Association between blood pressure levels and cardiovascular deaths: a 20-year follow-up study in rural China

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ABSTRACT

Objectives The 2017 American College of Cardiology/American Heart Association (ACC/AHA) hypertension guideline recommended 130/80 mm Hg as blood pressure (BP) target goals. However, the generalisability of this recommendation to populations at large with hypertension remains controversial. We assessed the association between BP and cardiovascular diseases (CVDs) mortality using a 20-year follow-up study among Chinese populations.

Design Prospective cohort study.

Participants 7314 participants were followed up for a median of 20 years in Fangshan District, Beijing, China.

Methods The primary outcome variable was death from cardiovascular causes. The adjusted HR for CVDs mortality associated with baseline BP was calculated using Cox regression analysis.

Results We identified 350 deaths from CVDs (148 stroke, 113 coronary heart disease and 89 other CVDs) during follow-up. Hypertension (defined by systolic BP (SBP)/diastolic BP (DBP) ≥140/90 mm Hg) was significantly associated with mortality due to CVDs (HR=2.49, 95% CI=1.77 to 3.50) among people aged 35–59 years rather than people aged ≥60 years. In addition, there was no significant association between stage 1 hypertension defined by the 2017 ACC/AHA (SBP/DBP of 130–139/80–89 mm Hg) and CVDs mortality when compared with SBP/DBP of <120/80 in neither the participants aged <60 years (HR=0.90, 95% CI=0.54 to 1.50) nor participants aged ≥60 years (HR=1.47, 95% CI=0.94 to 2.29).

Conclusion The study revealed hypertension of SBP/DBP≥140/90 mm Hg was an important risk factor of CVDs mortality, especially among people aged 35–59 years. However, stage 1 hypertension under the definition of 2017 ACC/AHA was not associated with an increased risk of CVDs mortality. This study indicated that whether adopting the new hypertension definition needs further consideration in rural Chinese populations.

INTRODUCTION

Hypertension is the first risk factor of cardiovascular diseases (CVDs), accounted for 7.8 million deaths and 148 million disability life years lost worldwide in 2015.1 It has been reported that hypertension affected nearly 30% of the adult population in Western countries as well as in China.2,3 The management of high blood pressure is a public health priority with implications for the prevention of CVDs.4,5 However, the optimal blood pressure, particularly for systolic blood pressure (SBP) treatment target is unclear worldwide. The 2017 American College of Cardiology/American Heart Association (ACC/AHA) Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults recommended 130/80 mm Hg as blood pressure target goals.6 However, the definition of hypertension remains ≥140/90 mm Hg in the European guideline.7

The Systolic Blood Pressure Intervention Trial (SPRINT) demonstrated intensive SBP lowering in adults without diabetes or stroke could result in significant decreases in cardiovascular events and all-cause mortality.8 A network meta-analysis conducted by Bundy et al also suggested that a more intensive
treatment target (eg, SBP of 120–124 mm Hg) showed improvement in the prevention of CVD complications and total mortality when compared with a standard SBP target (<140 mm Hg). However, the generalisability of SPRINT findings to populations at large with hypertension remains controversial. For example, a recent study showed that the treatment to achieve a target SBP of 110–139 mm Hg did not result in a lower rate of death than standard reduction to a target of 140–179 mm Hg in patients with hypertension with intracerebral haemorrhage.

Here, we aimed to assess the relative risk of CVDs mortality associated with different stages of hypertension according to 2017 ACC/AHA using a 20-year follow-up study in China, to further evaluate the generalisability of SPRINT findings and explore the target blood pressure levels among Chinese populations.

**METHODS**

**Study design**

The participants for these analyses came from a community-based follow-up study for the prevention and treatment of hypertension, which is being conducted in Fangshan District, Beijing, China. Verbal informed consent was obtained from all participants.

**Inclusion and exclusion of the participants**

From January 1997 through June 1999, 8189 participants aged 35–97 years were enrolled. We excluded 669 individuals with CVDs at baseline. In addition, we dropped the participants if any of the key variables required in the analysis (blood pressure, height, weight, demographic variables or potential risk factors including smoking, alcohol consumption or high salt intake) were missing. Finally, a total of 7314 participants (3346 males and 3968 females) were included in the analysis.

**Outcomes variables**

The primary outcome variable was death from CVDs. The information on death was continuously obtained from the Death Surveillance System in the Center for Disease Prevention and Control in Fangshan District. The date of death was ascertained from the record in the system. We determined survival times from the date participants investigated in the baseline survey through 31 December 2017. Participants who were alive at the end of this period contributed with censored observations to the survival analyses of time to death. The causes of death were coded using the International Classification of Diseases, Ninth Revision codes from 1997 to 2001, and International Classification of Diseases, Tenth Revision codes from 2002 to 2017.

**Data collection**

The primary exposure variables for these analyses included age at the enrolment and the blood pressure level at baseline. Data on sociodemographic characteristics, lifestyles and medical history of the participants were collected by questionnaire interviews by trained staff members.

Participants were defined as never smokers, former smokers and current smokers. Information on alcohol consumption was obtained through asking the participants to describe their drinking status: never, light (<two drinks a day) or heavy (≥two drinks a day). Furthermore, the salt intake of the participants was assessed according to the question of what kind of taste they liked (salty taste, moderate or light taste).

Physical measurements included height, weight and blood pressure. Blood pressure levels were measured three times using a mercury sphygmomanometer by trained investigators. The mean of the three recorded measurements was included in the analysis.

Hypertension was defined as SBP ≥140 mm Hg, diastolic blood pressure (DBP) ≥90 mm Hg, self-reported antihypertensive medication in the past 2 weeks or a self-reported history of hypertension. In addition, according to the 2017 ACC/AHA guidelines, the participants were divided into four categories: normal blood pressure (SBP<120 mm Hg and DBP<80 mm Hg), elevated blood pressure (120 mm Hg≤SBP<129 mm Hg and DBP<80 mm Hg), stage 1 hypertension (130 mm Hg≤SBP≤139 mm Hg or 80≤DBP<89 mm Hg), and stage 2 hypertension (SBP≥140 mm Hg/DBP≥90 mm Hg or taking antihypertensive medications).

**Statistical analysis**

Student’s t-test and χ² tests were used to test the differences between different baseline hypertensive history groups for continuous variables and categorical variables, respectively.

Person-years for each participant were calculated as the duration from the survey date at baseline through death date or date lost to follow-up, whichever came first. The Cox proportional hazards regression model for CVDs death included baseline blood pressure level, age, sex, education level, body mass index, smoking status, alcohol use, dietary salt intake, antihypertensive medications and family history of hypertension. Participants were classified as two groups according to baseline hypertensive status, and non-hypertension (<140/90 mm Hg) was treated as the reference. To test for possible interactions between age and hypertension, we categorised age with cutoffs of 60 years and hypertension as binary variables, and setting variable cross-product terms of hypertension (yes/no) with age (<60 and ≥60 years) in the model. Reference groups were SBP/DBP <140/90 mm Hg and age <60 years. We also performed a subgroup analysis according to baseline blood pressure levels (SBP/DBP: <120/<80, 120–129/<80, 130–139/80–89, 140–159/90–99 and ≥160/≥100 mm Hg), where SBP/DBP of <120/<80 was treated as the reference group.

All analyses were performed using R software (V.3.5.1). All p values for the tests were two-sided and p values <0.05 were considered as statistically significant.
RESULTS

Of the 7314 participants (aged 50.65±11.8 years), the prevalence of hypertension was 30.02%. According to the 2017 ACC/AHA guideline, the prevalence of hypertension was 58.96%. The proportion of people aged 60 years and above was higher in patients with hypertension (36.75%) when compared with participants without hypertension (19.05%, p<0.001). In addition, patients with hypertension were less educated than participants without hypertension (p<0.001). Moreover, there were more participants with tobacco smoking (49.27% vs 44.92%) and alcohol consumption (31.74% vs 30.15%) among patients with hypertension when compared with participants without hypertension. Furthermore, the percentage of obesity was higher among patients with hypertension when compared with participants without hypertension (p<0.001) (table 1).

During the median follow-up of 20 years, we have identified 609 deaths, of which 350 deaths were from CVDs (148 stroke, 113 coronary heart disease and 89 other CVDs). In the multivariable model adjusting for age, sex, educational level, smoking, alcohol consumption, dietary salt intake, body mass index (BMI), use of antihypertensive medications and family history of hypertension, we detected statistically significant association between hypertension and mortality from CVDs (HR=1.35; 95% CI 1.08 to 1.69). In the subgroup analysis based on baseline age, we found that, for people aged 35–59 years, patients with hypertension had a higher risk of mortality from CVDs when compared with those without hypertension (HR=2.49; 95% CI 1.77 to 3.50) (table 2). However, there was no significant association between hypertension and mortality due to CVDs among people aged 60 years and over (p>0.05) (table 2). Thus, age may significantly modify the association between hypertension and mortality from CVDs (p for interaction <0.001). We also assessed the association between hypertension and all-cause, coronary heart disease and stroke mortality (online supplementary table 1).

Stratified analysis according to different baseline blood pressure showed that patients with hypertension with SBP/DBP of 140–159/90–99 and ≥160/100 mm Hg were more likely to die of CVDs (HR=1.44; 95% CI 1.02 to 2.03; HR=1.74; 95% CI 1.22 to 2.48) when compared with participants with SBP/DBP of <120/80 mm Hg. However, we failed to detect significant associations between SBP/DBP of 130–139/80–89 mm Hg (HR=1.18; 95% CI 0.85 to 1.64, p=0.32) and 120–129/<80 mm Hg (HR=1.38; 95% CI 0.93 to 2.05, p=0.11) and mortality from CVDs, respectively. Furthermore, among participants aged <60 years at baseline, a similar trend was observed between hypertension and mortality due to CVDs, where HR was 2.32 (p<0.001) for SBP/DBP of 140–159/90–99 mm Hg and 3.25 (p<0.001) for ≥160/100 mm Hg, respectively.

However, there was no significant association between hypertension and mortality from CVDs with different baseline blood pressure levels for those aged ≥60 years (p for interaction <0.001) (table 3).

DISCUSSION

The present 20-year prospective study filled the gaps for implying the generalisability of the 2017 ACC/AHA hypertension guideline to rural Chinese populations. The results showed there was no significant association between stage 1 hypertension defined by the 2017 ACC/AHA and CVDs mortality when compared with SBP/DBP of <120/80 mm Hg. In addition, we detected high blood pressure was associated with higher mortality from CVDs among people aged 35–59 years rather than those aged 60 years and over. The findings may contribute to the optimal management of hypertension to address the...
Table 2. Multivariable HRs of mortality from CVDs according to baseline history of hypertension

| CVDs mortality | N   | Deaths | Adjusted HR (95% CI) | P value |
|----------------|-----|--------|----------------------|---------|
| Total          |     |        |                      |         |
| Baseline hypertension status |     |        |                      |         |
| No             | 5118 | 189    | Reference            |         |
| Yes            | 2196 | 161    | 1.35 (1.08 to 1.69)  | 0.01    |
| Age <60 years  |     |        |                      |         |
| Baseline hypertension status |     |        |                      |         |
| No             | 4143 | 80     | Reference            |         |
| Yes            | 1389 | 64     | 2.49 (1.77 to 3.50)  | <0.001  |
| Age ≥60 years  |     |        |                      |         |
| Baseline hypertension status |     |        |                      |         |
| No             | 975  | 109    | Reference            |         |
| Yes            | 807  | 97     | 1.01 (0.76 to 1.33)  | 0.96    |

Table 3. Multivariable HRs of mortality from CVDs according to baseline blood pressure levels

| CVDs mortality | N   | Deaths | Adjusted HR (95% CI) | P value |
|----------------|-----|--------|----------------------|---------|
| Total          |     |        |                      |         |
| <120/80 mm Hg  | 2132| 61     | Reference            |         |
| 120–129/<80 mm Hg | 920 | 43    | 1.38 (0.93 to 2.05)  | 0.11    |
| 130–139/80–89 mm Hg | 2180 | 91   | 1.18 (0.85 to 1.64)  | 0.32    |
| 140–159/90–99 mm Hg | 1239 | 80   | 1.44 (1.02 to 2.03)  | 0.04    |
| ≥160/100 mm Hg  | 843 | 75     | 1.74 (1.22 to 2.48)  | <0.01   |
| Age <60 years  |     |        |                      |         |
| <120/80 mm Hg  | 1813| 32     | Reference            |         |
| 120–129/<80 mm Hg | 727 | 21    | 1.46 (0.84 to 2.55)  | 0.18    |
| 130–139/80–89 mm Hg | 1691 | 29   | 0.90 (0.54 to 1.50)  | 0.70    |
| 140–159/90–99 mm Hg | 818  | 34   | 2.31 (1.41 to 3.79)  | <0.001  |
| ≥160/100 mm Hg  | 483 | 28     | 3.25 (1.92 to 5.50)  | <0.001  |
| Age ≥60 years  |     |        |                      |         |
| <120/80 mm Hg  | 319 | 29     | Reference            |         |
| 120–129/<80 mm Hg | 193 | 22    | 1.28 (0.74 to 2.24)  | 0.38    |
| 130–139/80–89 mm Hg | 489 | 62   | 1.47 (0.94 to 2.29)  | 0.09    |
| 140–159/90–99 mm Hg | 421  | 46   | 1.16 (0.72 to 1.85)  | 0.55    |
| ≥160/100 mm Hg  | 360 | 47     | 1.41 (0.88 to 2.26)  | 0.16    |

Growing burden of CVDs morbidity and mortality among rural Chinese populations, suggesting a large implication both to clinicians and public health practitioners.

In the current study, we first examined the association between hypertension of ≥140/90 mm Hg and mortality from CVDs. The result showed a higher risk of mortality from CVDs in patients with hypertension when compared with participants without hypertension (HR=1.35), which was comparable with previous studies.4 14–16 Furthermore, the stratified analysis according to age groups showed that the associations between hypertension and CVDs mortality were stronger among participants aged 35–59 years than those aged 60 years and above. A previous study also showed the association was significant in the age groups of 35–44 and 45–59 years rather than in the group of ≥60 years.12 Besides, a study based on pooling data from seven diverse US cohort studies showed that individuals who experienced blood pressure increases prior to middle age have associated higher remaining lifetime risk for CVDs when compared with those who had developed hypertension later in age 55 years.17 Similarly, a previous meta-analysis of 13 prospective cohort studies involving 396 200 participants showed that prehypertension was not associated with CVDs risk among older populations with age ≥60 years.18 It is reported that the cardiovascular risk for patients with hypertension decreased as the age of onset increased from 40 to 69 years.19 Possible explanations for the age-specific association between hypertension and mortality from CVDs needs further studies to explore. In addition, it is important to consider the influence of age in the diagnosis of hypertension.

In clinical practice, the staging of hypertension defined by SBP and DBP corresponds with the graded increased risk of cardiovascular disease and events and is in relation to pathophysiological mechanisms, prognostic implications and therapeutic approaches.20–22 For example, the initiation of pharmacological therapy is recommended for adults with stage 2 hypertension.22 ACC/AHA Task Force on Clinical Practice Guidelines released the 2017 hypertension guideline, which defined SBP of 130–139 mm Hg or DBP of 80–89 mm Hg as stage 1 hypertension supported by the evidence from SPRINT.6 8 Based on the new criterion, the prevalence of hypertension would increase substantially in many countries.23–25 Although intensive blood pressure control was beneficial to cardiovascular events and total mortality, it was associated with an increased number of newly diagnosed patients with hypertension who may not develop CVD events in the future.23 In particular, with a large ageing population, there was a high prevalence of hypertension in China.26–28 It is estimated that 2.33 million cardiovascular deaths were attributable to increased blood pressure in China.14 Furthermore, contrary to western countries that...
CVD mortality has decreased significantly during the past years, CVD mortality has increased during the same period in China.3-5 Thus, whether the results of SPRINT apply to rural Chinese populations is a critical question to answer among Chinese populations.

In the current analysis by different blood pressure levels at baseline, the HR of CVDs mortality related to stage 1 hypertension defined by the 2017 ACC/AHA hypertension guideline (130–139/80–89 mm Hg) was not statistically higher than that related to SBP/DBP of <120/<80 mm Hg. Previous studies have demonstrated diagnosed patients with hypertension tended to prescribe antihypertensive medications despite the lifestyle modifications patients with hypertension under the definition of smoking, alcohol consumption, salt intake and the use of antihypertensive drugs was relatively simple due to limited information in the baseline questionnaire. Second, hypertension was defined by SBP/DBP at baseline while we failed to acquire blood pressure measurements during follow-up, which may underestimate the strength of the associations we observed. Next, we had an insufficient sample size to explore whether the effects of hypertension on CVDs mortality differ by baseline comorbidities including diabetes or chronic kidney disease. In addition, information of death was obtained from the Death Surveillance System, the participants lost to follow-up were hard to detect and may cause potential bias. Therefore, further studies with a larger sample size are needed to validate the results in the study. More importantly, our study only included participants in rural China, which might limit the generalisability of the results to other populations with different socioeconomic status, environmental exposures or genetic background.

**Limitations of the study**

Nevertheless, the study has several limitations. First, we cannot exclude the influence of some potential confounding factors despite the fact that we conducted the analysis with careful adjustment. In particular, the definition of smoking, alcohol consumption, salt intake and the use of antihypertensive drugs was relatively simple due to limited information in the baseline questionnaire. Second, hypertension was defined by SBP/DBP at baseline while we failed to acquire blood pressure measurements during follow-up, which may underestimate the strength of the associations we observed. Next, we had an insufficient sample size to explore whether the effects of hypertension on CVDs mortality differ by baseline comorbidities including diabetes or chronic kidney disease. In addition, information of death was obtained from the Death Surveillance System, the participants lost to follow-up were hard to detect and may cause potential bias. Therefore, further studies with a larger sample size are needed to validate the results in the study. More importantly, our study only included participants in rural China, which might limit the generalisability of the results to other populations with different socioeconomic status, environmental exposures or genetic background.

**CONCLUSION**

In conclusion, the current study revealed hypertension of ≥140/90 mm Hg was an important risk factor of CVDs mortality, especially among people aged 35–59 years. However, stage 1 hypertension under the definition of 2017 ACC/AHA was not associated with an increased risk of CVDs mortality. This study indicated that adopting the new hypertension definition needs further consideration among rural Chinese populations.

**Contributors** MW, TW and Y-HH conceived and designed the paper. L-ML, WC, JL, YW, XQ, XT, QZ, SH, SZ, Y-HH, TW and DY coordinated the data acquisition and contributed to critical revision of the manuscript for important intellectual content. MW, PG, WG and CY analysed the data. MW and TW drafted the manuscript. MW, TW, LL and Y-HH were responsible for the overall content of article and data analysis. The manuscript is approved by all authors for publication.

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**Competing interests** None declared.

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information. All data relevant to the study are included in the article.

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REFERENCES

1. Forouzanfar MH, Liu P, Roth GA, et al. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990-2015. JAMA 2017;317:165–82.

2. Mills KT, Bundy JD, Kelly TN, et al. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. Circulation 2016;134:411–50.

3. Lewington S, Lacey B, Clarke R, et al. The burden of hypertension and associated risk for cardiovascular mortality in China. JAMA Intern Med 2016;176:824–32.

4. Blood Pressure Lowering Treatment Trialists’ Collaboration. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. Lancet 2014;384:591–8.

5. Kølle SS, Dyer RA, Li W, et al. A public health approach to global management of hypertension. Lancet 2015;385:825–7.

6. Whelton PK, Carey RM, Aronow WS, et al. Impact of baseline prehypertension and systolic blood pressure change during middle age on the remaining lifetime risk of cardiovascular disease: the cardiovascular lifetime risk pooling project. Circulation 2012;125:37–44.

7. Wang S, Wu H, Zhang Q, et al. Impact of baseline prehypertension on cardiovascular events and all-cause mortality in the general population: a meta-analysis of prospective cohort studies. Int J Cardiol 2013;168:4857–60.

8. Buck C, Baker P, Bass M, et al. The prognosis of hypertension according to age at onset. Hypertension 1987;9:204–8.

9. Rapsomaniki E, Timmis A, George J, et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1.25 million people. Lancet 2014;383:1699–911.

10. Kulenthiran S, Ewen S, Böhm M, et al. Status of hypertension in China: recent findings and lessons from the sixth national population census of the People’s Republic of China. Lancet 2018;7:e008888.

11. National Bureau of Statistics of the People’s Republic of China. The sixth national population census of the People’s Republic of China, 2010. Available: http://www.stats.gov.cn/tjsj/pcsj/rkpc6/rkpc6index.pdf [Accessed 5 Dec 2018].

12. Lu J, Lu Y, Wang X, et al. Prevalence, awareness, treatment, and control of hypertension in China: data from 1·7 million adults in a population-based screening study (China peace millions persons project). Lancet 2017;390:2549–58.

13. Wang JG, Liu L. Global impact of 2017 American College of Cardiology/American heart association (ACC/AHA) guideline. J Am Heart Assoc 2018;7:e008888.

14. Wang Z, Chen Z, Zhao L, et al. Status of hypertension in China: results from a nationwide population-based survey of 0.5 million people. J Hum Hypertens 2018;32:608–16.

15. Bakris G, Sorrentino M. Redefining hypertension: assessing the new 2017 American College of Cardiology/American heart association guidelines. JAMA Cardiol 2017;3:124–8.

16. Williams B, Mancia G, Spiering W, et al. ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J 2018;39:2011–104.

17. Wright JT, Williamson JD, Whelton PK, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015;373:2103–16.

18. 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;2:775–81.

19. Kølle SS, Dyer RA, Li W, et al. Impact of baseline prehypertension and systolic blood pressure change during middle age on the remaining lifetime risk of cardiovascular disease: the cardiovascular lifetime risk pooling project. Circulation 2012;125:37–44.

20. Allen N, Berry JD, Ning H, et al. Impact of blood pressure and blood pressure change during middle age on the remaining lifetime risk for cardiovascular disease: the cardiovascular lifetime risk pooling project. Circulation 2012;125:37–44.

21. Wang S, Wu H, Zhang Q, et al. Impact of baseline prehypertension on cardiovascular events and all-cause mortality in the general population: a meta-analysis of prospective cohort studies. Int J Cardiol 2013;168:4857–60.

22. Buckley C, Baker P, Bass M, et al. The prognosis of hypertension according to age at onset. Hypertension 1987;9:204–8.

23. Wang M, et al. BMJ Open 2020;10:e035190. doi:10.1136/bmjopen-2019-035190