

## REVIEW ARTICLE

**Hypertension Control: Which way We Go?**

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With the unfolding of the 21st century hypertension remains a serious health problem worldwide. The global prevalence of raised blood pressure (BP), defined as systolic blood pressure  $\geq 140$  mm Hg or diastolic blood pressure  $\geq 90$  mm Hg, is estimated as 24% in men and 20% in women in 2015 according to pooled analysis of population-based cohort studies. This included 19.1 million adults from 1,479 worldwide cohort studies which were assessed for prevalence of raised blood pressure (BP) between 1975 and 2015.<sup>1</sup> Also, it was detected that more than 50% of people aged 60-69 years and about 75% of people  $\geq 70$  years old have hypertension<sup>1</sup>

Another significant finding is that the highest prevalence has shifted from high-income western and Asia-Pacific regions to low- and middle-income countries in south Asia and sub-Saharan Africa which constitutes a huge burden on such less developed countries.<sup>1</sup>

Sadly, about 10 million people die every year from causes relating to hypertension, thus being the strongest modifiable risk factor for cardiovascular disease worldwide. Despite extensive knowledge about ways to prevent as well as to treat hypertension, the global incidence and

prevalence of hypertension and, more importantly, its cardiovascular complications are not reduced. This is partly because of shortcomings in prevention, diagnosis, and control of hypertension in an ageing world population.<sup>2</sup> The basic fact that hypertension is associated with increased cardiovascular morbidity and mortality including cardiovascular death, myocardial infarction, heart failure and stroke still holds. Recently, it has been found that worldwide the prevalence of SBP  $\geq 140$  mm Hg (per 100,000 people) increased from 17,307 (95% CI 17,117-17,492) in 1990 to 20,526 (95% CI 20,283-20,746) in 2015. Also, the annual mortality associated with SBP  $\geq 140$  mm Hg (per 100,000 people) increased from 97.9 (95% CI 87.5-108.1) to 106.3 (95% CI 94.6-118.1). Thus, elevated systolic blood (SBP) pressure is the leading global health risk and therefore, the estimation of the levels of SBP is important to guide prevention policies and interventions<sup>3</sup>.

- Therefore, every effort should be exercised in order to achieve optimal blood pressure control (BP)<sup>4</sup>. However, in spite of a flood of guidelines, still we did not succeed in achieving the recommended BP targets even in high resource countries. This is both intriguing

and constitutes a big disappointment. Knowing that good BP control reduce CVAs by 40%. Coronary heart disease by 25%, and heart failure by 50%, we should strive to be more aggressive in treating hypertension knowing that awareness of hypertension and pharmacologic treatment rates are lower in low-income countries compared to all other countries ( $p < 0.001$  for each)<sup>5</sup>

The first Guidelines for the management of hypertension have been developed about 30 years ago by the American Joint National Committee (JNC)<sup>6</sup>. They were then followed, one year later, by the World Health Organization / International Society of Hypertension Guidelines<sup>7</sup>. Since then Guidelines on Hypertension have been revised and updated every 4 to 6 years with the aim of incorporating the larger amount of information on the pathophysiology, diagnosis and treatment of the hypertensive disease<sup>8-13</sup>. The most recent guideline is that issued by the Canadian society of hypertension in 2017. It is a more comprehensive and practical document<sup>14</sup>.

Therefore, with this flood of guidelines, the hot question one would naturally ask is why the hypertension control is not up to the recommended target?

What is the recommended target BP?

The answer is: the target BP varies among different guidelines as follows:

- According to the JNC8: Patients <60 years of age:, the target blood pressure (BP) < 140/90 mm Hg is recommended for all even those with increased cardiovascular risk or comorbidities<sup>13</sup>.

- Patients aged > 60 years: initiate treatment at SBP  $\geq$  150 or DBP  $\geq$  90 reduces stroke, heart failure, and CHD (Grade A)

Comparison of different guidelines for treatment of the elderly:

- **JNC8:** > 60 y/o = < 150/90
- **ESH/ESC:** >80 y/o or elderly < 80 y/o = < 150/90
- **CHEP:** >80 y/o = < 150/90
- **NICE:** > 80 y/o = < 150/90
- **ASH/ISH:** > 80 y/o = < 150/90

### Special populations<sup>8-15</sup>:

- In selected patients, with **increased cardiovascular risk** and without diabetes who are  $\geq$  50 years old, systolic blood pressure target less than 120 mm Hg reduces risk of cardiovascular events and mortality compared to target systolic blood pressure below 140 mm Hg (level 1)
- **Patients with diabetes**
  - Here guidelines vary but targets range from < 130/80 mm Hg to < 140/90 mm Hg
  - BP targets < 140/90 mm Hg (based primarily on diastolic BP) not associated with reduced mortality or morbidity (level 2 [mid-level] evidence), except in patients with diabetes (level 2 [mid-level] evidence)
- **Patients with chronic kidney disease**
  - Current guidelines recommend < 140/90 mm Hg, with multiple guidelines suggesting < 130/80 mm Hg if proteinuria or diabetes is present
  - lower blood pressure targets associated with reduced risk of end-stage renal disease in patients with

proteinuria (level 2 [mid-level] evidence)

- **Patients with coronary artery disease**, targeting systolic BP  $\leq$  130 mm Hg is associated with reduced risk of heart failure and stroke but no improvement in risk of death or myocardial infarction (level 2 [mid-level] evidence)

#### The choice of drug therapy:

- In Caucasians (non-blacks), the best initial therapy consists of thiazide diuretics, calcium channel blockers(CCB). Angiotensin converting enzyme inhibitors (ACE-I) or angiotensin receptor blockers(ARB).
- In persons with African origin (black populations), thiazide diuretics and CCB are the first initial choice. Others can be added.
- Persons with chronic kidney disease (CKD), ACE-I or ARB are the first initial or add-on therapy and then CCB may be added.
- Beta blocker especially atenolol should not be used to treat hypertension .First-line beta-blockers lead to modest reductions in stroke and have no significant effects on total mortality and coronary heart disease. In addition, beta-blockers are inferior to calcium-channel blockers and renin-angiotensin system inhibitors for various important outcomes<sup>15</sup>

#### The SPRINT Study<sup>16</sup>:

Then came the SPRINT study. It compared the effects of antihypertensive treatment with a systolic blood pressure (SBP) target of <120 mm Hg (intensive treatment) versus

<140 mm Hg (standard treatment) in 9361 hypertensive adults

$\geq$ 50 years of age who had a SBP range of 130–180 mm Hg and were at additional risk for cardiovascular disease (CVD). SPRINT was designed to recruit study participants with an average CVD risk of  $\approx$ 2% per year, equivalent to a Framingham 10-year CVD risk score of 20%. Individuals with diabetes mellitus, stroke, and polycystic kidney disease were excluded because of other ongoing National Institutes of Health–funded trials.

The main finding in SPRINT was that a primary composite outcome of myocardial infarction, non–myocardial infarction acute coronary syndrome, stroke, acute decompensated heart failure, and CVD death was reduced by  $\approx$ 25% in the intensive treatment group compared with the standard treatment group. Similarly, all-cause mortality was reduced by  $\approx$ 27% in the intensive treatment group.

The ACCORD study<sup>17</sup>

One of the most common questions about SPRINT will likely be whether the trial results apply to adults with diabetes. The Action to Control Cardiovascular Risk in Diabetes Blood Pressure trial<sup>3</sup> (ACCORD BP) used the same SBP goals used in SPRINT to determine the value of intensive compared with that of standard BP reduction in 4733 adults with diabetes mellitus, additional risk of CVD, and an average systolic BP of 130 to 180 mm Hg. In ACCORD BP, the composite CVD outcome (myocardial infarction, stroke, or CVD death) was 12% lower in the intensive treatment group, but this difference was not statistically significant.

The evidence accrued to date strongly supports the superiority of a more intensive versus a less intensive BP lowering policy for the prevention of stroke and myocardial infarction.

Cardiovascular death and heart failure are likely to be reduced by a more intensive blood pressure-lowering strategy, but evidence is not yet conclusive<sup>18</sup>

**Take home messages: The following points should be the roadmap for better diagnosis & hypertension control:**

It is mandatory to measure BP using the recommended automated device outside the office and at home. An average of 3 office BP readings taken with proper cuff size with the person seated with the back supported after 5 minutes of rest before measurement, and no conversation during the rest period or BP determinations. Accurate BP readings & recognizing white coat and masked hypertension is imperative” Masked hypertension is defined by the European Society of Hypertension/European Society of Cardiology (ESH/ESC) guidelines as: normal office blood pressure (< 140/90 mm Hg) but elevated blood pressure on home blood pressure monitoring or ambulatory blood pressure monitoring (ABPM)<sup>11</sup>.

- Also, home BP monitoring (HBPM) and whenever indicated, ambulatory BP monitoring (ABPM) correlate better with HTN outcomes than office based BP measurement (OBPM).
- The up-to-date definition of hypertension is based on the readings at different settings:
- Prevention of hypertension complications is mainly the result of

the magnitude of the drop blood pressure reduction "per se" and only partly from the type of drug used.

- The assessment of both clinical & subclinical organ damage, crucial for assessing total cardiovascular risk, which is the main aim of treatment.
- There are two "new" measures recommended to assess the risk of end-organ damage, the ankle-brachial ratio and the pulse wave velocity. These should be used in clinical practice whenever available.
- lifestyle changes, should be implemented before and during the pharmacological approach
- Following relevant guidelines should lead to optimal or near-optimal blood pressure control.
- The use of proper combination drug therapy should be the first-line treatment option, and not only when monotherapy fails<sup>18</sup>.
- Very recently in early 2017, a quarter-dose quadruple combination therapy for initial treatment of hypertension was found to be effective & this will pave the way for more larger studies addressed to this new combination therapy<sup>19</sup>.
- And finally, Commentaries and editorials have proliferated, and numerous calls have been coming forward to swiftly change current hypertension guidelines.
- Can we accept the notion that the goal of hypertension treatment in 2017 and beyond will be a systolic BP between 120 and 129 mmHg, and for lower risk patients or patients younger than the age of 50 years similar guidelines may be adopted,

leading to intensive BP lowering as suggested recently?<sup>20</sup>

<b>Home or ABPM Blood Pressure Thresholds for Hypertension:</b>		
<b>Setting</b>	<b>Systolic Blood Pressure</b>	<b>Diastolic Blood Pressure</b>
Home	135 mm Hg	85 mm Hg
Day (ABPM)	135 mm Hg	85 mm Hg
24-hour (ABPM)	130 mm Hg	80 mm Hg

Abbreviation: ABPM, ambulatory blood pressure monitoring.

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