Hypertension Research (2019) 42:1644–1646
https://doi.org/10.1038/s41440-019-0286-7

COMMENT

Cardiovascular events associated with stage 1 hypertension in Asian populations: is this a more critical issue in younger adults?

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Received: 19 May 2019 / Revised: 24 May 2019 / Accepted: 25 May 2019 / Published online: 4 July 2019

The 2017 American College of Cardiology (ACC)/American Heart Association (AHA) blood pressure (BP) guidelines define an "elevated BP" as a clinic-measured systolic BP (SBP) of 120–129 mmHg and a diastolic BP (DBP) < 80 mmHg and "stage 1 hypertension" as a SBP of 130–139 mmHg or a DBP of 80–89 mmHg [1]. These new definitions lower the BP thresholds for hypertension from SBP/DBP ≥ 140/90 mmHg to SBP/DBP ≥ 130/80 mmHg [1]. Nonpharmacological and pharmacological interventions are recommended for adults with stage 1 hypertension, who also have an estimated 10-year atherosclerotic cardiovascular disease risk of 10% or higher. The guidelines recommend a BP treatment goal of <130/80 mmHg in almost all patients, except for older adults (≥ 65 years of age), with high comorbidity burdens and limited life expectancies. The rationale for these recommendations is based on data from observational studies that assessed the association between BP and cardiovascular disease (CVD) risk, randomized controlled trials (RCTs) using lifestyle modifications to lower BP, and RCTs treating patients with antihypertensive medication to prevent CVD. However, most of the data are based on studies in the US and European populations. Therefore, little is known regarding whether the BP classification in the 2017 ACC/AHA guidelines is generalizable to Asian populations for the management of BP. If stage 1 hypertension is not associated with CVD events in Asian populations, it suggests the possibility of the overdiagnosis of hypertension in this population, which could result in unnecessary treatment. In this issue of *Hypertension Research*, Ji et al. have provided evidence that CVD risk is associated with the BP classification in the 2017 ACC/AHA guidelines in Chinese populations [2].

Ji et al. used data from the Chinese Kailuan cohort that recruited adults 18–98 years of age who also had no history of CVD ($n = 97{,}126$; mean age 51 years; 20.4% women) [2]. The participants were employees, including retired workers, who underwent a health checkup in 2006–2007. Trained research staff measured BP two times in the brachial artery of each participant's left arm at 5-min intervals, after the participant had been sitting for 15 min, using a mercury sphygmomanometer. The mean of the two measurements was used for the analysis. The normal BP group included participants with SBP < 120 mmHg and DBP < 80 mmHg. The elevated BP group included participants with SBP 120–129 mmHg and DBP < 80 mmHg. The stage 1 hypertension group included participants with SBP 130–139 mmHg or DBP 80–89 mmHg. The stage 2 hypertension group included participants with SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, or the use of antihypertensive medication. The primary outcome was composite CVD events (fatal and nonfatal myocardial infarction and stroke). Contact was maintained with participants once every 2 years to follow up regarding these events, and outcomes were available through December 2016. Over a mean follow-up of 9.5 years, 5550 incident CVD events occurred (more than 70% were strokes). The CVD incidence rates in the normal BP, elevated BP, stage 1 hypertension, and stage 2 hypertension groups were 2.24, 3.93, 3.89, and 9.75 per 1000 person-years, respectively. After multivariable adjustment, hazard ratios for CVD events for the elevated BP, stage 1 hypertension, and stage 2 hypertension groups versus the normal BP group were 1.19 (95% confidence interval, 1.01, 1.42), 1.25 (1.11, 1.40), and 2.3 (2.07, 2.56), respectively. The hazard ratios for CVD events in each group were similar when 9598 participants using antihypertensive medication were excluded. In secondary analyses, CVD risk associated with changes in the BP classification from 2006–2007 to 2010–2011 was assessed among 20,922 participants with stage 1 hypertension in 2006–2007. Of the 20,922 participants, 15.1% were in the normal BP group in 2010–2011 (this group was defined as

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Table 1 Cardiovascular disease risk associated with stage 1 hypertension in the 2017 ACC/AHA blood pressure guidelines in Asian populations

Study	Population/study design	Stage 1 hypertension			
		Prevalence	Risk for composite CVD compared with normal BP	Risk for CHD compared with normal BP	Risk for stroke compared with normal BP
Chinese Multi-provincial Cohort Study [5]	Chinese (*n* = 21,441; mean ± standard deviation age 48.8 ± 8.8 years; women 48.5%; antihypertensive medication use in overall 8.3%; a median follow-up of 14.7 years)	25.8%	Adjusted HR, 1.70; 95% CI, 1.45, 1.99	Adjusted HR, 1.69; 95% CI, 1.31, 2.20	Adjusted HR, 1.73; 95% CI, 1.42, 2.11
Singapore Chinese Health Study [7]	Chinese (*n* = 30,636; mean ± standard deviation age 63.0 ± 7.8 years; women 55.7%; antihypertensive medication use in the stage 1 hypertension group 34.2%; a mean follow-up of 12.9 years)	23.5%	Adjusted HR, 0.94; 95% CI, 0.81, 1.11	Adjusted HR, 1.01; 95% CI, 0.82, 1.25	Adjusted HR, 0.87; 95% CI, 0.64, 1.19
Korean National Health Insurance Service [6]	Korean (*n* = 248,8101; mean age 31, interquartile range, 27–36 years; women 31.7%; antihypertensive medication use 0%; a mean follow-up of 10 years)	37.7%	Men: adjusted HR, 1.25; 95% CI, 1.21, 1.28 Women: adjusted HR, 1.27; 95% CI, 1.21, 1.34	Men: adjusted HR, 1.23; 95% CI, 1.19, 1.27 Women: adjusted HR, 1.16; 95% CI, 1.08, 1.25	Men: adjusted HR, 1.30; 95% CI, 1.25, 1.36 Women: adjusted HR, 1.37; 95% CI, 1.29, 1.46

ACC/AHA American College of Cardiology/American Heart Association, *HR* hazard ratio, *CI* confidence interval, *JACC* Journal of the American College of Cardiology, *JAHA* Journal of the American Heart Association, *JAMA* Journal of the American Medical Association

In the Chinese Multi-provincial Cohort Study and the Korean National Health Insurance Service, stage 1 hypertension was defined as untreated systolic blood pressure (SBP) of 130–139 mmHg or untreated diastolic blood pressure (DBP) of 80–89 mmHg, and normal BP as untreated SBP < 120 mmHg and untreated DBP < 80 mmHg. The outcomes included incident cardiovascular disease (CVD), coronary heart disease (CHD), or stroke events. In the Singapore Chinese Health Study, stage 1 hypertension was defined as untreated/treated SBP of 130–139 mmHg or untreated/treated DBP of 80–89 mmHg, and normal BP as untreated/treated SBP < 120 mmHg and untreated/treated DBP < 80 mmHg. The outcomes included CVD, CHD, or stroke mortality

the reference group in the secondary analyses), 5.5% in the elevated BP group, 43.1% in the stage 1 hypertension group, and 36.3% in the stage 2 hypertension group. In an adjusted model comparing the normal BP group in 2010–2011, stage 1 and 2 hypertension in 2010–2011 were each associated with a significantly higher risk of CVD events (HR, 1.77; 95% CI, 1.16, 2.71 and HR, 3.02; 95% CI, 1.99, 4.58, respectively).

Table 1 shows the studies in Asian populations that have assessed the CVD risk associated with stage 1 hypertension, as defined in the 2017 ACC/AHA guidelines. Ji et al. have extended the previous knowledge by demonstrating the association in a Chinese population. In the Ji et al. study, participants with stage 1 hypertension in both 2006–2007 and 2010–2011 were at a higher risk for CVD events compared with those with stage 1 hypertension in 2006–2007 who, however, had nonhypertensive BP measurements in 2010–2011. The Ji et al. study has two limitations. First, the 2017 ACC/AHA guidelines recommend that two or more BP readings be obtained before classifying a person's BP. However, in the primary analyses of the Ji et al. study, participants' BP classification was determined after only a single measurement; thus, there may have been misclassification of participants. Second, the mechanisms underlying the changes in participants' BP levels from 2006–2007 to 2010–2011 were unknown. It remains to be determined whether the observed reductions in BP from 2006–2007 to 2010–2011 were due to nonpharmacological and/or pharmacological interventions.

In Asian populations, compared with older adults, younger adults have an increased prevalence of hypertension due to the lowering of BP thresholds for hypertension from SBP/DBP ≥ 140/90 mmHg to SBP/DBP ≥ 130/80 mmHg [3, 4]. The CVD risk associated with stage 1 hypertension has been consistent in younger adults, but inconsistent in older adults in Asian populations [5–7]. Consequently, the population-attributable risk (PAR) related to stage 1 hypertension is higher in younger adults than in older adults. For example, the PAR related to stage 1 hypertension for CVD events in China was 14% in adults aged 35–44 years versus just 1.8% in those aged ≥ 60 years [5]. Young adults with stage 1 hypertension have a higher cumulative exposure to elevated BP from young adulthood to midlife and old age, which may lead to an increased lifetime risk for CVD events. In the Ji et al. study, the hazard ratio associated with stage 1 hypertension for stroke events was higher than that for coronary events. Emerging evidence suggests that the incidence of ischemic stroke has substantially increased in young adults [8]. Young adults who have had a stroke can have a long life expectancy afterward, and the costs of long-term care can impose major burdens on their families and healthcare systems. Therefore,

there is a pressing unmet need to conduct RCTs to determine if a treatment benefit can be achieved in young adults with stage 1 hypertension in Asian populations [9]. Because of the consequent amount of time that must pass in order to accumulate a sufficient number of CVD events, studies in young adults evaluating subclinical CVD markers (e.g., left ventricular hypertrophy, coronary artery calcification) as outcomes would be an initial step toward providing evidence that pharmacological treatments are appropriate for young adults with hypertension [10]. Pharmacological treatment in all young adults with stage 1 hypertension over a lifetime may be impractical and costly. Researchers need to identify the subgroups of young adults with stage 1 hypertension (e.g., those with a high lifetime risk for CVD) who are most likely to benefit from treatment. Furthermore, considering that young adults with hypertension will require a lifetime of care for this chronic disease, studies are also needed to determine the optimal self-management strategies, including emotional and behavioral supports using m-Health (mobile health) and telemedicine.

Compliance with ethical standards

Conflict of interest Dr. Yano has no relationships relevant to the content of this paper to disclose.

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