Hypertension and cardiovascular disease: Is a treatment strategy focused on high risk sufficient?

The epidemic of cardiovascular disease continues to explode. Cardiovascular disease now accounts for more than one-third of all deaths worldwide, creating a global health crisis that must be addressed.1 The epidemic is driven by lifestyle changes over the last few decades, including an increase in consumption of calorie and sodium dense foods and a decrease in physical activity. Growing trends of overweight and obesity are associated with rapidly rising prevalence rates for hypertension, diabetes, and dyslipidemia.2 Obviously, the best solution for the problem is a reversal of these lifestyle issues, which would lead to primordial prevention of these risk factors and cardiovascular disease. However, several decades after recognizing this, the trends are moving in the wrong direction. Around the globe, more countries are facing the growing epidemic of obesity and the associated disorders. Gaining control of the root cause of this epidemic will require more effort, including leadership from the scientific and medical communities, increased health education and literacy, and strong political and policy actions at the local, national, and global levels. What follows in this commentary can be considered a second best option (a temporizing measure) for addressing these issues while increasing attempts to educate people on the importance of improving diet and increasing physical activity.

As the rates of cardiovascular disease and its known risk factors continue to increase globally, in the US and other advanced economic countries, age-adjusted CVD death rates have improved over the last 2 to 3 decades.3 Most of the improvement has come from treating patients with the highest risk.4 The strategies that have lead to improved rates include the use of catheter based interventions such as angioplasty and thrombolytic therapy for acute events, including myocardial infarction and stroke, as well as better management of hypertension and dyslipidemia. However, in the US, progress has slowed in recent years. Cardiovascular disease remains the leading cause of death, and CVD mortality rates have started to plateau. These trends indicate we are likely approaching the limits of progress attainable through the existing treatment strategies.

Part of what has driven the strategy of focusing on high-risk patients is the reliance on evidence from randomized controlled event-based clinical trials (RCTs). Over the last few years, almost all guideline groups around the globe have moved from consensus-based to evidence-based guidelines, focusing on event-based randomized trials as the best form of evidence. The era of evidence-based medicine has certainly moved us forward in many ways. However, there may be a fly in the ointment when it comes to reliance on this strategy in terms of managing hypertension. For the population of patients at risk from hypertension, the current strategy leaves a large residual risk.

In countries with effective programs for hypertension control, much progress has been made in recent years. This progress is marked by better hypertension control rates and a decrease in the mean blood pressure for the population at large, leading to lower age-adjusted cardiovascular disease event and death rates.5 In the US, these changes have been associated with important changes in the relationship between blood pressure and cardiovascular events at the population level. In pooled data from 3 large observational studies performed in the 1980s and 1990s, most of the CV events occurred in patients with a BP ≥ 140/90. Pooled data from three studies from the 2000s reveal a majority of CV events occurring in patients with BP < 140/90 (Table).6

Data from both observational studies and meta-analyses of achieved BP in RCTs demonstrate a continuous relationship between BP and CVD risk beginning at a SBP of about 115 mm Hg.7 It has not been feasible to perform event-based RCTs in young patients who are at lower risk. All the evidence from RCTs pertaining to hypertension therapy and CVD risk is from older patients at higher total risk because this is the population easiest to study and demonstrate benefit. A significant portion of the residual risk is related to BP treatment goals that fall short of ideal physiologic BP levels.

The relationship between BP and CVD risk is continuous. It is important to note that in most countries, SBP trends with age and the increase in SBP with age is seen in all countries where weight also increases with age and the diet is sodium dense. It is important to note that this increase in BP with age is neither physiologic nor inevitable.8 Because BP tracks with age relative to other risk factors, BP levels in young adults not only predict future BP, but predict mortality risk as well9 (Figure 1). We also know that both lifestyle therapy and pharmacotherapy in patients with SBP 120 to 140 can attenuate the rise in BP with time.10,11 Though short of evidence from event based trials in young patients, the evidence is compelling that intervening on BP at lower levels and younger ages could attenuate the rise in BP and prevent cardiovascular events in middle and older age.

An important step in dealing with some of the residual risk from hypertension was taken with the 2017 ACC/AHA Blood Pressure Management Guidelines.12 The reduction in the treatment goal from a SBP of 140 to 130 mm Hg offers opportunities to further reduce risk. However, the 2017 guidelines call for use of pharmacotherapy in patients with a SBP 130 to 140 mm Hg only in those with a 10-year CVD risk ≥10%. Because of the lack of evidence from RCTs for lower risk patients, the guidelines suggest lifestyle therapy only for patients at lower 10-year risk. This is not from evidence that suggests there is no benefit, but from the lack of trials addressing the question.
These realities raise important questions. Will current strategies lead to an ideal reduction in CVD event and death rates? Are there opportunities to craft strategies that go beyond the evidence from RCTs, especially since it is unlikely that early treatment of patients at lower risk will be tested in the near future? Can we leverage the availability of inexpensive, effective, and relatively safe pharmacotherapy to address the issue of residual risk? And, while we are considering this, can we make more progress on the core lifestyle issues driving the epidemic?

It is unlikely that guideline groups will soon move away from reliance on evidence from randomized controlled trials for offering recommendations for management of hypertension. I am both a co-author and enthusiastic endorser of the 2017 ACC/AHA guidelines. But, I do offer suggestions for clinicians to consider that go beyond these recommendations based exclusively on evidence from RCTs. (1) Offer patients maximum opportunities for responding to lifestyle therapy, including advice from a dietician. (2) Consider the addition of pharmacotherapy to achieve goal BP, regardless of calculated 10-year risk in patients who do not achieve a SBP ≤ 130 mm Hg after 6 months of lifestyle therapy.2 (3) Consider the addition of pharmacotherapy in patients with a family history of premature CVD or hypertension, dyslipidemia, or diabetes mellitus, if a SBP ≤ 120 mm Hg is not achieved with lifestyle therapy. (4) Join the World Hypertension League in their efforts to bring about policy changes leading to a healthier food and physical activity environment in countries around the globe.

Implementation of these strategies could go a long way toward reducing the residual risk of hypertension in individual patients and the overall population, and move us closer to a goal of lowering CVD events around the globe.

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CONFLICT OF INTEREST

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| CVD event | 1980s-1990s (%) | 2000s (%) |
|-----------|----------------|-----------|
| Stroke    | 23             | 63        |
| CHD       | 31             | 63        |
| HF        | 26             | 60        |

CHD, coronary heart disease; CVD indicates cardiovascular disease; HF, heart failure.
REFERENCES
1. Roth GA, Johnson C, Abajobir A, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990-2015. J Am Coll Cardiol. 2017;70:1-25.
2. Yatsuya H, Li Y, Hilawe EH, et al. Global trend in overweight and obesity and its association with cardiovascular disease incidence. Circ J. 2014;78:2807-2818.
3. Sidney S, Quesenberry Jr CP, Jaffe MG, et al. Recent trends in cardiovascular mortality in the United States and public health goals. JAMA Cardiol. 2016;1:594-599.
4. Alagona Jr P, Ahmad TA. Cardiovascular disease risk assessment and prevention: current guidelines and limitations. Med Clin North Am. 2015;99:711-731.
5. Nwankwo T, Yoon SS, Burt V, Gu Q. Hypertension among adults in the United States: National Health and Nutritional Examination Survey, 2011-2012. NCHS Data Brief. 2013;133:1-8.
6. Tajue GS, Booth JN, Colantonio LD, et al. Incident cardiovascular disease among adults with blood pressure <140/90 mm Hg. Circulation. 2017;136:798-812.
7. Bundy JD, Li C, Stuchlik P, et al. Systolic blood pressure reduction and risk of cardiovascular disease and mortality; a systematic review and network meta-analysis. JAMA Cardiol. 2017;2:775-781.
8. Gurven M, Blackwell AD, Rodriguez DE, Stieglitz J, Kaplan H. Does blood pressure inevitably rise with age?: longitudinal evidence among forager-horticulturalists. Hypertension. 2012;60:25-33.
9. Zhang WB, Pincus Z. Predicting all-cause mortality from basic physiology in the Framingham Heart Study. Aging Cell. 2016;15:39-48.
10. Whelton PK, Buring J, Borhani NO, et al. The effect of potassium supplementation in persons with a high-normal blood pressure. Results from phase I of the Trials of Hypertension Prevention (TOHP) Collaborative Research Group. Ann Epidemiol. 1995;5:85-95.
11. Julius S, Kaciroti N, Egan BM, Nesbitt S, Michelson EL; Trial of Preventing Hypertension (TROPHY) Investigators. TROPHY study: outcomes based on the Seventh Report of the Joint National Committee on Hypertension definition of hypertension. J Am Soc Hypertens. 2008;2:39-43.
12. Whelton PK, Carey RM, Aronow WS, 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. 2018;71:1269-1324.