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EDITORIAL COMMENT

Blood Pressure Levels Within Target

Not Just Good Control But Excellent Control Over Time

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High blood pressure (BP) is one of the leading preventable risk factors for cardiovascular disease (CVD), including ischemic heart disease and stroke and premature death. Elevated BP contributes to 8.5 million deaths each year.[1] CVD risk doubles for a 20-mm Hg increase in systolic blood pressure (SBP) above 115 mm Hg, and for a 10-mm Hg increase in diastolic BP above 75 mm Hg, the risk of CVD is 2-fold higher.[1] The burden of uncontrolled hypertension globally has made it a major public health challenge.

Recent evidence advocates for stricter hypertension treatment targets, given the additional benefits of more intensive BP lowering for prevention of CVD and deaths.[2] The 2017 American guidelines for diagnosis and management of hypertension lowered the diagnostic threshold from 140/90 to 130/80 mm Hg and proposed a more aggressive BP target of 130/80 mm Hg for hypertensive patients.[3] The European guidelines define "elevated BP" as an office SBP of 120 to 139 mm Hg or diastolic BP of 70 to 89 mm Hg, and "hypertension" as office SBP of ≥140 mm Hg or diastolic BP of ≥90 mm Hg.[4] In addition, it advocates an SBP target of 120 to 129 mm Hg among adults receiving BP-lowering medications.[4] However, the guideline accepts a more lenient BP target for selected cases caused by medication intolerance or some comorbidities, still recommending a BP target that is "as low as reasonably achievable."[4]

Poor guideline implementation remains a major challenge, contributing to suboptimal control of hypertension.[4] In the global INTERASPIRE (International Action on Secondary Prevention through Intervention to Reduce Events) study, only 38.5% of patients achieved normal BP <130/80 mm Hg, whereas 32.4% had BP ≥140/90 mm Hg.[5] However, even strict implementation of the current guidelines may not be enough. Simply achieving target BP levels may not be sufficient for full mitigation of hypertension-related risk. The net hypertension-related health risks depend on sustained longitudinal BP control, and are influenced by the previous duration of raised BP and ongoing BP fluctuations (ie. BP trajectories), which interact with age and sex.[6] Even childhood BP trajectories influence subclinical cardiovascular risk in adulthood.[6] In contrast, late-life BP decreased for 14 to 18 years before death in patients dying at age 60 years and older, with these BP decrease trajectories unattributable to age, hypertension treatment, or better survival without hypertension.[7] Sex differences matter for the impact of BP trajectories, with women being more sensitive to repeated BP deviations than men, starting early in life.[8] Upward long-term BP trajectories are associated with a greater risk of developing hypertension-related complications, such as AF, in women, compared with men.[9]

More recently, there has been a shift away from the focus on single BP measurements toward BP dynamics over time. Hence, the BP time-in-target range (TTR) concept has been proposed, and was found to allow better risk profiling of major adverse cardiovascular events.[10] Achieving high BP TTR lowered CVD risk and mortality in adults with hypertension and high cardiovascular risk,[10] as well as in those with heart failure.[11,12] In contrast, accumulated hypertension burden has also been associated with an increased risk of manifestations of hypertension-related target organ damage, such as dementia[13] and AF.[14]

In this issue of *JACC: Asia*, Han et al[15] investigated the time-in-target range of systolic blood pressure (SBP-TTR) between 120 and 140 mm Hg in

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9,552 participants of the community Kailuan. For every SD increase in SBP-TTR, there was a 19% reduction in the risk of CVD and a 24% reduction in premature CVD, as well as a 17% decrease in the risk of premature death. When an SBP target of 110 to 130 mm Hg was modelled, for a 1-SD increase in SBP-TTR, there was a 23% reduction in the risk of CVD and a 30% reduction in premature CVD, as well as a 27% decrease in the risk of premature death. Hence, Han et al[15] suggested that TTR could serve as a useful indicator of effective BP control, especially if seamlessly integrated into calibrated wearable BP measurement devices for widespread use in the general population.

The novel concept of SBP-TTR can be particularly attractive with the ongoing development of digital technologies and increasing routine use of electronic health records. The technologies can allow easy automated assessment for longitudinal profiling of hypertension management. There are multiple potential clinical benefits of such applications. For example, they may help identify suboptimal compliance with antihypertensive treatments and select patients who may need more vigorous overall BP reduction to accommodate its fluctuations. The approach may also allow is to move away from the emphasis on one-off measurements that may be inadequate due to suboptimal BP measuring techniques and measurements taking during acute illness. These possibilities will need to be explored in more detail in the future.

Some practical considerations are needed for clinical implementation of SBP-TTR. Besides SBP, extremely excessively low diastolic BP has been associated with increased adverse cardiovascular events (the so-called diastolic J-shape phenomenon).[16,17] Thus, an optimal diastolic BP target of between 70 and 80 mm Hg has been recommended according to the 2018 European Society of Cardiology (ESC)/European Society of Hypertension guidelines for patients with all risk levels,[18] and this level also applies to patients with treated SBP below 130 mm Hg.[19] Nevertheless, the 2024 new ESC guidelines define a diastolic BP of <70 mm Hg as non-elevated BP, but avoids terms like “normal BP,” “optimal BP,” or “normotension,” considering that the relative risk for CVD starts to increase at BP below this threshold (even as low as 90 mm Hg SBP).[4] Additionally, mean BP and pulse pressure (ie, difference between SBP and diastolic BP) have been associated with poor cardiovascular outcomes.[20,21] Thus, each pressure component (systolic, diastolic, mean pressure, and pulse pressure) should be further considered in terms of its optimum target. Diastolic BP and mean BP are not part of SBP-TTR, and further work is needed to whether and how their values can help even better definition of BP treatment targets.

Finally, hypertension-related risk is not static, but is dynamic in nature, changing over time. Similarly, one-off BP measurements are not reflective of the BP “load” on the body. Over 24 hours, ambulatory BP monitoring provides some indication of this “load.” Over time, assessment of hypertension burden using metrics such as SBP-TTR may prove a better indication of the impact of high BP and the risk of hypertension target organ damage. However, it remains unclear how often BP measurements should ideally be taken to maximize SBP-TTR precision, but without overburdening patients; what should be the optimal duration of SBP-TTR assessment periods; and how these could be affected by sex and ethnicity. These questions need to be answered to advance benefits of SBP-TTR into practice.

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