Received: 31 December 2020 | Revised: 27 January 2021 | Accepted: 3 February 2021

DOI: 10.1111/jch.14225

ORIGINAL PAPER

WILEY

Blood pressure and long-term subclinical cardiovascular outcomes in low-risk young adults: Insights from Hanzhong adolescent hypertension cohort

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Funding information
This work was supported by the National Natural Science Foundation of China No. 81870319 and No. 81700368 (CC), National Key R&D Program of China (2016YFC1300100); Grant 2017YFC1307604 from the Major Chronic Non-communicable Disease Prevention and Control Research Key Project of the Ministry of Science and Technology of the People's Republic of China; Grant 2017ZDXM-SF-107 from the Key Research Project of Shaanxi Province, and Clinical Research Award of the First Affiliated Hospital of Xi'an Jiaotong University, China(No. XJTU1AF-CRF-2019-004).

Abstract

Stage 1 hypertension, newly defined by the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) hypertension guideline, has been the subject of significant interest globally. This study aims to assess the impact of the new blood pressure (BP) stratum on subsequent subclinical cardiovascular outcomes in low-risk young adults. This longitudinal study consisted of 1020 young adults (47.7% female; ages 18–23 years) free of cardiovascular disease from the Hanzhong Adolescent Hypertension Cohort with up to 25-year follow-up since 1992–1995. Outcomes were available through June 2017. Young adults with stage 1 hypertension accounted for 23.7% of the cohort. When it comes to middle adulthood, subjects with early life stage 1 hypertension were more likely to experience BP progression, and they had a 1.61-fold increased risk of high-risk brachial-ankle pulse wave velocity (baPWV) and a 2.92-fold risk of left ventricular hypertrophy (LVH) comparing with their normotensive counterparts. Among participants without any active treatment in midlife, the risk associated with stage 1 hypertension for BP progression was 2.25 (95% confidence interval [CI] = 1.41–3.59), high-risk baPWV was 1.58 (95% CI = 1.09–2.79), LVH was 2.75 (95% CI = 1.16–6.48), and subclinical renal damage (SRD) was 1.69 (95% CI = 1.02–2.82) compared with the normal BP group. Overall, young adults with stage 1 hypertension had significantly higher risks for midlife subclinical cardiovascular outcomes than normotensive subjects. BP management targeting low-risk young adults is of importance from both clinical and public health perspectives.

1 | INTRODUCTION

Hypertension represents a public health crisis worldwide and is the most common preventable risk factor for all-cause morbidity and mortality. [1-4] Elevated blood pressure (BP) causes insidious multi-organ injuries that take place long before any awareness and contributes to cardiovascular disease (CVD).[5-10] Although the detrimental impact of hypertension has been well established, most studies focus on high-risk populations or older people, whereas the evidence for young adults, those who were traditionally considered as the low-risk population, is still limited.[11,12] However, the awareness and management levels of hypertension are low in the young, which now becomes a significant concern as elevated BP in early life could increase CVD risk in their later life.[11,13-16]

In 2017, an updated guideline was given by the American College of Cardiology (ACC)/ American Heart Association (AHA), recommending the BP thresholds for hypertension shifting from systolic BP (SBP)/diastolic BP (DBP) of 140/90 mm Hg to 130/80 mm Hg.[17] This lower threshold for hypertension directly implicated the estimates of the association between BP categories and CVD and subclinical CVD risk.[18-20] However, the evidence is also mainly based on studies among older people, and in the limited number of studies among young adults, evidence from the Chinese population is lacking.[11,21-27] It is uncertain to what extent this new BP stratum affects subclinical cardiovascular risk in the young population in China.

The current study, utilizing data from the Hanzhong Adolescent Hypertension Cohort, aims to examine the risk of subclinical cardiovascular outcomes associated with BP categories on the bias of 2017 ACC/AHA guidelines in Chinese young adults.

2 | METHOD

2.1 | Study sample

The Hanzhong Adolescent Hypertension Cohort was established in 1987 when 4623 schoolchildren aged 6 to 15 years were enrolled from three rural towns in Hanzhong, Shaanxi, China, focusing on the natural development of cardiovascular risk factors. Detailed study design and procedures (Figure S1) have been published elsewhere. [9,10,28] For the present investigation, participants attending at least one examination during their early adulthood (1992–1995) were eligible. Among a total of 4131 participants with available data, we excluded those who were under 18 years (n = 2699), had diabetes, dyslipidemia, or use of antihypertension treatment (n = 22), remaining 1410 participants comprising our baseline sample. The assessment of subclinical CVD outcomes was performed at the most recent examination (2017), including brachial-ankle pulse wave velocity (baPWV), carotid intima-media thickness (cIMT), electrocardiograph (ECG), and biochemical examinations. Participants missing 2017 measurements were also excluded (n = 390), leaving 1020 participants included in the analysis (Figure 1).

This study was supported and approved by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University (Reference number: XJTU1AF2015LSL-047) and was clinically registered (Reference number: NCT02734472, date of registration: 12/04/2016). Written informed consent was obtained from each participant.

2.2 | BP measurement and classification

Standardized protocols were used to measure SBP and DBP at each visit. Participants were required to avoid coffee/tea, alcohol, cigarette smoking, and strenuous exercise for at least 30 minutes before the measurements. Trained staff repeated three BP measurements on the right arm with the participant in a relaxed sitting position after a 5-minute rest and at 2-minute intervals. The mean value from the three readings was used for analysis. SBP and DBP were recorded using a mercury sphygmomanometer at baseline and an Omron M6 (Omron, Kyoto, Japan) device for the last follow-up in 2017. [29,30] Participants were stratified by baseline SBP/DBP category: normal BP (<120/<80 mm Hg), elevated BP (120 to 129/<80 mm Hg), stage 1 hypertension (130 to 139 or 80 to 89 mmHg), and stage 2 hypertension (≥140 or ≥ 90 mm Hg).[18,27,31]

2.3 | Definition of midlife subclinical cardiovascular outcomes

Midlife subclinical CVD outcomes tracked in this study, including traditionally defined hypertension, high-risk baPWV, high-risk cIMT, left ventricular hypertrophy (LVH), and subclinical renal damage (SRD), were assessed in 2017 using standard cutoffs. Traditionally defined hypertension was classified according to the current Chinese hypertension guideline as having an SBP of ≥ 140 mmHg or DBP of ≥ 90 mmHg or currently using antihypertension medications.[32] High-risk baPWV and high-risk cIMT were defined as values at or above the age and sex-specific 90th percentile.[33,34] LVH was defined as the product of QRS duration times the Cornell voltage combination (RaVL + SV3, with 8 mm added in women) >2440 mm/ms[33] SRD was defined as an estimated glomerular filtration rate (eGFR) between 30 and 60 mL/min per 1.73 m^2 and/ or a urinary albumin-to-creatinine ratio (uACR) of at least 2.5 mg/mmol in men and 3.5 mg/mmol in women.[10,35,36] A detailed description of the measurements for baPWV, cIMT, LVH, and biochemical assays is presented in Supplementary Methods.

2.4 | General examination

Data on demographic characteristics, occupation, married status, education levels, use of medicines, cigarette smoking, alcohol intake, and family history were collected using a standard questionnaire.

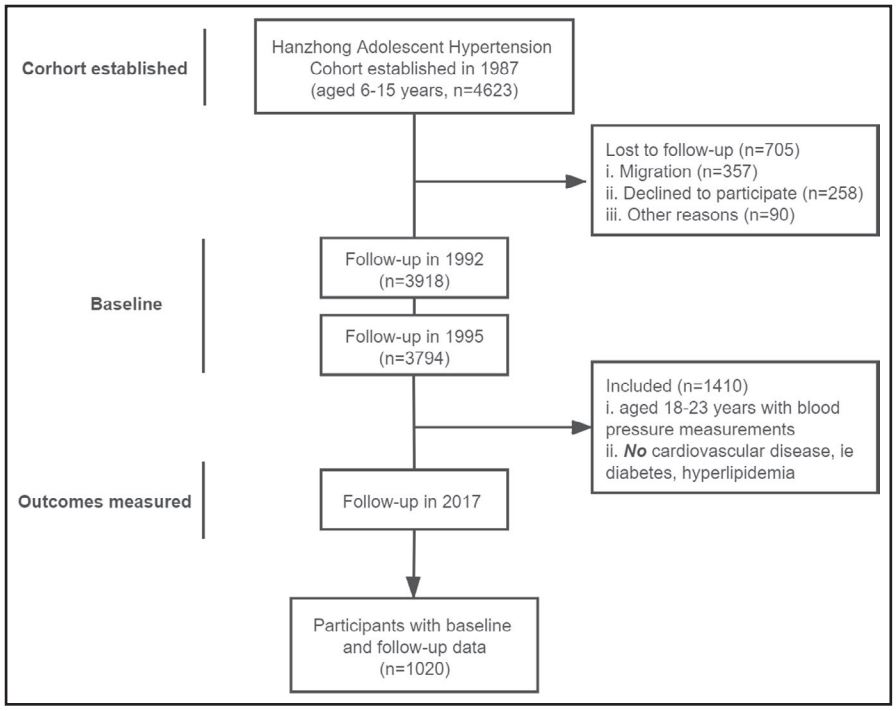


FIGURE 1 Flowchart for inclusion/exclusion of study participants

Height and weight were measured using standardized protocols at each visit. The definitions of each dichotomous risk factor used in this study are available in Supplementary Methods.

2.5 | Statistical methods

Continuous data were presented as mean ± SD if normally distributed; otherwise, they were shown as median with interquartile ranges. Categorical variables were shown as frequency and percentage. Statistically significant differences among the groups were assessed using one-way ANOVA or Kruskal-Wallis test for continuous variables and chi-square test for categorical variables. Test for trend with increasing BP level was based on the variable containing the median value for each group for continuous data or by Mantel-Haenszel chi-square test for categorical data. Logistic regression was performed to explore the association between BP categories and midlife subclinical CVD outcomes shown as odds ratio (OR) and their 95% confidence intervals (95% CIs). Several cardiovascular risk factors including age, sex, adult socioeconomic status, body mass index (BMI), serum uric acid (UA), plasma blood glucose (GLU), total cholesterol (TC), and triglyceride (TG) levels were adjusted in the regression model, and the low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were excluded from the model due to high collinearity.

To test the robustness of the results, we performed sensitivity analyses by excluding participants with active treatment, including antihypertensive, antidiabetic, or lipid-lowering agents. Statistical significance was set as a two-sided p-value < .05. Statistical analyses were performed using R (version 3.6.3) and SPSS software (version 22.0, SPSS Inc).

3 | RESULTS

3.1 | Characteristics of study participants

Table 1 presented the demographic characteristics and cardiovascular risk factors of participants by BP categories. The median age of study participants was 19.4 (18.7, 20.3) years at baseline, and 487 participants (47.7%) were women. At baseline, the median level was 117.3 (110.0, 126.0) mmHg in SBP and 72.0 (66.0, 79.3) mmHg in DBP. With increasing BP category, the proportion of women in each group decreased (p for trend < .05), while the age and BMI level increased (both p for trend < .05). In middle adulthood, higher baseline BP categories were positively associated with smoking rate, BMI, SBP, DBP, and higher levels of LDL-C and serum uric acid (p for trend < .05 for all). However, there was no significant difference in the prevalence of diabetes or hyperlipidemia, the rate of alcohol drinking, the socio-economic status, and levels of GLU, total cholesterol (TC), triglyceride (TG), and HDL-C, among BP categories (p >.05 for all).

Table 2 showed the cardiovascular variables of interest in midlife by sex and BP categories. The levels of baPWV, Cornell index, and uACR were significantly different among the BP categories (p < .05 for all) except for a borderline significant difference in uACR among males (p = .059). However, there was no significant difference in cIMT and eGFR among BP categories for males and females.

TABLE 1 Participant Characteristics by blood pressure categories

Parameter	All participants (n = 1020)	Normal BP (n = 530)	Elevated BP (n = 171)	Stage 1 hypertension (n = 242)	Stage 2 hypertension (n = 77)	*p*-value	*p for trend
Blood pressure range	–	SBP < 120 mmHg and DBP < 80 mmHg	SBP 120–129 mmHg and DBP < 80 mmHg	SBP 130–139 mmHg or DBP 80–89 mmHg	SBP >=140 mmHg or DBP >=90 mmHg		–
Women, n (%)	487 (47.7%)	303 (57.2%)	69 (40.4%)	95 (39.3%)	20 (26.0%)	<.001	<.001
Baseline							
Age, yr	19.4 (18.7, 20.3)	19.3 (18.6, 20.2)	19.4 (18.7, 20.4)	19.5 (18.7, 20.3)	19.5 (18.7, 20.3)	<.001	.044
BMI, kg/m^2	20.5 (19.3, 21.8)	20.3 (19.0, 21.6)	20.8 (19.7, 21.6)	20.8 (19.6, 22.4)	21.0 (19.8, 22.6)	<.001	<.001
Heart Rate,	78.0 (72.0, 84.0)	78.0 (72.0, 84.0)	78.0 (72.0, 84.0)	80.0 (72.0, 84.0)	82.0 (72.0, 88.0)	<.001	<.001
SBP, mmHg	117.3 (110.0, 126.0)	110.7 (104.0, 105.3)	124.6 (121.3, 126.7)	132.0 (130.0, 135.3)	142.7 (140.7, 148.2)	<.001	<.001
DBP, mmHg	72.0 (66.0, 79.3)	68.2 (62.0, 72.0)	73.3 (68.7, 77.3)	80.7 (79.3, 84.0)	90.0 (80.3, 91.7)	<.001	<.001
Family history of hypertension	545 (53.4%)	275 (51.9%)	79 (46.2%)	141 (58.3%)	50 (64.9%)	.045	.022
Follow-up (2017)							
Age, yr	43.7 (42.8, 45.0)	43.7 (42.8, 44.8)	43.9 (42.8, 45.0)	43.9 (42.7, 45.0)	43.9 (42.7, 44.6)	.866	.124
Occupation (%)							
Farmer	186 (18.2%)	102 (19.2%)	26 (15.2%)	43 (17.8%)	15 (19.5%)	.825	.752
Worker	400 (39.2%)	193 (36.4%)	71 (41.5%)	102 (42.1%)	34 (44.2%)	.691	.268
Businessman	145 (14.2%)	82 (15.5%)	25 (14.6%)	30 (12.4%)	8 (10.4%)	.59	.176
Governor	32 (3.1%)	19 (3.6%)	4 (2.3%)	6 (2.5%)	3 (3.9%)	.83	.903
Other	257 (25.2%)	134 (25.3%)	45 (26.3%)	61 (25.2%)	17 (22.1%)	.922	.604
Education (%)							
Primary school or less	58 (5.7%)	26 (4.9%)	13 (7.6%)	13 (5.4%)	6 (7.8%)	.687	.587
Middle school	738 (72.4%)	387 (73.0%)	128 (74.9%)	174 (71.9%)	49 (63.6%)	.334	.140
High school	173 (17.0%)	89 (16.8%)	24 (14.0%)	43 (17.8%)	17 (22.1%)	.523	.267
College or more	51 (5.0%)	28 (5.3%)	6 (3.5%)	12 (5.0%)	5 (6.5%)	.816	.491
Marital status (%)							
Married	973 (95.4%)	508 (95.8%)	163 (95.3%)	229 (94.6%)	73 (94.8%)	.983	.753
Divorced	31 (3.0%)	16 (3%)	4 (2.3%)	9 (3.7%)	2 (2.6%)	.876	.794
Unmarried or other	16 (1.6%)	6 (1.1%)	4 (2.3%)	4 (1.7%)	2 (2.6%)	.796	.339
Smoking (%)	420 (41.2%)	174 (32.8%)	82 (48.0%)	119 (49.2%)	45 (58.4%)	.005	.001
Drinking (%)	288 (28.2%)	127 (24.0%)	51 (29.8%)	80 (33.1%)	30 (29.0%)	.564	.376
Diabetes (%)	35 (3.4%)	18 (3.4%)	5 (2.9%)	11 (4.5%)	1 (1.3%)	.44	.598
Hyperlipidemia (%)	364 (35.7%)	180 (34.0%)	60 (35.1%)	93 (38.4%)	31 (40.3%)	.806	.331

(Continues)

TABLE 1 (Continued)

Parameter	All participants (n = 1020)	Normal BP (n = 530)	Elevated BP (n = 171)	Stage 1 hypertension (n = 242)	Stage 2 hypertension (n = 77)	*p*-value	*p for trend
BMI, kg/m^2	23.8 (22.1, 25.8)	23.6 (21.7, 25.6)	23.8 (22.4, 26.2)	24.2 (22.6, 26.1)	24.2 (22.4, 26.1)	.03	.015
Heart Rate,	73.0 (66.0, 79.0)	73.0 (66.0, 79.5)	72.0 (64.0, 79.0)	73.0 (67.0, 79.0)	73.5 (65.5, 82.0)	.263	.996
SBP, mmHg	122.3 (113.3, 132.3)	119.0 (110.0, 129.0)	123.0 (114.7, 132.3)	126.7 (118.3, 136.2)	134.0 (120.9, 145.7)	<.001	<.001
DBP, mmHg	76.3 (69.3, 84.0)	74.3 (67.2, 81.0)	75.3 (70.7, 84.0)	80.7 (74.0, 87.3)	82.0 (77.2, 87.8)	<.001	<.001
GLU, mmol/L	4.6 (4.3, 4.9)	4.6 (4.3, 4.9)	4.6 (4.3, 4.9)	4.7 (4.2, 5.0)	4.6 (4.2, 5.0)	.198	.971
TC, mmol/L	4.5 (4.1, 5.0)	4.6 (4.1, 5.1)	4.5 (4.0, 4.9)	4.6 (4.2, 5.1)	4.5 (3.9, 5.1)	.26	.845
Triglycerides, mmol/L	1.3 (1.0, 1.9)	1.3 (0.9, 1.9)	1.3 (0.9, 1.8)	1.4 (1.0, 2.0)	1.3 (1.0, 2.0)	.456	.292
LDL-C, mmol/L	2.5 (2.1, 2.9)	2.4 (2.1, 2.9)	2.5 (2.1, 2.9)	2.5 (2.2, 3.0)	2.6 (2.0, 3.1)	.019	.042
HDL-C, mmol/L	1.2 (1.0, 1.4)	1.2 (1.0, 1.4)	1.1 (1.0, 1.4)	1.1 (1.0, 1.3)	1.1 (1.0, 1.3)	.206	.057
Serum uric acid, mmol/L	272.3 (222.9, 326.1)	264.2 (217.5, 314.7)	283.0 (227.6, 331.0)	286.0 (237.1, 331.8)	297.5 (254.5, 360.5)	<.001	<.001

Note: Continuous variables are expressed as median with interquartile range. Categorical variables are expressed as numbers and percentages of subjects.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; GLU, fasting plasma blood glucose; HDL-C, HDL cholesterol; HR, heart rate; LDL-C, LDL cholesterol; SBP, systolic blood pressure; TC, total cholesterol.

*Test for trend was based on variable containing median value for each group for continuous data and assessed by Mantel-Haenszel chi-square test for categorical data.

3.2 | Association of BP groups with midlife subclinical CVD outcomes

Compared with their normotensive counterparts, young adults with stage1 and stage 2 hypertension had worse cardiovascular profiles in their midlife (Figure 2). In the fully adjusted model (Table 3), the ORs (95% CIs) for traditionally defined hypertension, high-risk cIMT, high-risk baPWV, LVH, and SRD comparing stage 1 hypertension to normal BP (reference) were 2.21 (1.45–3.34), 0.88 (0.39–1.98), 1.61 (1.07–2.70), 2.92 (1.35–6.35), and 1.31 (0.81–2.10), respectively. Similarly, the fully adjusted ORs (95% CIs) for those outcomes of stage 2 hypertension were 3.14 (1.76–5.63), 0.99 (0.87–1.12), 3.08 (1.55–6.12), 4.66 (1.78–12.22), and 1.88 (1.06–3.69), respectively, compared with the normal BP group. Among young adults with elevated BP, the risks of all those subclinical CVD outcomes were similar to those with normal BP (ORs close to 1).

Results were similar after excluding participants who were receiving antihypertensive, antidiabetic, or lipid-lowering treatments in midlife (n = 44); young adults with stage 1 and stage 2 hypertension experienced higher risks of subclinical CVD outcomes (Table 4). It was worth noting that young adults with stage 1 hypertension had nearly 1.7 times the risk for SRD compared with those with normal BP (OR = 1.69, 95% CI = 1.02–2.82; p = .04), of whom the increased risk was not significant in the full sample analysis. Consistently, the risk of midlife high-risk cIMT associated with early adulthood BP categories was not detected.

Further, we assessed the associations between the BP categories with the midlife outcomes load (classified as 0, 1, ≥2) using sex- and age-adjusted ordinal logistic regression (Figure 3). The predicted probability of participants with no midlife outcome decreased from 0.65 to 0.29 as the BP category changed from normal to stage 2 hypertension. Conversely, the probability of having ≥ 2 outcomes in midlife increased from 0.12 (normal BP) to 0.37 (stage 2 hypertension).

4 | DISCUSSION

In this 25-year prospective cohort study of Chines young adults, there was an association between BP categories in early adulthood, classified using the 2017 ACC/AHA guideline, and subclinical CVD outcomes by middle age. Stage 1 hypertension and stage 2 hypertension in early adulthood were significantly associated with higher risks for traditionally defined hypertension, high-risk baPWV, LVH, and SRD in midlife, compared with normal BP.

Beyond the increased prevalence of hypertension under the 2017 ACC/AHA guideline, the other concern lies in the influence of the new BP stratum on cardiovascular risk in the population, which is critical to determine whether the new threshold could be applied to the populations.[37] However, data are still lacking among the low-risk young adults. We hypothesized that elevated blood pressure in early life could increase subclinical CVD risk in later life. The current study was able to follow individuals from early adulthood to middle age

TABLE 2 Cardiovascular variables in midlife by sex and blood pressure categories

Parameter	Normal BP	Elevated BP	Stage 1 hypertension	Stage 2 hypertension	*p-value
Men (n = 533)					
eGFR, ml/min per 1.73 m^2	98.6 (89.7, 112.0)	99.8 (91.5, 112.0)	96.1 (86.3, 112.2)	105.5 (83.8, 118.7)	.341
uACR, mg/mmol	0.9 (0.7, 1.6)	0.9 (0.7, 1.5)	1.0 (0.7, 1.7)	1.1 (0.7, 2.2)	.059
cIMT, mm	0.7 (0.6, 0.8)	0.7 (0.6, 0.8)	0.7 (0.6, 0.8)	0.8 (0.6, 0.9)	.678
Cornell Index, mm/ms	1181.7 (838.5, 1635.0)	1296.0 (890.3, 1657.8)	1337.5 (1017.6, 1725.0)	1695.6 (1110.2, 2233.8)	<.001
baPWV, cm/s	1271.0 (1152.0, 1429.0)	1300.0 (1174.5, 1415.6)	1351.5 (1250.0, 1500.0)	1356.6 (1211.0, 1614.0)	<.001
Women (n = 487)					
eGFR, ml/min per 1.73 m^2	99.4 (88.6, 117.8)	97.7 (86.8, 113.2)	98.3 (84.3, 110.3)	108.1 (84.0, 123.6)	.743
uACR, mg/mmol	1.0 (0.7, 1.8)	1.2 (0.8, 1.9)	1.4 (0.9, 2.6)	1.8 (1.1, 3.0)	.011
cIMT, mm	0.6 (0.5, 0.7)	0.7 (0.6, 0.8)	0.6 (0.5, 0.7)	0.6 (0.5, 0.8)	.537
Cornell Index, mm/ms	1444.8 (1053.0, 1710.0)	1430.8 (1044.0, 1750.0)	1682.0 (1313.6, 1893.0)	1767.5 (1283.1, 2527.6)	<.001
baPWV, cm/s	1142.0 (1032.5, 1274.0)	1201.5 (1066.0, 1356.5)	1213.0 (1095.5, 1380.5)	1292.0 (1115.4, 1474.0)	<.001

Note: Continuous variables are expressed as median with interquartile range.

*Statistically significant differences among the groups were assessed using Kruskal-Wallis test. eGFR, estimated glomerular filtration rate; uACR, urinary albumin-to-creatinine ratio; cIMT, carotid intima-media thickness; baPWV, Brachial-ankle pulse wave velocity.

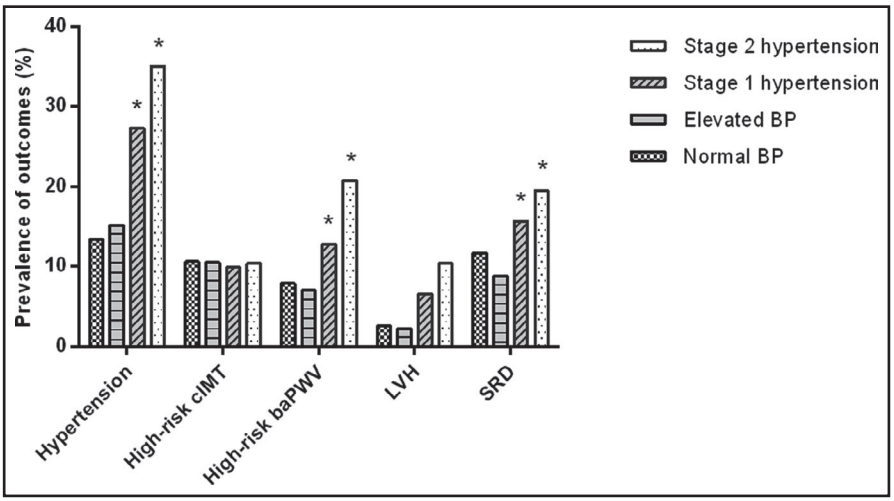


FIGURE 2 Proportion of participants with midlife subclinical CVD outcomes by baseline BP category

and assessed the performance of the 2017 ACC/AHA BP categories, especially the stage 1 hypertension, in the prediction of midlife outcomes.

Previous longitudinal studies suggest that elevated BP tracks from early life into later life.[38,39] In a recent meta-analysis of 39 714 participants, Yang et al found elevated BP in early life (3–19 years) increased the risk of adulthood hypertension in (18–57 years) by approximately two times.[38] In our previous study, we also found subjects with BP ≥ age- and sex-specific 90th percentile during 6–18 years experienced an increased risk of adult hypertension (SBP ≥ 140 mm Hg and/or DBP ≥ 90 mm Hg; OR = 2.01; 95%CI, 1.53-2.65).[39] Our present results agree with those of studies illustrating the BP tracking phenomenon among the general population. Importantly, we expanded previous observations by finding that under the 2017 ACC/AHA guidelines, young adults with stage 1 hypertension who would otherwise be assigned to the non-hypertensive category by prior criteria had over twice the risk of progression to higher BP category in midlife (OR = 2.21; 95%CI = 1.45–3.34). Our data also suggest the potential importance of BP control strategies for stage 1 hypertension in young adults to prevent subsequent severe hypertension in midlife.

Our findings also supported the advantage of the 2017 ACC/AHA guidelines in early identifying individuals with higher cardiovascular risks, who would be classified as non-hypertensive subjects by the current Chinese guidelines.[32,40] Young adults with stage 1 hypertension had a 1.6-fold increased risk for high-risk baPWV and 2.92-fold increased risk for LVH in their midlife. Antihypertensive medication in middle age did not completely mitigate the subclinical

TABLE 3 Odds ratio (and 95% CIs) of midlife outcomes by blood pressure categories

Outcome and blood pressure group	Sex-age-adjusted model[a]			All adjusted model[b]		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Hypertension[c]						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	1.01	0.62–1.65	.47	1.01	0.60–1.72	.96
Stage 1 hypertension	2.16	1.47–3.18	<.001	2.21	1.45–3.34	<.001
Stage 2 hypertension	2.83	1.64–4.86	<.001	3.14	1.76–5.63	<.001
High-risk cIMT						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	0.69	0.40–1.19	.54	0.62	0.35–1.08	.09
Stage 1 hypertension	0.93	0.42–2.05	.85	0.88	0.39–1.98	.75
Stage 2 hypertension	0.99	0.88–1.12	.93	0.99	0.87–1.12	.88
High-risk baPWV						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	0.88	0.45–1.72	.71	0.86	0.43–1.72	.67
Stage 1 hypertension	1.72	1.04–2.83	.03	1.61	1.07–2.70	.04
Stage 2 hypertension	3.12	1.63–5.98	.00	3.08	1.55–6.12	.01
LVH						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	0.98	0.32–3.05	.97	1.04	0.33–3.29	.95
Stage 1 hypertension	2.97	1.40–6.28	.00	2.92	1.35–6.35	.01
Stage 2 hypertension	4.70	1.84–12.0	.00	4.66	1.78–12.22	.00
SRD						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	0.68	0.37–1.24	.21	0.71	0.38–1.33	.29
Stage 1 hypertension	1.33	1.05–2.07	.03	1.31	0.81–2.10	.27
Stage 2 hypertension	1.66	1.08–3.13	.02	1.88	1.06–3.69	.04

[a]Adjusted for sex and baseline age;

[b]Further adjusted for smoking, alcohol drinking, occupation, married status, education, BMI (kg/m^2), GLU (millimoles per liter), UA (micromoles per liter), TC (millimoles per liter), TG (millimoles per liter) in adulthood.

[c]Traditional defined hypertension was classified according to the current Chinese hypertension guideline.

CVD outcomes risk among those young adults with stage 1 hypertension except for SRD (OR = 1.69, 95% CI = 1.02–2.82 *vs*. OR = 1.31, 95%CI = 0.81–2.10).

As the major change in the guidelines, the newly defined stage 1 hypertension has been the subject of significant interest globally.[11,25-27] Recent data showed that stage 1 hypertension significantly increases the risk of cardiovascular incidence and mortality.[18,25,26] Our findings align with previous studies suggesting that stage 1 hypertension, along with stage 2 hypertension, has a long-term detrimental impact on target organs.[7-10,39,41,42] On the basis of these findings, it appears that the 2017 guideline contributes to risk stratification during BP management among young adults and may be of great importance for CVD prevention in China.

Taken together, the high risk of BP category progression and the subclinical CVD risk associated with stage 1 hypertension underline the importance of early BP control in young Chinese adults. In this context, epidemiological data showed that the prevalence of hypertension had increased rapidly in recent decades among the young Chinese.[43-45] Data from the China Hypertension Survey between 2012 and 2015 reported that the prevalence of hypertension based on the 2017 ACC/AHA guideline was 23.0% among the young Chinese aged 18–24 years, in whom barely 0.0% achieved BP control.[46] In addition, in this same study the awareness, treatment, and control rates were only 5.7%, 3.4%, and 0.6%, respectively, even by the higher threshold of the 2010 Chinese guidelines.[46] Our findings, together with these results, highlight the urgency for health education, early detection, and subsequent intervention targeting young adults in order to retard hypertension progression, protect against organ damage, and ultimately attenuate CVD risk effectively and economically.

Limitations of the study require careful consideration. First, the odds ratio may be underestimated based on baseline BP levels due to

TABLE 4 Odds ratio (and 95% CIs) of midlife outcomes by blood pressure categories (Sensitivity analysis)

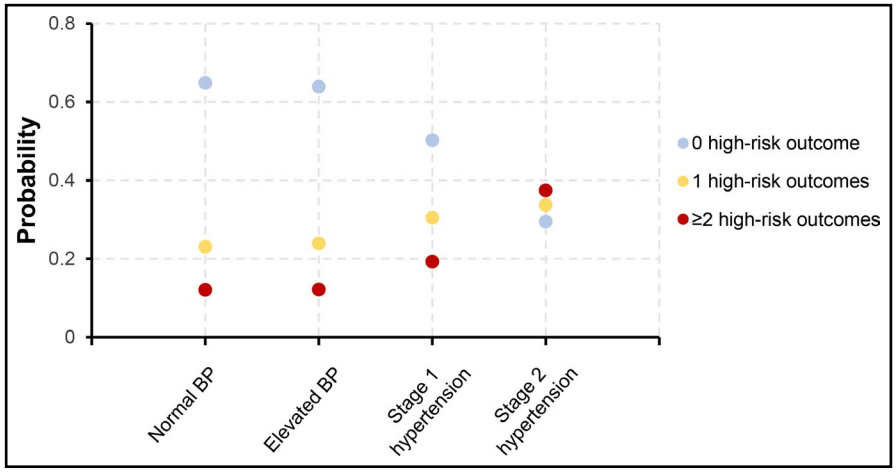
Outcome and blood pressure group	Sex-age-adjusted model[a]			All adjusted model[b]		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Hypertension[c]						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	1.15	0.67–1.98	.61	1.13	0.63–2.03	.68
Stage 1 hypertension	2.20	1.43–3.39	<.001	2.25	1.41–3.59	<.001
Stage 2 hypertension	2.83	1.56–5.15	<.001	3.22	1.70–6.12	<.001
High-risk cIMT						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	0.67	0.38–1.19	.17	0.62	0.35–1.08	.11
Stage 1 hypertension	0.85	0.37–1.98	.71	0.80	0.34–1.88	.61
Stage 2 hypertension	0.98	0.87–1.11	.73	0.98	0.86–1.11	.71
High-risk baPWV						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	0.67	0.30–1.48	.32	0.62	0.27–1.43	.26
Stage 1 hypertension	1.63	1.04–2.82	.03	1.58	1.09–2.79	.02
Stage 2 hypertension	2.60	1.26–5.36	0.01	2.59	1.20–5.59	.01
LVH						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	1.23	0.39–3.93	.72	1.30	0.40–4.23	.67
Stage 1 hypertension	2.76	1.2–6.36	.02	2.75	1.16–6.48	.02
Stage 2 hypertension	4.42	1.55–12.65	.01	4.29	1.16–12.58	.01
SRD						
Normal BP	1.00	–	–	1.00	–	–
Elevated BP	0.74	0.38–1.44	.37	0.73	0.36–1.47	.37
Stage 1 hypertension	1.69	1.05–2.73	.03	1.69	1.02–2.82	.04
Stage 2 hypertension	2.03	1.02–4.02	.04	2.21	1.1.07–4.58	.03

[a]Adjusted for sex and baseline age.

[b]Further adjusted for smoking, alcohol drinking, occupation, married status, education, BMI (kg/m^2), GLU (millimoles per liter), UA (micromoles per liter), TC (millimoles per liter), TG (millimoles per liter) in adulthood.

[c]Traditional defined hypertension was classified according to the current Chinese hypertension guideline.

FIGURE 3 Predicted probability of midlife subclinical CVD outcomes load: 0 (n = 618), 1 (n = 253), and ≥ 2 (n = 149) based on sex- and age-adjusted ordinal logistic model



regression dilution bias, which is a common problem in long-term cohort studies. Second, the sample size of individuals with an elevated cIMT was relatively small, resulting in limited statistical power to detect weak associations. Large-scale population studies are required to validate our findings. Third, evidence from large randomized controlled trials is still needed to determine the benefit of BP-lowering strategies among young Chinese adults with stage 1 hypertension.

We conclude that the use of the 2017 ACC/AHA definition of stage 1 hypertension in early adulthood, allowed the detection of a significant increase in the risk of BP aggravation and of subclinical CVD outcomes in midlife in the Chinese population. Our findings suggest that the new BP guidelines could contribute to early detection of future adverse CVD risk and emphasize the importance of BP management in young adults.

ACKNOWLEDGMENTS

The authors thank Ruihai Yang, Jun Yang, Yong Ren, Bo Yan, and Ying Deng for assistance with data collection.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

Yu Yan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Yu Yan, Qiong Ma, and Jianjun Mu designed the study; Yu Yan, Wenling Zheng, Qiong Ma, Jiawen Hu, Wenling Zheng, and Chao Chu collected the epidemiological data; Yu Yan, Jiawen Hu, Keke Wang, Yueyuan Liao, Chen Chen, and Yue Sun performed biochemical parameter measurements; Yu Yan, Yueyuan Liao, and Ting Zou analyzed the data; Yu Yan and Jianjun Mu drafted and revised the paper; Jianjun Mu, Yang Wang and Chao Chu obtained funding; all authors approved the final version of the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Yan Y, Ma Q, Liao Y, et al. Blood pressure and long-term subclinical cardiovascular outcomes in low-risk young adults: Insights from Hanzhong adolescent hypertension cohort. *J Clin Hypertens*. 2021;23:1020–1029. https://doi.org/10.1111/jch.14225