



Controversies in Hypertension

Potential benefits and harms of various arterial hypertension guidelines

Maria Dorobantu^{*}, Nicoleta-Monica Popa-Fotea

ARTICLE INFO

Keywords:

Hypertension
Guidelines
Benefits

Without doubt, hypertension is a leading cause of mortality and morbidity and a risk factor for coronary heart disease, heart failure, cerebrovascular and chronic kidney disease. Seen the major impact of hypertension in the reduction of cardiovascular disease (CVD), many cardiology societies focused on the development of guidelines to assure optimal management. Based on major follow-up studies [1,2] that showed significant association between increased cardio-vascular risk and blood pressure (BP) higher than 130/80 mmHg, the American Heart Association/American College of Cardiology (AHA/ACC) changed the BP thresholds for diagnosis and treatment [3]. In the 2017 AHA/ACC guideline the cut-off value for the definition of hypertension is $\geq 130/80$ mmHg, with hypertension grade 1 defined between 130 and 139/80–89 mmHg [3]. Compared to these cut-offs, in the 2020 International Society of Cardiology (ISH) global hypertension practice guideline as well as in the European Society of Cardiology/European Society of hypertension (ESC/ESH) recommendations, the definition of hypertension is $\geq 140/90$ mmHg [4,5].

The emerging question is the potential impact of this change in definition and the resulting benefit/harm ratio. The first novelty generated refers to a variation in the overall prevalence of hypertension from 32% when the BP threshold was $\geq 140/90$ mmHg to 46% when it is lowered to $\geq 130/80$ mmHg [6,7]. Moreover, the most important effect rests the impact on the reduction of CV events in subjects with BP $> 130/80$ mmHg and a CVD risk higher than 10% that will benefit earlier from BP-lowering medication. However, there exists the risk of overdiagnosis and overtreatment of young adults who do not meet the criteria for prescribing antihypertensives, namely those with a CVD risk lower than 10% and no history of chronic kidney disease, diabetes mellitus, or CV events. Notwithstanding, the number of subjects using antihypertensive drugs among US adults increased only slightly after the 2017 ACC/AHA hypertension guideline, precisely an increment

estimated at 2%, as not all subjects with mild hypertension need treatment, but only those at high risk for CVD [6]. On the other hand, one study showed that the ACC/AHA BP definition helped to identify young adults at higher risk for CVD [8].

Based on a systematic review of Sundström [9], 7.8% of people with new diagnosed hypertension according to the new ACC/AHA guideline will have a modest benefit translated into an absolute reduction of CVD events by 1.4% for those with a baseline 10-year risk of CVD of 10–15%, while around 17%, represented by those with a risk $> 15\%$, will have a large benefit (a reduction of the absolute CVD risk between -2.41% and -3.84%).

But are there also possible incremental harms that may result from the new thresholds?

At least three drawbacks result from the new definition of hypertension and the increasing number of subjects needing antihypertensives. Firstly, there is a vicious cycle between hypertension and anxiety, knowing that anxiety predispose individuals to develop high BP and the diagnosis of hypertension on its turn induces anxiety, even if by an indirect effect [10]. Labelling especially young people with a chronic diagnosis induces anxiety and depression compared with those without a diagnosis of hypertension. Secondly, newly treated patients or those with intensified are at higher risk to experiment inconvenient related to therapy and polypharmacy. In the SPRINT trial, on which 2017 ACC/AHA mostly basis, lower BP targets resulted in adverse events such as syncope or acute kidney injury [1].

In accordance with the Hippocratic “*primum non nocere*”, a main focus must be put on protection of patients from complications. Unlike the ISH and ESC/ESH guidelines which take more personalized BP thresholds according to age, the ACC/AHA recommends similar BP cut-offs irrespectively of age, excepting those ≥ 65 years where the threshold of SBP is set at < 130 mmHg. Although SPRINT [1] and HYVET [2] trial included a great proportion of elderly subjects, supporting the

^{*} Corresponding author.

E-mail address: maria.dorobantu@gmail.com (M. Dorobantu).

use of antihypertensives to reduce the risk of death, stroke or heart failure, these data are not supported by metanalysis, which determined other hypertension societies to be more prudent [11]. In elderly the side effects of an intensified treatment could be numerous predominantly in those frail subjects, systematically excluded from existing studies. The real benefits of such treatment in this category is unknown as evidences come from old individuals, but without frailty, meaning that we may underestimate the risk of side effects resulting from the new definition. Patients and physicians should put in balance the benefits and risks altogether in a team about the opportunity to initiate treatment and its intensity. If the subject has defined CVD or high risk for CVD, the evidence favors treatment, but if none of the above are encountered potential benefits and harm should be discussed.

Thirdly, the costs of treating an increasing number of hypertensives puts supplementary stress on healthcare insurance systems, mainly in poor countries. The impossibility to assure continuity of treatment through insurances will lead to treatment discontinuation and even much harm in those treated with drugs having significant rebound effects after cessation.

How we should protect patients from complications? The first and most important step remains the identification of subjects with high CV risk who would have benefits rather than raising adverse effects; therefore this target population should be a priority for intensive treatment. Accurate assessment of CV risk is essential in order to avoid over-treatment. If the 2017 AHA/ACA guideline recommend the Atherosclerotic Cardiovascular Disease Risk (ASCVD) calculator, the ESC guideline utilize the Systematic Coronary Risk Evaluation (SCORE) based on a large representative European cohort of subjects. SCORE permits the addition of correction factors in order to reflect CV risk in the first generation of immigrants to Europe, compared with ASCVD calculator, which admits the highest risk in certain ethnic groups, but does not have the possibility to refine the score with additional variables. Also, the European guideline gives more attention to the assessment of hypertension-mediated organ damage and their impact on CV risk, assuring a more refined global risk. These differences in the assessment of CV risk could furthermore impact the proportion of people treated with antihypertensives and therefore the adverse effects.

Apart from a correct evaluation of the CV risk, physicians can protect patients from adverse effects by taking sufficient time to discuss lifestyle modifications they should adopt, as many subjects with grade 1 hypertension need only changes of lifestyle, as well as the majority of those with uncontrolled hypertension.

Despite the tendency of the AHA/ACC guideline to “fit all into one size” with the aim to prevent CV events, only individualized treatment differentiated upon age, clinical status, organ damage or other conditions can respond to the needs of the individual. ESC/ESH hypertension guideline, unlike ACC/AHA recommending similar BP targets across all ages, indicates in older adults (≥ 65) a BP of less than 140/90 mmHg compared with those < 65 years old where a BP between 120 and 129/70–79 is targeted. The cautiousness of the European guidelines derives from the observation that some old individuals can reach a BP of less than 130/80 mmHg, but others with low vascular compliance and high pulse pressure may not, essential aspect as these were excluded from SPRINT or HYVET studies because presented orthostatic hypotension. Albeit setting different BP targets across ages is still debatable, as systematic reviews of controlled, randomized trials do not support the recommendations [11], this remark being valid also for diabetes mellitus [12]. Both European and American guidelines ascertain that tolerability to treatment and biological age are of upmost importance in BP management.

All recommendations, either coming from the European or the American continent are only a guide for physicians' daily practice and not a substitute of clinical judgment and good communication with patients. The best manner to protect our patients remain the engagement of the individual in the treatment of the disease, without neglecting that the biggest issue to achieve proper BP control rests the unwillingness to adopt healthy lifestyles. This goal can be achieved only if health-care related personnel takes more time to discuss and debate with the patient instead of prescribing more drugs.

Declaration of Competing Interest

The authors declare that they have no competing interests.

References

- [1] T.S.R. Group, A randomized trial of intensive versus standard blood-pressure control, *N. Engl. J. Med.* 373 (2015) 2103–2116, <https://doi.org/10.1056/NEJMoa1511939>.
- [2] N.S. Beckett, R. Peters, A.E. Fletcher, J.A. Staessen, L. Liu, D. Dumitrascu, V. Stoyanovsky, R.L. Antikainen, Y. Nikitin, C. Anderson, A. Belhani, F. Forette, C. Rajkumar, L. Thijs, W. Banya, C.J. Bulpitt, Treatment of hypertension in patients 80 Years of age or older, *N. Engl. J. Med.* 358 (2008) 1887–1898, <https://doi.org/10.1056/NEJMoa0801369>.
- [3] P.K. Whelton, R.M. Carey, W.S. Aronow, D.E. Casey, K.J. Collins, C. Dennison Himmelfarb, S.M. DePalma, S. Gidding, K.A. Jamerson, D.W. Jones, et al., 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of cardiology/American heart association task force on clinical practice guidelines, *Hypertension* 71 (6) (2018) 1269–1324, <https://doi.org/10.1161/HYP.0000000000000065>.
- [4] T. Unger, C. Borghi, F. Charchar, N.A. Khan, N.R. Poulter, D. Prabhakaran, A. Ramirez, M. Schlaich, G.S. Stergiou, M. Tomaszewski, R.D. Wainford, B. Williams, A.E. Schutte, 2020 international society of hypertension global hypertension practice guidelines, *Hypertension* 75 (2020) 1334–1357, <https://doi.org/10.1161/HYPERTENSIONAHA.120.15026>.
- [5] B. Williams, G. Mancia, W. Spiering, E. Agabiti Rosei, M. Azizi, M. Burnier, D.L. Clement, A. Coca, G. de Simone, A. Dominiczak, et al., 2018 ESC/ESH Guidelines for the management of arterial hypertension, *Eur. Heart J.* 39 (2018) 3021–3104, <https://doi.org/10.1093/eurheartj/ehy339>.
- [6] P. Muntner, R.M. Carey, S. Gidding, D.W. Jones, S.J. Taler, J.T. Wright, P.K. Whelton, P.K. Whelton, Potential US population impact of the 2017 ACC/AHA high blood pressure guideline, *Circulation* 137 (2018) 109–118, <https://doi.org/10.1161/CIRCULATIONAHA.117.032582>.
- [7] S. Garies, S. Hao, K. McBrien, T. Williamson, M. Peng, N.A. Khan, R.S. Padwal, H. Quan, A.A. Leung, Committee for H.C.R. and E., Prevalence of hypertension, treatment, and blood pressure targets in Canada associated with the 2017 American College of cardiology and American heart association blood pressure guidelines, *JAMA Netw. Open* 2 (2019), <https://doi.org/10.1001/JAMANETWORKOPEN.2019.0406>.
- [8] Y. Yano, J.P. Reis, L.A. Colangelo, D. Shimbo, A.J. Viera, N.B. Allen, S.S. Gidding, A.P. Bress, P. Greenland, P. Muntner, D.M. Lloyd-Jones, Association of blood pressure classification in young adults using the 2017 American College of cardiology/American heart association blood pressure guideline with cardiovascular events later in life, *JAMA* 320 (2018) 1774, <https://doi.org/10.1001/jama.2018.13551>.
- [9] J. Sundström, H. Arima, R. Jackson, F. Turnbull, K. Rahimi, J. Chalmers, M. Woodward, B. Neal, Effects of blood pressure reduction in mild hypertension, *Ann. Intern. Med.* 162 (2015) 184, <https://doi.org/10.7326/M14-0773>.
- [10] A.T. Ginty, D. Carroll, T.J. Roseboom, A.C. Phillips, S.R. de Rooij, Depression and anxiety are associated with a diagnosis of hypertension 5 years later in a cohort of late middle-aged men and women, *J. Hum. Hypertens.* 27 (2013) 187–190, <https://doi.org/10.1038/jhh.2012.18>.
- [11] A. Qaseem, T.J. Wilt, R. Rich, L.L. Humphrey, J. Frost, M.A. Forciea, Clinical Guidelines Committee of the American College of Physicians and the Commission on Health of the Public and Science of the American Academy of Family Physicians, Pharmacologic treatment of hypertension in adults aged 60 Years or older to higher versus lower blood pressure targets: a clinical practice guideline from the American College of physicians and the American academy of family physicians, *Ann. Intern. Med.* 166 (2017) 430–437, <https://doi.org/10.7326/M16-1785>.
- [12] C. Thomopoulos, G. Parati, A. Zanchetti, Effects of blood-pressure-lowering treatment on outcome incidence in hypertension, *J. Hypertens.* 35 (2017) 922–944, <https://doi.org/10.1097/HJH.0000000000001276>.