such as normotension, prehypertension, and hypertension stage 1 and 2. A new category designated as prehypertension was added, which was defined as a systolic BP of 120 to 139 mmHg or a diastolic BP of 80 to 89 mmHg, because of prehypertension's increased risk for progression to hypertension.<sup>6)</sup> Those people with high normal BP (130/80 to 139/89 mmHg BP range) are at almost twice the risk of developing hypertension as those people with lower values.<sup>8)</sup>

The prevalence of hypertension in persons older than 30 years is as high as 34.4% in men and 26.5% in

women, and the prevalence of prehypertension is 39.4% in men and 30.6% in women. Therefore, the percentage of normotension is merely 28.4% in men and 47.3% in women (Table 2).<sup>4)</sup>

#### BP control rates

Hypertension is the most common disease in Korea, affecting 1/3 of the men and 1/4 of the women who are aged more than 30 years and more than 1/2 of the elderly who are 60 years old or older. However, although improved, the current control rate (a systolic BP <140 mmHg and a diastolic BP <90 mmHg), is still only 10% (Table 3),<sup>4)</sup> and this is still far below the rate of Western Society, i.e., 30%.<sup>10)</sup>

### Clinical evaluation

#### BP measurement and the cutoff point of hypertension

The use and the method of BP measurement at medical settings, ambulatory BP monitoring and self-measurement is in line with the recent JNC VII guidelines.<sup>10)</sup> BP measurement with a properly calibrated and validated instrument should be done at a medical office and at least 2 measurements should be taken. The home BP values are usually lower by about 12/7 mmHg than clinic readings. Individuals with a mean BP of more than 135/85 mmHg as measured at home are generally considered to be hypertensive. Home BP measurement may benefit patients by providing information on the response to antihypertensive medication, improving patient compliance with therapy and for evaluating white-coat hypertension. Ambulatory BP monitoring provides information about BP during daily activities and sleep. Ambulatory BP monitoring is warranted for the evaluation of 1) white-coat hypertension in the absence of target-organ injury, 2) patients with apparent drug resistance, 3) episodic hypotensive/hypertensive symptoms and 4)

**Table 1.** Classification of blood pressure in adults

Classification	Systolic BP (mmHg)		Diastolic BP (mmHg)
Normal	<120	and	<80
Prehypertension	120-139	or	80-89
Stage 1 hypertension	140-159	or	90-99
Stage 2 hypertension	≥ 160	or	≥ 100

BP: blood pressure

**Table 2.** Hypertension prevalence in Korean adults ≥ 30 years of age

Classification	Men	Women
Normal (<120 and <80 mmHg)	28.4	47.3
Prehypertension (120-139 or 80-89 mmHg)	39.8	30.6
Stage 1 hypertension (140-159 or 90-99 mmHg)	22.5	15.4
Stage 2 hypertension (≥ 160 or ≥ 100 mmHg)	9.4	6.8

2002 Korean national health and nutrition survey report

**Table 3.** Hypertension control rates in Korean adults ≥ 30 years of age

Classification	Men	Women
Treatment	25.2	39.5
Control in all hypertension	7.6	16.6
Control on medication	30.2	42.0

**Table 4.** Cutoff value of hypertension according to method of BP measurement

	Systolic BP (mmHg)	Diastolic BP (mmHg)
BP at office	≥ 140	≥ 90
24 hour-ambulatory BP monitoring		
24 hour	≥ 125	≥ 80
Day-time	≥ 135	≥ 85
Night-time	≥ 120	≥ 75
Home BP	≥ 135	≥ 85

BP: blood pressure

autonomic dysfunction. Hypertensive individuals have a mean BP of more than 135/85 mmHg during a waking state and more than 120/75 mmHg during sleep (Table 4).

#### Patient evaluation

Evaluation of patients with documented hypertension has 3 objectives: 1) to assess their lifestyle and to identify other cardiovascular risk factors or concomitant disorders that may affect the prognosis and guide treatment, 2) to reveal identifiable causes of hypertension, and 3) to assess the presence or absence of target-organ damage and CVD (Table 5). The data that is needed is acquired through taking a thorough medical history, conducting a physical examination, routine laboratory tests and other diagnostic procedures and most of these procedures are similar to those of the other guidelines.<sup>10)12)</sup> Screening for secondary hypertension, unless it is indicated, is usually not recommended because of secondary hypertension's low prevalence.

## Hypertension treatment

### Lifestyle modifications

Adoption of healthy lifestyles by all individuals is critical for the prevention of high BP and it is an indispensable part of the management for those individuals with hypertension. The major lifestyle modifications that have been shown to lower BP include weight reduction in those individuals who are overweight or obese, adoption of the "Dietary Approaches to Stop Hypertension" eating plan, which is a diet rich in potassium and calcium, dietary sodium reduction, physical activity and moderation of alcohol consumption (ethanol less than 30 gram/day) (Table 6). Lifestyle modifications decrease BP, enhance antihypertensive drug efficacy and decrease the cardiovascular risk. Most of the recommendations on lifestyle modification are similar to those of the JNC VII.<sup>10)</sup> Because the average Korean eats 15-20 grams of salt per day, which is much higher than other nationalities, we placed greater emphasis on salt restriction.

**Table 5.** Cardiovascular risk factors and target organ damage

Major risk factors	
Hypertension	
Cigarette smoking	
Diabetes mellitus (fasting glucose $\geq 126$ mg/dL, 2-hour postprandial glucose $\geq 200$ mg/dL)	
Dyslipidemia (LDL $\geq 160$ mg/dL, total cholesterol $\geq 240$ mg/dL, HDL cholesterol $<40$ mg/dL for men and $<50$ mg/dL for women)	
Microalbuminuria (30-300 mg/24 hour or estimated GFR $<60$ mL/min, serum creatinine men $>1.5$ mg/dL, women 1.3 mg/dL)	
Obesity (BMI $\geq 25$ kg/m <sup>2</sup> , waist circumference men $>90$ cm, women $>80$ cm)	
Physical inactivity	
Age (men $>55$ years, women $>65$ years)	
Family history of premature CV death (men $<55$ years, women $<65$ years)	
C-reactive protein $\geq 1$ mg/dL	
Target organ damage	
Heart: left ventricular hypertrophy, angina or prior myocardial infarction, prior coronary revascularization, heart failure	
Brain: stroke or transient ischemic attack	
Chronic renal disease: diabetic nephropathy, renal insufficiency, proteinuria $>300$ mg/24 hour	
Peripheral arterial disease	
Retinopathy: hemorrhage, exudates, retinal edema	
Carotid IMT $\geq 0.9$ mm or plaque	
BMI indicates body mass index calculated as weight in kilograms divided by the square of height in meters. Estimated GFR=(140-age) $\times$ weight/72/serum creatinine (90% for women). GFR: glomerular filtration rate, IMT: intimomedial thickness, LDL: low density lipoprotein, HDL: high density lipoprotein, CV: cardiovascular	

**Table 6.** Lifestyle modifications to prevent and manage hypertension

Modification	Recommendation	Approximate SBP reduction
Weight reduction	Maintain normal body weight (BMI: 18.5-24.9 kg/m <sup>2</sup> )	5-20 mmHg/10 kg weight loss
Adopt DASH eating plan	Consume a diet rich in fruits, vegetables and low-fat dairy products with a reduced content of saturated and total fat	8-14 mmHg
Dietary sodium reduction	Reduce dietary sodium intake to 6 g sodium chloride	2-8 mmHg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day on most days of the week)	4-9 mmHg
Moderation of alcohol consumption	Limit consumption to less than 30 mL/day in most men and to less than 15 mL/day in women and the lighter-weight persons	2-4 mmHg

DASH: dietary approaches to stop hypertension, BMI: body mass index, SBP: systolic blood pressure

The committee recommends a combination of 2 or more lifestyle modifications to achieve better results.

### Pharmacologic treatment

All people with hypertension and prehypertension should be advised on how to achieve lifestyle modifications. Initiating antihypertensive drug therapy is recommended if the BP is persistently sustained at  $\geq 140/90$  mmHg. If there are any complications, target organ damage or if diabetes is combined even in stage I hypertension, then more aggressive treatment is recommended. The optimal goals for blood pressure treatment are  $<140$  for the systolic BP and  $<90$  mmHg for the diastolic BP. For people with diabetes mellitus or renal disease, the optimal goal is to reduce the BP to less than  $130/80$  mmHg.

The outcome data from many clinical trials (this data is not still established for Koreans), have proven that lowering BP with most classes of drugs, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs),  $\beta$ -blockers, calcium channel blockers (CCBs), and diuretics, has similar BP lowering effects and all these classes of medications reduce the complications of hypertension. However, individuals may respond in a different way; they can show diversity in morbidity and mortality and there can be the development of adverse effects when taking these drugs. If the patients signs and symptoms are not combined with other compelling indications, the committee recommends the use of a treatment algorithm based on the AB/CD rule to initiate the first antihypertensive drug and then to make good use of logical combinations of drugs. For example, ACE inhibitors or ARBs (or  $\beta$ -blockers) are recommended for patients who are younger than 55. CCBs or diuretics are more effective first line agents for the patients aged 55 or older.<sup>13)</sup> If the BP is still insufficiently controlled with one drug, the combination of A (or B) + C or D is recommended by adding a different class drug, and then A (or B) +

C+D is added if necessary (Fig. 1). The selection of drugs for high-risk conditions is based on the favorable outcome data from the reported clinical trials. In case of diabetes or renal disease, ACE inhibitors are recommended as an initial drug, ACE inhibitors and diuretics are appropriate for heart failure patients, thiazide-type diuretics and long-acting CCBs are appropriate for systolic hypertension in the elderly, and  $\beta$ -blockers and ACE inhibitors are appropriate for patients who have suffered myocardial infarction.

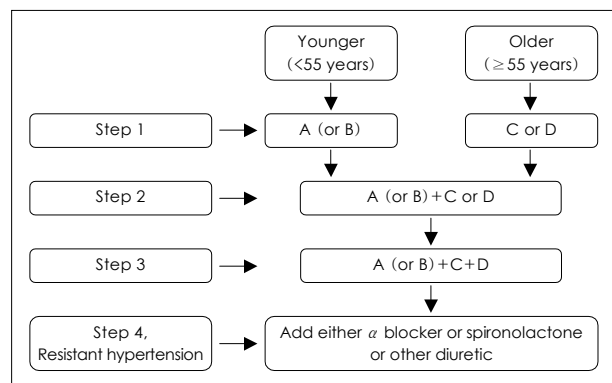
Low-dose aspirin therapy can be considered for the patients who are over the age of 50 years and who are in a high risk condition, but who are not at risk for gastrointestinal bleeding. However, aspirin should be used only when the BP is controlled. Statins are recommended for patients with coronary artery disease, peripheral arterial disease, stroke or type 2 diabetes if the low density lipoprotein (LDL) cholesterol level is higher than  $130$  mg/dL. In patients with combined hypertension and diabetes, the goal is less than  $110$  mg/dL for the fasting glucose and a HbA<sub>1c</sub>  $<6.5\%$ .

### Follow-up and monitoring

Once antihypertensive drug therapy is initiated, most patients should return for follow-up and adjustment of medications at approximately monthly intervals until the final BP goal is reached. More frequent visits will be necessary for patients suffering with stage 2 hypertension or for those patients with complicating comorbid conditions. After the BP has reached the goal and is stable, follow-up visits can usually be conducted at 3- to 6-month intervals. Serum potassium and creatinine should be monitored at least 1 to 2 times per year. If the BP is persistently less than  $120/80$  mmHg for more than a year or on 4 follow-up visits and the pretreatment BP is mild, the dosage of antihypertensive drugs can be reduced and tapered out for those patients without other risk factor or target organ damage. After withdrawal, the BP should be frequently monitored with reinforcing the lifestyle advice.

### Perspective

The prevalence of hypertension is increasing steadily as our society ages and becomes more complicated. However, the Korean national surveys are still disappointing, and they show considerable underdiagnosis, undertreatment and poor control rates of hypertension in Korea<sup>4)</sup>; further, compliance with antihypertensive treatment is still low.<sup>14)</sup> In spite of insufficient clinical outcome data pertaining to the Korean people, the committee recognizes the necessity of the Korean Hypertension Treatment Guidelines and these guidelines come at an opportune time. The 2 key goals of the Korean guideline is 1) to reduce or minimize the CV events that come

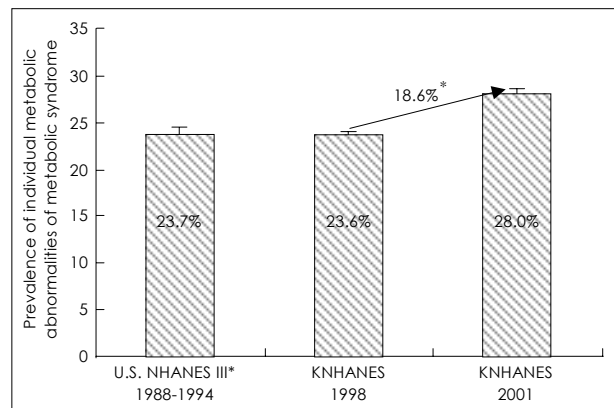


**Fig. 1.** Algorithm for the treatment of hypertension. A: ACE inhibitors or ARBs, B:  $\beta$ -blocker, C: calcium channel blocker, D: diuretics. ACE: angiotensin-converting enzyme, ARBs: angiotensin-receptor blockers.

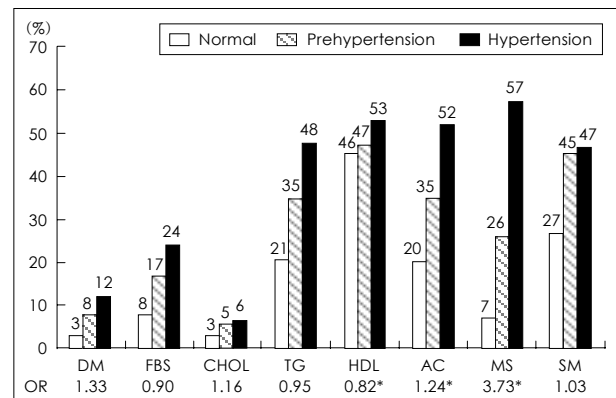
about from hypertension by increasing patients' and physicians' awareness and by emphasizing the importance of prehypertension. Promoting healthy lifestyles should be advised for the population that is at high risk, 2) to increase the control rate of hypertension by simplifying drug prescription. The treatment algorithm based on the AB/CD rule should be instituted to guide physician's decisions.

Even though the Korean people have a different genetic and environmental background, our guidelines share many similarities with those of the JNC VII, ESH, WHO/ISH, and BHS guidelines. Although there may be variability in the absolute cardiovascular risk of hypertension among diverse societies, we believe that the relative risk of hypertension for CVD is similar irrespective of racial, ethnic, cultural, religious and social differences. The higher the BP, the greater is the chance of CVD and hypertension-related target organ damage. Treatment of hypertension has shown similar reductions of cardiovascular events in the worldwide population.

Salt intake and obesity are very different in Koreans than in Caucasians. Obesity related co-morbidities such as hypertension, diabetes and hyperlipidemia have been shown to increase proportionately to the increase of the body mass index in our 8 years follow-up study, and this is similar to the trends noted in the western populations.<sup>15)</sup> Metabolic syndrome (MS) is a clustering of central obesity, glucose intolerance, hypertension and dyslipidemia; this is a constellation of metabolic abnormalities associated with an increased risk for cardiovascular disease (CVD). Even though Koreans have a lower frequency of obesity than do Caucasians, our nationwide surveys have demonstrated a persistent increase of prevalence of MS, i.e., an 18.6% increase between 1998 and 2001 (Fig. 2).<sup>16)</sup> Another characteristics of metabolic syndrome in Korea is that much MS exists even in people with low waist measurements or a low BMI.<sup>17)</sup> Therefore, insulin resistance underlies the development of metabolic syndrome, and then obesity boosts and accelerates it. The prevalence of metabolic syndrome is now about 28%, which is similar to that of Caucasians, when the modified Third National Health and Nutrition ATP III criteria (body mass index  $25 \text{ kg/m}^2$ ) or the Asia-Pacific abdominal obesity criterion (waist circumference  $>90 \text{ cm}$  in men and  $>80 \text{ cm}$  in women)<sup>18)</sup> is applied. The prevalence of hypertension and low HDL cholesterol comprises 37.7% and 49.3%, respectively, of the metabolic risk factors among the individual metabolic abnormalities of MS.<sup>15)</sup> The vast majority of individuals with MS fall into the categories of prehypertension or stage I hypertension. According to the data of the 2002 Korean National Health and Nutrition Examination Survey (NHANES), among such factors as diabetes (DM), fasting blood sugar (FBS), lipid profiles, abdominal circumference (AC), metabolic syndrome



**Fig. 2.** Prevalence of metabolic syndrome in Korea in comparison with the US NHANES study. \*: the modified Third National Health and Nutrition ATP III criteria (a body mass index of  $25 \text{ kg/m}^2$ ) or the Asia-Pacific abdominal obesity criterion (a waist circumference  $>90 \text{ cm}$  in men and  $>80 \text{ cm}$  in women) was applied. US NHANES: United States National Health and Nutrition Examination Survey, KNHANES: Korean National Health and Nutrition Examination Survey, ATP: adult treatment panel.



**Fig. 3.** Odds ratios of metabolic syndrome and abdominal circumference for prehypertension (Korean NHANES 2002,  $n=5613$ ) (male/female=2380/3233). \*:  $p<0.05$ , normal vs prehypertension, adjusted for age and gender. NHANES: National Health And Nutrition Examination Survey, FBS: fasting blood sugar, HDL: high density lipoprotein, AC: abdominal circumference, MS: metabolic syndrome, DM: diabetes mellitus, CHOL: cholesterol, TG: triglyceride, SM: smoking.

and smoking for prehypertension, the odds ratio was the highest at 3.73 for the metabolic syndrome; the odds ratio was 1.24 for abdominal circumference and low HDL-C showed also a significant risk (Fig. 3). Therefore, awareness of the importance of prehypertension will be imperative to prevent our society from being overwhelmed with high BP and to prevent BP- or metabolism derangement-derived CVD.

Several key initiatives introduced here will serve to guide patients and physicians towards better healthcare. Our society has been working in a systematic and structured way to advise, educate and support patients and physicians on effectively implementing this guideline.

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