

ABSTRACT

Management of hypertension will continue to evolve as new studies provide us more evidence on many relevant aspects of care for this very common condition. To define hypertension, we need to be able to measure blood pressure (BP) accurately and make it easily reproducible. The mercury sphygmomanometer has been a standard tool to measure BP, but it is evident that it will be phased out soon and replaced by electronic BP devices — both for clinic and home use. There is increasingly more awareness of the benefits of out-of-office (clinic) BP measurement to estimate extent of BP control and also prognosis. The goal for BP treatment has also evolved and, for the first time in decades, there has been a suggestion that a lower-than-140/90 mmHg target is associated with further reduction in adverse cardiovascular outcomes. There is, however, a need for more pills and an increased risk of treatment-related side effects. The choice of which anti-hypertensive to use, as well as the goal of treatment, should be individualised and discussed with the patient.

Keywords: Hypertension; Blood Pressure Goal; Guidelines;

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INTRODUCTION

The management of hypertension will continue to evolve despite great progress made in the last few decades. In the last 3 years, various professional organisations have published updated guidelines on the management of hypertension. We do need to accept and understand that none of the guidelines are perfect and that one is not more precise than the other. It is because the science of a condition like hypertension is not complete and the interpretation of available evidence will have some degree of inevitable subjectivity.

Despite the various differences and emphases, it is necessary to educate ourselves in these new updates and to apply them sensibly to each of the patients we treat. Each of the guidelines published is of considerable length but they serve to provide excellent guidance, and all physicians treating hypertension should read at least the summary recommendations.

This article is not intended to provide a comprehensive review of all aspects of hypertension but will focus on a few selected

issues that will have significant impact on our practice. These pertinent issues are some of the newer additions and changes in the latest guidelines.

BLOOD PRESSURE MEASUREMENT

The mercury sphygmomanometer has been the traditional gold standard in the measurement of blood pressure (BP). However, because of occupational health and environmental safety reasons, electronic devices will gradually replace it in the clinic, as in the home. Electronic BP devices help avoid auscultation errors and also minimise white-coat hypertension, as BP can now be taken without the health professional in attendance. The list of electronic BP devices that have been validated is published at www.bhsoc.org.

The technique for taking the correct BP has also been published in many of the guidelines. The emphasis on appropriate cuff size, the necessary environmental condition, having the patient seated in the right position and well rested, are steps that should be consistently applied each time a BP is measured. In addition, if the patient is a new consult and the BP measurement is being taken for the first time, the measurement should be taken from both arms. If there is a difference of >5 mmHg, the arm with the higher BP should be the reference for all future BP recordings. In patients with risk for or existing postural hypotension, BP must be done in the standing position as well (with at least a 2-minute standing duration). The BP measurement of patients with atrial fibrillation will need to be repeated several times for better accuracy.

What has also become a consistent feature in the latest guidelines is the use of out-of-clinic BP measurement. Home BP monitoring (HBPM) and also 24-hour ambulatory BP measurements (ABPM) are advantageous for certain clinical indications as they provide more measurement points over different time periods and are recorded in a more representative environment for the patient. Because of this, the threshold for the diagnosis of hypertension is set a little lower if based on out-of-clinic BP readings. However, the BP readings used in cardiovascular (CV) risk calculators were all validated based on clinic BP. Hence, it is the clinic BP that is used in estimating total CV risks using these population-studies-derived calculators (Framingham Heart Study).

HBPM is easy to accomplish and patients should be encouraged to have that done. Home BP should be taken across 3 time periods during the day. The first reading should be done early, upon waking up (and before taking any anti-hypertensive agents if they are on it). The second BP reading should be taken in the afternoon and the last in the evening. For most people, the evening BP is the lowest, and if a patient only checks the home BP once daily after work in the evening, it may seem well controlled but in actual fact is not. HBPM is ideal for the

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diagnosis of masked and white-coat hypertension. It is also used in patients who may have symptoms at home and HBPM can help determine if the symptoms are related to BP being high or low. It will promote better awareness to ensure good BP control and improve compliance to treatment.

Although ABPM is not widely available in primary care practice, patients can be referred to centres specialising in hypertension and cardiovascular medicine to have it done. It will automatically record BP every 30 minutes, throughout a 24-hour period (day and night). ABPM will allow calculation of BP variability, detection of early-morning surge and circadian BP patterns (nocturnal BP during sleep and nocturnal dipping vs. non-dipping pattern). The additional information from the ABPM is of proven prognostic value and will help in determining choice of treatment and also timing of the dosing. The early-morning BP surge (detected by ABPM) should be managed by long-acting anti-hypertensive agents or by an evening dosing schedule.

BLOOD PRESSURE TARGET

It has been quite awhile since the question of an appropriate BP target has been asked. The publication of a meta-analysis in 2002 of more than a million patients from 61 prospective studies on BP treatment suggested a lower optimal BP than the 140/90 mmHg that has been the goal for BP management for many decades (since JNC IV that was published in 1988). The latest JNC VIII guidelines (2014) and the results of randomised study like SPRINT perhaps created more confusion than clarity.

JNC VIII started the task of updating the hypertension guidelines in 2008 and finally, after much delay, recommended a treatment goal of less than 150/90 mmHg for those older than 60 years of age. This was based primarily on some 6 studies of BP control in older individuals. Although many of those studies had recruited patients much older than 60 years, the JNC VIII panel felt that it was enough to justify a recommendation that currently available studies (up to 2013) did not support a lower BP goal of 140/90 mmHg for individuals older than 60 years old. Not everyone agrees with that and, till today, there is still much controversy surrounding this. The American Heart Association and the American College of Cardiology never did endorse the JNC VIII.

The latest recommendations for BP goals from different guidelines are given in the table below for comparison. For most individuals, the guidelines recommend a BP goal below 140/90 mmHg; the exceptions being older individuals (which is defined as those 80 years and older by ASH and ESH, but 60 years or older in JNC VIII). There also exists some degree of uncertainty and controversy in the BP goal for those with diabetes mellitus (DM) and chronic kidney disease (CKD). Some expert panels felt that the evidence was enough to recommend a lower than 140/90 mmHg BP goal for individuals with DM and those with CKD. However, JNC VIII again felt that the strength of the evidence was weak (many arising from post-hoc analysis) and did not recommend different BP goals for these two groups.

Table 1: Comparative BP Goals

Guideline	Population	Goal blood pressure (mm Hg)	Initial treatment options	Grade of recommendation*
American Diabetes Association (2013) ³	Patients with diabetes mellitus	< 140/80	ACE inhibitor or ARB	B
American Society of Hypertension/ International Society of Hypertension (2014) ²	General ≥ 80 years	< 150/90	Nonblacks: thiazide diuretic, ACE inhibitor, ARB, or CCB	NA
	General < 80 years	< 140/90	Blacks: thiazide diuretic or CCB	NA
Eighth Joint National Committee (2014) ¹	General ≥ 60 years	< 150/90	Nonblacks: thiazide diuretic, ACE inhibitor, ARB, or CCB	A
	General < 60 years	< 140/90	Blacks: thiazide diuretic or CCB	Systolic: E
	Patients with diabetes	< 140/90	ACE inhibitor or ARB	Diastolic: A
	Patients with CKD	< 140/90	ACE inhibitor or ARB	E
European Society of Hypertension/ European Society of Cardiology (2013) ⁴	General ≥ 80 years	< 150/90	Thiazide diuretic, beta blocker, CCB, ACE inhibitor, or ARB	A
	General < 80 years	< 140/90	ACE inhibitor or ARB	B
	Patients with diabetes	< 140/85	ACE inhibitor or ARB	A
	Patients with CKD without proteinuria	< 140/90	ACE inhibitor or ARB	B
	Patients with CKD with proteinuria	< 130/90		B
Kidney Disease: Improving Global Outcome (2012) ⁵	Patients with CKD without proteinuria	≤ 140/90	ACE inhibitor or ARB	B
	Patients with CKD with proteinuria	≤ 130/80		C

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; CKD = chronic kidney disease; NA = not applicable.

*—A = strong recommendation; B = moderate recommendation; C = weak recommendation; D = recommendation against; E = expert opinion.

Information from references 1 through 5.

When the SPRINT (Systolic BP Intervention) trial was published in November 2015,¹ it again generated quite a bit of excitement and discussion. This was a randomised trial comparing intensive BP control (SBP less than 120 mmHg) versus standard BP control (SBP less than 140 mmHg) in patients with higher CV risk (defined as patients aged 75 years or older, those with existing CVD except stroke, those with eGFR of 20-60 ml/min/1.73m², those with a 10-year Framingham Risk Score of at least 15%). Over 9000 patients were randomised for a follow-up period of close to 4 years. The study population excluded individuals younger than 50 years, those with DM, those with eGFR <20ml/min/1.73m², those with previous history of stroke, those with LVEF <35 percent and those with proteinuria of >1g/day. The mean age of the study population was 68 years, with about 28 percent in both arms of the trial aged 75 years or older.

The study reported a significantly better outcome for the group treated to a lower-than-standard BP goal. It achieved a 25-percent reduction in hazard ratio for the primary outcome (a composite of myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from CV disease). The patients treated to a lower BP received more anti-hypertensive agents (3 vs. 2) over the course of the study period. Although the final outcome was in favour of the intensive treatment arm, patients in the lower BP arm did experience more side effects such as hypotension, syncope, electrolyte abnormality, and acute kidney injury.

The result from SPRINT was published after the latest guideline revisions and was not part of the body of evidence that was reviewed. It is still arguable whether the balance tips in favour of the benefit of more intensive BP lowering in view of the higher risk of side effects. Experts have suggested perhaps to consider an SBP target of 120 mmHg for those who are above 50 years old, non-diabetic or have other factors that are associated with higher CV risk. All practitioners must adhere strictly to monitoring

closely for occurrence of side effects and must make it known to patients the possibility of such events before a final decision is made to pursue this more-intensive treatment goal. It must also be noted that the study population in SPRINT had a baseline mean SBP close to 140 mmHg and it is uncertain if a more-intensive BP target is attainable in patients who have a higher grade of BP without increasing the risk of harm. There is also inadequate clarity on DBP, what the accompanying DBP should be, and whether there is a level below which it is harmful and should be avoided.

SPRINT excluded patients with diabetes in their study population because there was already a study of intensive BP control in diabetic patients done — the ACCORD study (published in 2010).² Unlike SPRINT, the intensive BP control arm (SBP less than 120 mmHg) in ACCORD did not manage to show significant advantage over the standard arm (SBP less than 140 mmHg) although it did significantly reduce the occurrence of stroke as part of the secondary outcome. It must be noted that the populations differed in age (ACCORD recruited patients aged 40–79 years old) and the final number randomised in ACCORD was only about half the study population in SPRINT. It is unclear if the result of ACCORD would have been different if there had been a larger study population size. All the recently revised guidelines did not change the SBP goal for individuals with DM because ACCORD did not manage to achieve a positive result in the primary outcome measure. The DBP goal was set lower than 90 mmHg in some guidelines based on the favourable results from the ABCD (Appropriate BP Control in Diabetes) trial that was published in the '90s.

BLOOD PRESSURE TREATMENT

There were no major changes in recommendation for pharmacological treatment in the latest revised guidelines. Essentially, any of the following can be used as first-line therapy — thiazide diuretics (TD), calcium channel blockers (CCB), angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB). Beta-blockers (BB) are generally not offered as first-line therapy unless there is concomitant specific indication for their use. Therapy can be initiated alone or in combination. Risk stratification is useful to help determine urgency for pharmacologic therapy. Patients can be stratified by the severity of their BP at the time of diagnosis, presence of additional CV risk factors, diabetes, and evidence of organ damage. The ESH/ESC Hypertension Guidelines (2013) have a table that is easy to use for everyday clinical practice.³

The classes of anti-hypertensives as listed above have all been demonstrated to reduce CV morbidity and mortality. Various randomised prospective trials done support this and show that the benefit seen is related to BP lowering more than any particular mechanism of action of a specific class.^{4,5,6} There are, however, differences in components of CV outcome (such as heart failure or stroke risks) and of organ protection (progressive kidney disease) that may be influenced by specific classes of anti-hypertensive agents more than others. Most of the revised guidelines do provide guidance on what is considered to be the preferred choice of anti-hypertensive agents in various categories

of patients (such as for those with diabetes, stroke, post myocardial infarction, heart failure, and chronic kidney disease; and for the elderly). The initial drug choice should be based on patient's age, presence of other co-morbid conditions or organ damage, affordability, and ease of maintaining long-term compliance. It is a decision that should be discussed with each patient.

Many of the patients with hypertension may need more than one agent to lower their BP to goal. Most classes do form synergistic combinations that provide more efficacious lowering of BP. Prospective randomised studies showed that the combination of ACEi and CCB is more effective in reducing CV endpoints than combining ACEi with TD, or BB with TD. However, the context of patient selection is important as different classes and combinations may be of added benefit in patients with different co-morbidities. It is useful to remember that using two classes of anti-hypertensives will lower BP more than doubling the dose of a single agent. When two anti-hypertensive agents are needed, there is the option of using a 2-in-1 fixed-dose combination pill or to start the drugs separately before progressing to a single fixed-dose combination for ease and compliance. A few combinations to avoid include ACEi and ARB, ACEi or ARB with direct renin inhibitor (DRI), and non-dihydropyridine CCB with BB.

Ensuring compliance is a key challenge in achieving and maintaining optimal BP control. Useful strategies in helping patients remain on BP treatment (which is usually lifelong for most) include a good and uncomplicated explanation of:

- what hypertension is;
- what serious harm it can cause if untreated;
- the fact that a high BP is usually asymptomatic and silent;
- the fact that anti-hypertensive agents can reduce risk of CV disease;
- how the side-effects from one agent does not mean all anti-hypertensive agents are bad;
- why they can be honest in sharing their concerns and perspectives;
- the need to voice their objections if treatment cost is too high;
- the need to make it known if they feel the treatment regimen is too complex to follow; and
- how patients can be empowered to participate in the overall treatment of the condition.

Whatever the pharmacologic approach, one must remember to advocate for lifestyle changes to accompany the treatment prescribed. These include dietary salt and fat restriction, smoking cessation, moderate alcohol intake, planned physical activity, and maintaining an ideal body mass index. These may seem clichéd, but they have been proven effective when done deliberately and consistently.

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LEARNING POINTS

- **Clinic BP is subject to considerable error and variances. HBPM and ABPM are 2 means of measuring out-of-clinic BP and provide better representation of the BP profile. Out-of-clinic BP measurements should be an inherent part of our practice.**
 - **There is new evidence to suggest that intensive SBP control in a population with certain characteristics is associated with a greater reduction in adverse CV outcomes. However, this must be balanced against the increased incidence of treatment side effects.**
 - **Successful treatment and attainment of good long-term BP control will require careful selection of the most effective and appropriate anti-hypertensive agents or combination of such; taking into consideration the unique demographic and medical backgrounds of each patient.**
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