Justice Came to Hypertension. Or Did It?

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Recomendations of the major guidelines in Hypertension (HT, with the meaning of systemic arterial hypertension) until November 2017 indicate almost uniform blood pressure (BP) therapeutic targets for the majority of pathologic conditions. Figure 1 makes a comparison between guidelines as in the year 2014 (1). The compared guidelines are the 2013 European Guideline (2), two North American Guidelines from 2014 (3, 4), one old American Guideline from 2003 (5) and the Canadian Guideline from 2013 (6). As we see, most of the blood pressure (BP) therapeutic targets were 140/90 mm Hg, with few timid exceptions: 140/85 mm Hg (only!) for diabetics in ESC/ESH Guideline (2), 130/80 mm Hg for diabetics in CHEP (6) and 130/90 mm Hg in patients with renal involvement in ESC Guideline (2). For the rest of the guidelines, till that date the targets are 140/90 for everybody, except for older people, for whom the accepted target could be 150/90 mm Hg.

It is curious that former guidelines, the cited JNC 7 guideline (5) and the ESC/ESH Guideline from 2007 (7) indicated other BP targets, such as 130/80 mm Hg, for some special conditions, like diabetes (5, 7). The argument for higher BP targets in the subsequent guidelines was that there were not sufficient data from large clinical trials to support lower BP targets. But we think that not every medical item which rises some questions finds a financial support for a new trial quickly enough to give a definitive answer. In our thought, the analysis from 2003 (5) or 2007 (7) to indicate a BP target of less than 130/80 for diabetics had enough scientific substance not to be necessarily replicated with new large clinical trials.

In 2015, the SPRINT clinical trial (8) changed the rationale of hypertension therapy as perceived until then. This was an important trial on

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<th>BP Goal</th>
<th>JNC-7</th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>ESC/ESH</th>
<th>CHEP</th>
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Figure 1. Comparison between guidelines. Modified from (1)
more than 9000 hypertensive patients followed for 3.26 years. Patients in the intensively treated group (systolic BP target under 120 mm Hg) had a clearly better outcome than those in the standard therapy group (BP target under 140 mm Hg). The hypertensive patients included were at high risk for cardiovascular disease, but the trial did not include diabetics. Cardiovascular mortality at 3.26 years was reduced by 27% (from 0.43% per year to 0.25% per year, p=0.003) in the intensively treated group and the primary composite endpoint (myocardial infarction, other acute coronary syndromes, stroke, heart failure, or death from cardiovascular causes) was reduced from 2.19% per year to 1.65% per year (p<0.001). There were more adverse effects in the intensively treated group, but no important difference in serious adverse effects (SAEs). Overall, benefit exceeded harm.

Effect of SPRINT trial on Guidelines

Since the publication of SPRINT trial, hundreds of pages in serious journals appeared with Pro or Con comments to this study. However, as to date (October 2017), no official point of view regarding possible lower BP targets was communicated at the great European and North American Congresses on Hypertension or Cardiology. Key opinion leaders who participated in Task Forces responsible for the development of European and American Guidelines on Hypertension (2-4) published their opinions which seemed to show agreement with the higher therapeutic targets of those guidelines (9-11).

However, some official guidelines which appeared since 2015 began to promote another opinion.

The Canadian Hypertension Guideline from 2016 (12) indicates a target for BP treatment of under 120 mm Hg for systolic BP (without a specified target for diastolic BP) for the population considered at high risk, under 130/80 mm Hg for diabetics, and under 140/90 mm Hg for the rest of the patients, including those with chronic kidney disease, respectively. High risk patients include clinical or subclinical cardiovascular disease, estimated 10 years global cardiovascular risk of more than 15%, kidney disease patients with some characteristics, but also people over 75 years of age. Elderly often do not tolerate low BP levels.

The Australian Guideline for the diagnosis and management of hypertension in adults (13) recommends that all patients receiving treatment should reach a target of less than 140/90 mm Hg. However, in those who were judged on clinical grounds to be at high risk and in whom more intense treatment was considered to be clinically safe and therapy was well tolerated, a target of less than 120 mm Hg systolic BP was considered to be reasonable. The guideline makes comments on this. Firstly, the diastolic target is not suggested by the new trials taken into consideration, e.g., the SPRINT trial. The diastolic target remains less than 90 mm Hg. Secondly, reaching a target of 120 mm Hg could be difficult in patients with a very high initial BP or with a long history of HT, and could involve some risk in patients with several comorbidities. Thirdly, the calculation of the Australian algorithm of the total cardiovascular risk differs from that applied in the SPRINT trial. The Australian guideline concludes that the current recommendation to take a less than 120 mm Hg BP target in the selected population mentioned is subject to review in accordance with new information. To date it was not reviewed.

The American Guideline on Heart Failure revised in 2017 (14) is most decided in recommending low for BP targets for patients with heart failure (HF). For patients with increased risk among those with Stage A HF (high risk for HF), the target BP would be less than 130/80 mm Hg. High risk is defined as a population with established cardiovascular disease, those over 75 years of age, those with a Framingham risk score over 15% or those with chronic renal disease. Again, the taken age limit is 75 (like in CHEP – 12), and lowering BP at 130/80 in such a fragile population is an interesting new point of view. To note that the Class of recommendation is the best (Class I) and the strength is good enough (Level of Evidence B-R). This guideline recommends a target for systolic BP under 130 mm Hg for all patients with reduced systolic function or even preserved systolic function in stage C of HF (structural heart disease with symptoms of HF). In this case there is no diastolic threshold. Again, the Class is I, but with level of evidence C.

Two Types of Hypertension?

It is unusual that the results of clinical studies are so different from study to study and guide-
lines constructed on their basis have to change dramatically in short time intervals. And this happens today in a very clear clinical condition, which is hypertension.

Or maybe things are not yet completely understood or analysed. Let us make a short judgement regarding the distribution of hypertension with age. According to most of the epidemiological studies, HT becomes evident in a population at the age of 40 and increases continuously until the age of 80. The overall prevalence in all the adult population, including young people, is about 40–45% (2, 3). We may say, according to a AHA Statistics, that HT is present in 35% of adults at the age of 45, 55% at the age of 55, 65% at the age of 65 and 75% at the age of 75 (15, page e114). At the age of 65, the number of hypertensive patients is twice that of people with HT at the age of 45.

We may consider that HT developed over the age of 65 is mainly due to stiffness of the great arteries, is mainly systolic and accounts for half of the hypertension at the advanced age (about 40% of the total population). This category is added to the other half of the hypertensive patients at that age who had high BP starting with the adult age and whose HT is systolo-diastolic. We may approximate that at the age of 75, 20% of the population is normotensive, 40% has systolo-diastolic HT and 40% has mainly systolic HT (Figure 2).

As it is known from epidemiologic studies and guidelines, systolic HT has different mechanisms, appears in a more fragile population and has to be treated in a different way than the systolo-diastolic HT of the middle age. The last one appears at a more robust population who has a much longer natural duration of life than old people.

We may conclude that there are two main types of hypertension: the middle age people HT, systolo-diastolic and present in a most robust population with a long expectancy of life, and the old people HT, half systolic due to stiffness and half coming from the middle age, systolo-diastolic with a new systolic component. The old people are more fragile and have a shorter expectancy of life.

Together, these two types of hypertension appear in more than three quarters of the population who have attained the age of 75.

The bomb

On the 13th of November 2017, AHA, ACC and other 11 North American Medical organizations published their new “High Blood Pressure Clinical Practice Guideline” (16). It is a monograph of more than 150 pages analysing the evidence in hypertension available until mid-2017. After an analysis of more than 100 pages, the final table indicates a target BP for different categories of patients with a single value: 130/80 mm Hg.

Here are the categories of patients (16):

- clinical CVD or 10-year ASCVD risk ≥10%
- no clinical CVD and 10-year ASCVD risk <10%
- older persons (≥65; noninstitutionalized, ambulatory, community-living adults)
- diabetes mellitus
- chronic kidney disease
- chronic kidney disease after renal transplantation
- heart failure
- stable ischemic heart disease
- secondary stroke prevention
- secondary stroke prevention (lacunar)
- peripheral arterial disease.

For each of these categories, the target therapeutic BP is 130/80 mm Hg, except for the "older persons" one, for whom only the systolic BP target of less than 130 mm Hg is indicated.

I want to say from the beginning that I consider this radical change in the philosophy of treatment of hypertension as very positive. However, some curious things still exist.

Firstly, in 2014, over 40 North American medical societies claimed in JNC 8 that the almost uniform BP therapeutic target should be 140/90 mm Hg (3). Since then, no major evidence appeared, except the SPRINT trial, in
which the „good” systolic BP target is... under 120 mm Hg. However, the re-appraisal of analyses of all the other available proofs leads today to a completely different conclusion.

Secondly, there is not enough differential analyses of the systolo-diastolic HT of the middle age and the systolic HT of the advanced age. As discussed before, the mechanism is different and the therapeutic consequences could be different. And different BP therapeutic targets should be probably defined for these two huge categories of hypertensive patients.

Conclusion

To date, we see that the same school of medicine, the North American one (it is right – with different groups of scientists), changed the philosophy of hypertension therapy from an almost uniform target of 140/90 in 2014 towards an almost uniform target of 130/80 mm Hg in 2017. This happened taken into account mainly a clinical study in which the „best” BP target was... under 120 mm Hg for systolic BP. 2018 is the year in which the European guidelines are announced to be re-appraised. I think some confusion remains in this field of pathology, which includes hundreds of millions of patients worldwide.

Till then, I want to conclude with my own analyses of the main points of view. I think there enough arguments for the following:

• for middle age (40-65) hypertensive patients with little comorbidity and a long life expectancy, the BP therapeutic target should be under 120 mm for systolic BP;
• for middle age (40-65) hypertensive patients with diabetes, ischemic heart disease, mild to moderate heart failure or chronic kidney disease, the target BP should be 130/80 mm Hg;
• in old (over 65) hypertensive people with little comorbidity, the target BP should be 140/90 mm Hg;
• in frail old (over 65) hypertensive people with important comorbidities, the target BP should be under 150/90 mm Hg.

Not neglecting the guidelines, let us always look at the patient in face of us, and act according to his/her particular status, arguing our decision in written!

References