High normal blood pressure and prehypertension: The debate continues

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Subjects with high normal blood pressure are at high risk of developing hypertension. Thus, the criteria of the Canadian Hypertension Education Program for diagnosis of hypertension and recommendations for follow-up now recommend that patients with high normal blood pressure (130 mmHg to 139 mmHg systolic and/or 85 mmHg to 89 mmHg diastolic) be followed up annually for the development of hypertension. Clinical trial data from subjects with high normal blood pressure show that 40% over two years and 63% over four years developed hypertension (140/90 mmHg or higher). These data are consistent with observational data from the Framingham Heart Study, which found a similar risk. Besides annual follow-up, the Canadian Hypertension Education Program recommends lifestyle therapy for individuals with high normal blood pressure. Ongoing research will establish whether any further management is required.

Key Words: *Clinical practice guidelines; High normal blood pressure; Hypertension; Lifestyle therapy; Prehypertension*

La pression artérielle normale élevée et la préhypertension artérielle : Le débat se poursuit

Les personnes ayant une pression artérielle (PA) normale élevée sont fortement prédisposées à l'hypertension artérielle (HTA). C'est pourquoi on recommande dans les critères relatifs au diagnostic d'hypertension et les recommandations sur le suivi, exposés dans le Programme d'éducation canadien sur l'hypertension, que les patients présentant une PA normale élevée (PA systolique : 130 – 139 mm Hg ; PA diastolique : 85 – 89 mm Hg) soient suivis chaque année afin de déceler l'apparition d'HTA. D'après des données d'essais cliniques, 40 % et 63 % des personnes ayant une PA normale élevée sont atteintes d'HTA au cours des deux et quatre années suivantes, respectivement (≥ 140/90 mm Hg). Ces données vont dans le même sens que les données d'observation de l'étude de Framingham, qui révèlent un risque comparable. En plus du suivi annuel, il est recommandé, dans le Programme, que les personnes présentant une PA normale élevée modifient leur mode de vie. La poursuite de la recherche permettra de déterminer si d'autres mesures s'imposent.

As a new addition to the criteria for diagnosis of hypertension and recommendations for follow-up published in the current issue of the *Journal* (pages 529-538 [1]), it is recommended that patients with high normal blood pressure (BP) (130 mmHg to 139 mmHg systolic and/or 85 mmHg to 89 mmHg diastolic) should be followed up annually for the development of hypertension.

This new recommendation acknowledges the finding that over two and four years, 40% and 63% of patients, respectively, with BP in the high normal range develop hypertension (ie, clinic BP 140/90 mmHg or higher) (2) with the attendant well-documented increased risk for cardiovascular events. This finding is supported by earlier observations obtained from the Framingham Heart Study (FHS). The FHS showed that over four years, hypertension developed in 39% of subjects 35 to 64 years of age and in 53% of subjects 65 to 94 years of age who had baseline clinic BPs of 130-139/85-89 mmHg. Even in subjects with baseline BPs of 120-129/80-84 mmHg, hypertension developed in 18% of those 35 to 64 years of age and in 29% of those 65 to 94 years of age (3). These data were considered sufficient evidence by the Canadian Hypertension Education Program (CHEP) to recommend the annual follow-up of patients who have high normal BP, so as not to miss their progression to hypertension. Although the FHS showed that the risk for a cardiovascular event is greater in individuals with high normal BP than in those with optimal BP (below 120/80 mmHg) (4), there are no data as to whether antihypertensive treatment would lower this increased risk in patients with high normal BP.

In recent years, lower levels of BP have been used to define hypertension. Experts continue to debate the exact level of BP that constitutes hypertension. This uncertainty exists because the relationship between BP and the risk of a cardiovascular morbid or fatal event is continuous. No definable threshold has been identified, down to a BP of 115/75 mmHg (5). BP is not unique in this regard, because other biological variables

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(eg, cholesterol levels) relate to risk in a similar continuous fashion. The question is: at what level does the benefit of BP therapy outweigh the risk? The answer to this must also consider potential hazards that may be attributed to the intervention.

However, to diagnose and treat hypertension in clinical practice, specific cut-off points for abnormal BP need to be defined. Currently, hypertension is defined as a clinic BP of 140/90 mmHg or higher, the level at which antihypertensive treatment significantly reduces cardiovascular morbidity and mortality.

Over the past decade, this well-established paradigm has been challenged, and the risks associated with BP below 140/90 mmHg have been put into focus. This trend of addressing increasingly lower BP is reflected in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (6), which defines BP of 120-139/80-89 mmHg as 'prehypertension'. The FHS results (3,4) and a meta-analysis of 61 prospective studies (5) involving one million adults provided the basis for this new classification. The European guidelines (7) classify BP levels of 130-139/85-89 mmHg as high normal. Although presently the identification of lower BP relates more to terminology than substance, it reflects some concern about the potential risk of these lower BP categories.

How should high normal BP or prehypertension be managed in practice? There are as yet no data to show whether treatment of high normal BP or prehypertension reduces the risk of cardiovascular events. At least 31% of the population in the United States has prehypertension (8), and this figure may be even higher in Europe (9). Therefore, recommendations for treating high normal BP or prehypertension need to be approached with great caution, considering the enormous health care costs involved. Therapeutic intervention must be balanced against a definite benefit. There is still no evidence for or against the latter.

So how should we, as clinicians, respond to the increasing popularization of these BP categories, particularly when it comes to managing an individual patient? As addressed in this year's CHEP recommendations (pages 529-538 and 539-550 of the current issue of the *Journal* [1,10], a yearly follow-up of patients with high normal BP will identify those who progress to established hypertension. It also addresses those who then need to be managed with lifestyle, and possibly medical, therapy according to the algorithm for the diagnosis of hypertension in the CHEP recommendations.

What about the individuals who are and remain in the high normal BP range, and for whom there are no evidence-based recommendations to guide their management? In the absence of data to support any pharmacological interventions, there are a few practical approaches that may be considered. Lifestyle measures, such as weight reduction, regular exercise and a low-salt diet, have been shown to lower BP (11) and will reduce the risk of progression to hypertension. There is also the potential for lifestyle therapy to move patients out of the high normal BP range, particularly when considering that high normal BP is associated with obesity and overweight (8). A great number of patients with high normal BP may have other cardiovascular risk factors, such as hypercholesterolemia or smoking, the treatment benefit of which are proven, irrespective of BP level. Therefore, elimination of these additional risk factors is both ethical and effective. Patients with a high normal BP and who at very high risk of cardiovascular events, such as those with diabetes or chronic kidney disease, should already be on antihypertensive treatment, because there is sufficient evidence showing the benefits of lowering high normal BP to a treatment target of below 130/80 mmHg. For patients who have 'only' high normal BP, for now, there is no evidence that treating their 'numbers' is associated with any proven benefits. An assessment of global risk, as described in the current issue of the *Journal* (1), may become an important factor in deciding how to approach patients with high normal BP. Also, further studies are required to provide evidence for therapeutic intervention in these patients.

What should we tell our patients? Today, information technology allows for a rapid transfer of information to the public at large. Daily practice shows that patients are aware of the terms 'high normal BP' and 'prehypertension', and this has the potential to raise concern. As clinicians, our first task is to clarify any misconception about this new terminology to ensure that information provided to the public is not biased or erroneous. We need to explain that a treatment benefit for these levels of BP has not yet been demonstrated. In discussions with interested or concerned patients, we can use this opportunity to recommend lifestyle changes or treatment of additional risk factors. Most importantly, and until we have evidence to the contrary, we need to avoid labelling these individuals as hypertensive or as having a disease. The negative consequences of such a stigma (increased absenteeism from work, increased clinic visits, increased anxiety, etc) are well known.

Before we give too much attention to high normal BP and 'prehypertension', and before we indulge in endless debates on treating numbers, we should remember that there are still many hypertensive patients who have not been diagnosed or treated, or who are poorly controlled (12). In this group of patients, there is abundant evidence proving that accurate diagnosis and appropriate treatment saves lives and prevents many cardiovascular catastrophes.

REFERENCES

1. Padwal RS, Hemmelgarn BR, McAlister FA, et al; for the Canadian Hypertension Education Program. The 2007 Canadian Hypertension Education Program recommendations for the management of hypertension: Part I – blood pressure measurement, diagnosis and assessment of risk. Can J Cardiol 2007;23:529-38.
2. Julius S, Nesbitt SD, Egan BM, et al; Trial of Preventing Hypertension (TROPHY) Study Investigators. Feasibility of treating prehypertension with an angiotensin-receptor blocker. N Engl J Med 2006;354:1685-97.
3. Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: A cohort study. Lancet 2001;358:1682-6.
4. Vasan RS, Larson MG, Leip EP, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. N Engl J Med 2001;345:1291-7.
5. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R; Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360:1903-13. (Erratum in 2003;361:1060).
6. Chobanian AV, Bakris GL, Black HR et al; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High

Blood Pressure: The JNC 7 report. JAMA 2003;289:2560-72. (Erratum in 2003;290:197).
7. European Society of Hypertension-European Society of Cardiology Guidelines Committee. 2003 European Society of Hypertension-European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens 2003;21:1011-53. (Errata in 2003;21:2203-4, 2004;22:435).
8. Wang Y, Wang QJ. The prevalence of prehypertension and hypertension among US adults according to the new joint national committee guidelines: New challenges of the old problem. Arch Intern Med 2004;164:2126-34.
9. Wolf-Maier K, Cooper RS, Banegas JR, et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada and the United States. JAMA 2003;289:2363-9.
10. Khan NA, Hemmelgarn B, Padwal R, et al; for the Canadian Hypertension Education Program. The 2007 Canadian Hypertension Education Program recommendations for the management of hypertension: Part 2 – therapy. Can J Cardiol 2007;23:539-50.
11. Sacks FM, Svetkey LP, Vollmer WM, et al; DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med 2001;344:3-10.
12. Joffres MR, Ghadirian P, Fodor JG, Petrasovits A, Chockalingam A, Hamet P. Awareness, treatment and control of hypertension in Canada. Am J Hypertens 1997;10:1097-102.